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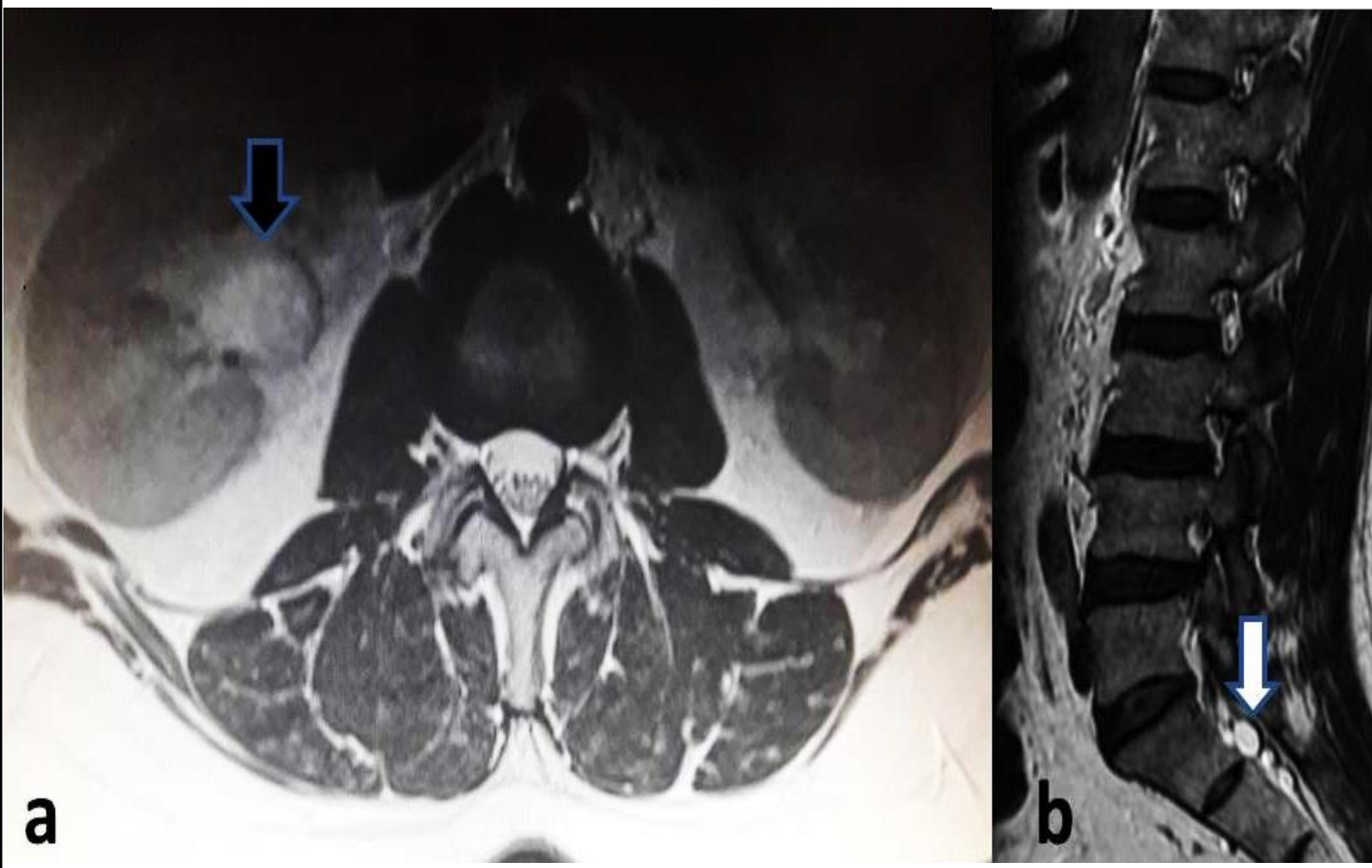

- **Compensation of MRI findings in asymptomatic patients with chronic low back pain**
- **Analysis of The Patients with Lichenoid Drug Reactions: A Retrospective Study.**
- **Stereotactic radiotherapy for patients with metallic implants on vertebral body: A dosimetric comparison**

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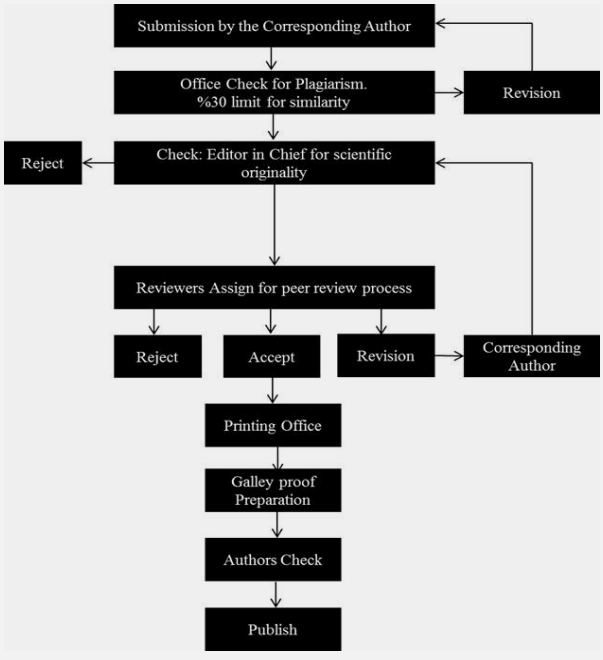

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Correlation of dyspeptic symptoms and endoscopic findings in diabetic patient

Ramazan Ilyas Oner[1]*, Melih Karincaoglu[2]

Abstract

Objective: We aimed to demonstrate the relationship between the endoscopically increased mucosal damage and the frequency of dyspeptic symptoms in patients with diabetes.

Material and Methods: The 42 diabetic patients with dyspeptic complain and 40 healthy dyspeptic people were involved in this study and evaluated with video endoscopes.

Results: Diabetic patients when compared with the control group according to the endoscopic evaluation and Glasgow Dyspepsia Symptom Scoring System no significant difference had been detected. The symptoms of the diabetic group and the control group were familiar and there was no significant difference between the frequencies of the symptoms in both groups. In dyspeptic diabetic patients a weak correlation between BMI and endoscopically detected hiatal hernia was reported. However there was no relation between BMI and the other gastrointestinal symptoms. Also there was no difference between the patients with neuropathy and without neuropathy in terms of endoscopic findings and gastrointestinal symptoms.

Conclusion: Endoscopic findings of diabetic patient and non-diabetic control group were compared statistically. Although gastric ulcus was significantly higher in diabetic group, there was no significant difference between two groups in terms of other endoscopic findings. Hovewer, gastric ulcus frequency in diabetic group is higher, there were no significant difference in terms of gastrointestinal symptoms, diabetic complications and glisemic control in patients with other endoscopic lesions when compared with the patients with gastric ulcus. Hiatal hernia frequency in diabetic patients was higher due to control group. In shed light on our findings, diabetic patients must be evaluated for the esophageal reflux symptoms.

Keywords: Diabetes mellitus, Dyspepsia, Endoscopy

Introduction

Diabetes mellitus (DM) is a chronic disease characterized by anomalies in carbohydrate, protein and lipid metabolism. Chronic and continuous exposure to these anomalies cause microvascular complications (retinopathy, neuropathy, nephropathy), macrovascular complications (myocardial infarction, stroke, peripheral artery disease) (1), gastrointestinal (gastroparesis, diarrhea), genitourinary (uropathy/sexual dysfunction) and dermatological complications.

Chronic hyperglycemia leads to complications in DM by increasing the activity of sorbitol pathway of metabolism, causing the formation of advanced glycosylation end products (AGE) by means of the non-enzymatic glycosylation of cellular proteins of increased intracellular glucose and increasing the formation of diacylglycerol by activating certain isoforms of protein kinase C (PKC) (1).

'Dyspepsia' expresses an exact definition; however, it is generally defined as the indicator of upper gastrointestinal symptoms and most of the patients with dyspepsia have an organic or functional disorder of upper gastrointestinal system. The symptoms of dyspepsia involve upper abdominal pain/discomfort, anorexia, bloating, early satiety, nausea and/or vomiting, and it affects up to 7- 40% of the general population.

Upper gastrointestinal endoscopy is the most convenient initial test to evaluate patients with dyspepsia (2). The factors leading to gastrointestinal symptoms in DM patients are autonomic neuropathy, poor glycemic control, psychiatric disorders and metabolic disorders secondary to diabetes. A significant association has been detected between gastric emptying and the severity of autonomic neuropathy.

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Parasympathetic dysfunction developing secondary to chronic hyperglycemia affected emptying function, and as well as, antroduodenal motor activity, gastroesophageal reflux activity and gastric secretion. In 1958, the reducing effect of diabetes associated with autonomic neuropathy on the gastric emptying was defined as 'Gastroparesis diabeticorum' and it has been encountered in almost 25% of the DM patients (3).

The incidence of diarrhea or constipation, abdominal pain or discomfort, heartburn, dysphagia, nausea, vomiting and fecal incontinence is higher in DM patients, and basal and stimulated gastric acid secretion has been reported to be normal or decreased (4). The secondary symptoms are gastroparesis, and alterations in motility of small and large intestine. The lesions, such as gastric ulcer, duodenal ulcer, gastritis and esophagitis, should be evaluated by GIS endoscopy before establishing a correlation between gastrointestinal symptoms and gastroparesis in DM patients (5).

In the present study, it was aimed to demonstrate the relation between the prevalence of dyspeptic symptoms and endoscopically increased mucosal damage in patients having DM with dyspeptic symptoms.

Material and method

The present prospective clinical studies were conducted on 42 DM patients, aged 35 to 76 years, who were admitted to Gastroenterology Outpatient Clinic of Turgut Ozal Medical Center, Inonu University Faculty of Medicine, between April 2004 and September 2005, with complaint of dyspepsia, and 40 control patients, aged 18 to 77 years, without a comorbid disease. The approval of the local ethics committee was obtained from the Inonu University, Faculty of Medicine.

Upper GIS endoscopy was performed with Olympus GF-XQ 200 (Olympus, Japan) in all patients by the gastroenterology specialists in our department. The spectrophotometric analysis of complete blood count and the nephelometric analysis of other biochemical parameters were performed with LH750-ANA device (Beckman Coulter, USA) analyzer and Olympus AU 600 analyzer (Olympus, USA) respectively.

The dyspeptic complaints of patients, involving pain, bloating, indigestion, gastric fullness, early satiety, excessive belching and burping, nausea, vomiting and heartburn were examined, and evaluated by using Glasgow Dyspepsia Severity Scale (GDSS) (Table 1) (6).

Patients who having any alarm symptoms such as weight loss, anemia, dysphagia, epigastric mass, persistent vomiting, patients having a concomitant severe systemic disease, pregnant or lactating women having the signs of being pregnant, patients having perception and adjustment disorder (mental disease or defect), and those having alcohol addiction or drug abuse were excluded from the study. one of 82 patients was excluded from the study due to intolerance to esophagogastroduodenoscopy.

Statistical analysis was performed by using SPSS 10.0 Windows package program. All data were calculated as mean ± standard deviation (SD). According to the findings of esophagogastroduodenoscopy, study and control groups were compared by using Pearson Chi-Square Test. A p-value of <0.05 was accepted as statistically significant.

Results

Forty-two DM patients with complaints of dyspepsia and 40 patients with dyspepsia having no comorbid diseases were included in this study. The mean age of study group, including 20 males (47.6%) and 22 females (52.4%), was 50.8 ± 9.2 years; the control group consisted of 17 males (42.5%) and 23 females (57.5%).

Twenty-three DM patients had a comorbid disease, such as hypertension, cardiac disease, osteoporosis (54.8%); 19 patients had no systemic disease (45.2%).

The drug list and habits of the patients in the study and control groups were presented in table 2 and table 3.

According to the diabetic complications, 6 patients had microalbuminuria (14.3%), 12 patients had retinopathy (28.6%) and 27 patients had polyneuropathy (64.3%).

There was no statistically significant difference between the GDSS of diabetic and non-diabetic patients (GDSS= 7.40 ± 3.54 and GDSS= 6.87 ± 3.29, respectively) (p= 0.487).

Esophagogastroduodenoscopic examination of diabetic patients revealed that 40 had antral gastritis (97.6%), the 13 had pangastritis (31.7%), the 4 had gastric ulcer (9.8%), the 4 had duodenal ulcer (9.8%), the 17 had bulbitis (41.5%), the 10 had cardiac insufficiency (24.4%), the 2 had hiatal hernia (14.6%), and two had esophagitis (4.9%).

In the patients of control group (non-DM), the 35 had antral gastritis (87.5%), the 8 had pangastritis (20%), the 4 had duodenal ulcer (10%), the 12 had bulbitis (30%), the 4 had cardiac insufficiency (10%), the 5 had hiatal hernia (12.5%) and the 4 had esophagitis (10%) according to the esophagogastroduodenoscopic examination, and none of them had gastric ulcer.

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The most common lesion was antral gastritis in both groups (97.6% in study group; 87.5% in control group). While esophagitis was detected in the diabetic patients (4.9%), gastric ulcer was not observed in none of the patients in non-diabetic dyspepsia group.

According to the findings of esophagogastroduodenoscopy, study and control groups were compared by using Pearson Chi-Square. There was no significant difference between the groups due to endoscopic findings, except the high frequency of gastric ulcer (p= 0.043) (Table 4).

Table 1: Glasgow Dyspepsia Symptom Scoring System

1- Frequency of dyspeptic symptoms	**Score**
How often have you complained of a dyspeptic complaint in the last six months?	
Never happened	0
Only 1 or 2 days	1
One day a month	2
One day per week	3
Approximately every two days	4
In the majority of days	5
2- Effect on normal activities	
Do your dyspeptic complaints affect your normal activities such as sleeping,	
eating or social activities?	
No, it does not affect	0
Sometimes it is affecting	1
Always affected	2
3-Time off work	
How many days did you go to work because of your dispeptic complaints in the last 6 months	
Therefore it was not the day I did not go to work	0
I did not go 1-7 days	1
I did not go over 7 days	2
4- Consultation with medical profession	
How often did you go to a doctor for the cause of your dyspeptic complaints in the last 6 months?	
I never went	0
Once	1
Two or more	2
5- Doctor visits to home	
Have you called your doctor for your dyspeptic complaints in the last six months?	
I never called	0
Once	1
Two or more	2
6- Tests for dyspepsia	
How many times have you tested for the cause of your dyspeptic complaints in the last 6 months?	
I never did it	0
Once	1
Two or more	2
7- Treatment for dyspepsia	
a- How often did you use medication without going to the doctor with your own decision?	
I've never used	0
Less than once a week	1
More than once a week	2
b- How long have you used prescription medication for your dyspeptic complaints	
in the last six months	
One or less per month	0
1-3 months	1
3 months more	2

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Table 2: Distribution of drugs and habits of diabetic patients

	User		Not Using	
	n	**%**	**n**	**%**
Cigarette	10	23,8	32	76,2
Alcohol	2	4,8	40	75,2
NSAID*	27	64,3	25	35,7
Aspirin	19	45,2	23	54,8
Steroid	0	0	42	100
OAD**	31	73,8	11	26,2
Insulin	12	28,6	30	71,4

*Nonsteroidal anti-inflammatory drugs
**Oral antidiabetic drugs

Table 3: Distribution of drugs and habits of non-diabetic patients

	User		Not Using	
	n	**%**	**n**	**%**
Cigarette	11	27,5	29	**72,5**
Alcohol	5	12,5	35	**87,5**
NSAİD*	20	50	20	**50**
Aspirin	1	2,5	39	**97,5**
Steroid	**0**	**0**	**40**	**100**

* Nonsteroidal anti-inflammatory drugs

Table 4: Comparison of endoscopic findings of patients according to Pearson Chi-Square test

OGD* Findings	Diabetic Patients		Control Group		P value
	n	%	n	%	
Antral Gastritis	40	97,6	35	87,5	0,084
Pangastritis	13	31,7	8	20	0,229
Gastric Ulcer	4	9,8	0	0	**0,043**
Duodenal Ulcer	4	9,8	4	10	0,971
Bulbitis	17	41,5	12	30	0,282
Cardiac Insufficiency	10	24,4	4	10	0,087
Hiatal Hernia	6	14,6	5	12,5	0,779
Esophagitis	2	4,9	4	10	0,379

*Esophagogastroduodenoscopy

Discussion

Gastric motor and sensory disorders associated with irreversible autonomic neuropathy, poor glycemic control, demographic and physiological characteristics are the indicators of gastric emptying and upper GIS symptoms in diabetic patients. Autonomic nerve functions and glycemic control have primary significant effects.

The relationship between GIS symptoms and glycemic control in diabetic patients has been shown in various studies. The prevalence of GIS symptoms was found to be higher in patients with poor glycemic control (7). Koch et al. reported in their study that glycemic control did not show any correlation with worsening gastrointestinal symptoms (8). Although, the diabetic patients had poor glycemic control in our study (HbA1C= 9.9 ± 2.8), Statistically significant difference between the groups in terms of GDSS and esophagogastroduodenoscopic findings were not found. The acute blood glucose alterations have major effects on the gastric emptying and upper GIS senses.

In a recent cohort study by Bharucha et al., a correlation was reported between HbA1C and delayed gastric emptying (9)

Schvarcz et al. showed that the prevalence of gastrointestinal symptoms was significantly higher in diabetic women than diabetic men (10). In the present study, statistically significant difference between the genders in terms of symptom scoring and endoscopic findings were not found.

Gastric emptying might be affected by body weight in healthy individuals, and may associate with eating habits, as well. Obesity might cause rapid or slow gastric emptying in healthy groups; however, gastric emptying was delayed in functional dyspepsia patients with low weight. In a meta-analysis published in 2012, significant associations were found between BMI and gastrointestinal symptoms, including reflux, diarrhea, upper abdominal pain, vomiting and heartburn, there was no relationship between BMI and the symptoms, including common abdominal pain, bloating, constipation, lower abdominal pain and nausea (11).

In the present study, a weak correlation was detected between BMI and hiatal hernia in the endoscopic assessment of the diabetic patients with dyspepsia (p= 0.02 and r = 0.35). However, there was no significant association between BMI and other endoscopic findings and frequency of GI symptoms.

Another factor causing abnormal gastric motor function is the receptive relaxation of the fundus and reduced antral motor activity. The postprandial antral motor activity (motility index) is decreased in diabetic patients (12). Despite of a slow tonus rhythm of fundus during starvation, fundic tonus is higher in diabetic patients in comparison to the healthy individuals. Prolonged phase-2 was observed in diabetic patients (12), and phase-3 was almost disappeared in 6-7 juvenile patients with Type-1 diabetic gastroparesis (13). In a study performed with 45 patients with cardiovascular autonomic neuropathy, semi-solid nutrients were given to the patients, the ratio of proximal/distal stomach was significantly decreased in 32 patients having prominent complaints of dyspepsia (14), and the abdominal ultrasound examination revealed significantly dilated gastric antrum in patients with Type-1 diabetes. These findings were also supported by manometric studies. All these findings indicate the presence of slow gastric emptying in diabetic patients.

It has been realized that blood glucose levels have a critical role on gastric motility. Gastric emptying was slower in the hyperglycemic stage of the Type-1 DM patients with regard to glycemic stage (15). Glycemic control was obtained with oral antidiabetics and insulin in Type-2 DM and Type-1 DM patients, respectively, and the rate of gastric emptying remained unchanged. These findings conflict with decreased rate of gastric emptying in hyperglycemic patients (16). In the present study, there was no difference between the diabetic patients using insulin and those not using insulin in terms of symptoms and esophagogastroduodenoscopy findings.

Although certain researchers cannot find an association between autonomic nerve and gastric dysfunctions, few detected that autonomic dysfunction had a poor predictive impact on gastric emptying (17). Cardiovascular autonomic neuropathy is significantly and directly proportional to the gastric motor disorders.

In a study performed on Type 1 DM patients, abnormal gastroesophageal reflux activity was observed in 12 of 31 patients with cardiac autonomic dysfunction, and 2 of 19 patients with no cardiac autonomic dysfunction. This ratio was found to be higher in the diabetic patients comparing to the normal population (18). In the meta-analysis by Sun et al. in 2015, the incidence of gastroesophageal reflux disease was significantly higher in diabetic patients (19). In the present study, the incidence of hiatal hernia was higher in diabetic patients in comparison to the control group. Diabetic patients should be carefully examined in terms of gastroesophageal reflux and reflux symptoms due to the increased prevalence of hiatal hernia.

In the 5-year follow-up study, Marie-France Kong et al. reported higher duration of diabetic, autonomic neuropathy score and esophageal transit in deaths (n=21) in comparison to the living patients; however, no difference was detected between the groups in terms of gastric emptying. In this study, they did not a find an association between gastroparesis and poor prognosis. In most of the patients, the presence of gastroparesis and upper GIS symptoms was found to be not associated with poor diagnosis (20).

Diabetic gastroparesis has a significant clinical importance as it leads to alterations in GIS symptoms, glycemic control and oral drug absorption (21). Alipour et al. found the prevalence of gastroparesis as 64% in diabetic patients (22). In the present study, there was no significant difference between patients with/without neuropathy in terms of endoscopic findings and GIS symptoms.

The symptoms are not characteristic in diabetic patients and even it is similar to those in non-diabetic individuals. The symptoms of diabetic gastropathy is mainly related to the upper GIS system. These symptoms involve diarrhea or constipation, abdominal pain or discomfort and heartburn according to their prevalence in diabetic patients. The symptoms of dyspepsia, nausea and vomiting shows similarities among diabetic and non-diabetic patients. Certain symptoms might vary in diabetic patients or they do not display any symptoms due to visceroreseptor malfunction. In certain studies, the number of symptoms in diabetic patients with slow gastric emptying were shown to be higher and divergent in comparison to the normal population (23). In our study, the GIS symptoms were similar in diabetic and control groups, and there was no significant difference between diabetic and non-diabetic patients in terms of the incidence of the symptoms.

Schvarcz et al. stated that the severity of upper GIS symptoms was higher in diabetic patients and patients with elevated levels of HbA1c had higher prevalence of symptoms (10). Khoshbaten et al. detected a correlation between the prevalence of GIS symptoms and glycemic control, duration of diabetes and diabetic complications (23). It was shown that patients with neuropathy had higher prevalence of symptoms. The severity of symptoms was found to directly proportional to the neuropathy, and the severity of symptoms had correlation with the glycemic control (24).

In the survey study of Peter Bytzer et al., the increased prevalence of GIS symptoms was found to

be significantly associated with poor glycemic control level; however, the duration, type or treatment of diabetes were not related to the type of diabetes (7).

The increased prevalence of *H. pylori* was associated with higher exposure to the pathogens in diabetic patients when they were compared to the control group. The factors of delayed gastric emptying and gastric mucosal damage might cause bacterial overgrowth in the upper GI track in diabetic patients. Basal and stimulated acid secretion were reported as normal or decreased in diabetic patients (25).

Roussos et al. did not establish any significant difference between diabetic and non-diabetic patients in terms of *H. pylori* infection (26). They found higher incidence of gastric ulcer and lower incidence of peptic ulcer in diabetic patients comparing to the non-diabetics; however, these findings were not statistically significant. The prevalence of *H. pylori* infection in diabetic patients was serologically increased (27), and it has been shown in the histological study of Malecki et al. that *H. pylori* infection had a minor role in the upper GIS symptoms (28). Li et al. reported in their meta-analysis study that the prevalence of *H. pylori* infection in diabetic patients was significantly higher than the non-diabetic individuals and this difference was only associated with Type-2 DM (29).

In a study conducted in Ireland, the infection rate of *H. pylori* infection by histology of gastrointestinal mucosa was 74.4% in diabetic patients and 50% in the control group (ulcer 71%, gastritis 43.5%, simple dyspepsia 35%) (27). Persico et al. determined a significant association between *H. pylori* infection and autonomic neuropathy (84.7%), and the early prevalence of *H. pylori* infection in diabetic patients with dyspepsia was found to be higher than the non-diabetic individuals (30). Devrajani et al. showed that diabetic patients were more susceptible to the *H. pylori* infection (31).

Conclusion

In the present study, endoscopic findings were compared between diabetic patients with dyspepsia and non-diabetic individuals, and as the prevalence of gastric ulcer was significantly higher in diabetic group (p=0.04), there was no statistically significant difference in terms of other endoscopic findings, including antral gastritis, pangastritis, duodenal ulcer, bulbitis, cardiac insufficiency, hiatal hernia and esophagitis. Despite of high prevalence of gastric ulcer in the diabetic group, there was no significant difference between GIS symptoms, diebetic complications and glycemic control among the patients having other endoscopic lesions.

Meantime, no significant difference was determined between diabetic patients with non-ulcer dyspepsia and diabetic patients with dyspepsia and duodenal ulcer in terms of GIS symptoms. The prevalence of hiatal hernia in the diabetic patients was higher than the control group. Diabetic patients should be carefully examined in terms of gastroesophageal reflux and reflux symptoms due to the increased prevalence of hiatal hernia.

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Coincidental Lesions that have been seen in Patients with Lumbar Discopathy at Spinal MR Examination

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Abstract

Objective: The present Study has been made in order to investigate and examine the prevalence and type of the coincidental findings seen in patients with lumbar discopathy subjected to Lumbar Spinal Magnetic Resonance Imaging (MRI).

Material and Method: the 613 patients who were thought to have been Lumbar discopathy and who were subjected to Lumbar MRI have been examined. Lumbar MRIs were reported by musculoskeletal radiologists. Vertebra hemangiomas, tarlov cysts, Renal cysts, schmorl nodules, liver cysts were included in this study.

Findings: Total 613 patients (male-female rate, 354: 259; age range, 16-79 years of age) were assessed. Vertebra Hemangiomas at 5.7% of the patients (n=35) vertebra hemangioma, at 3.5% of patients (n=22) tarlov cyst, at 2.2% (n=14) kidney cyst, at 1.4% (n=9) schmorl nodule, at 0.3% (n=2) of the patients liver cyst were found.

Conclusion: Detected coincidental findings have seen quite common at the examination of MRI of the patients with lumbar discopathy. Although the most of the coincidental findings which were detected at MRI of Lumbar Spine have been benign, the awareness of their prevalence is helpful in diagnosing the lesions which are not related with the symptoms.

Keywords: Lumbar, MRI, Discopathy, Tarlov Cyst

Introduction

Lumbar discopathies are one of the common causes of lumbar (back) pain and disability seen in our society nowadays, approximately 60 percent to 80 percent of adults suffer lumbar (back) pain throughout their lifetime (1,2). Lumbar disc hernia is among the main causes of the lumbar/back pain, which are at the upper ranks. Gradual degeneration of Nucleus Pulposus and Anulus Fibrosus which are the disc components paves the way for this disease. Disc, which becomes degenerated in time depending on age and peripheral factors, shows tendency to herniation (2). Lumbar disc hernia is diagnosed in accordance with clinical symptoms and findings supported by radiological examinations (2). The lumbar disc and neighboring anatomic structures have been displayed in detail with imaging of MRI and Lumbar anatomy at different dimensions, HD Image of the soft tissue and by utilizing different MRI sequences (3). In this study, our objective was to investigate lesions independent from the main complaint falling within the imaging areas of the patients undergone to Lumbar MRI because of the Lumbar/Back Pain and to examine layout and distribution of these lesions.

Material and method

Pre-diagnosis of Lumbar Discopathy and radiological examination of 613 patients whom Lumbar MRI applied have been assessed in the present study. The scrutiny on MRI has been carried out by musculoskeletal radiologists who are well experienced in the field of spinal lumbar MRI. The coincidental finding has been defined as any abnormal finding included in the imaging field which was not associated with the main complaint. Vertebral hemangioma, tarlov cyst, Renal cyst, schmorl nodule, liver cyst were included in the study. Imaging data were obtained by the same MR Device (Avanto 1.5 Tesla, Siemens, Germany).

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Results

the 354 (57.7%) male patients and 259 (42.3%) female patients were subjected into this study. We have come across with coincidental findings in 82 patients. There were vertebra hemangioma at 5.7% (n=35) of the vertebra patients, tarlov cyst at 3.5% (n=22), Renal cyst at 2.2% (n=14), schmort nodule at 1.4% (n=9), liver cyst at 0.3% (n=2).

There were 4 patients with Vertebral Hemangioma+, 4 patients with Tarlov Cyst, 3 patients with Vertebral Hemangioma+ Renal Cyst at the same time. Renal (Figure 1a,b). There was not any coincidental lesion in 531 patients (Table 1). Patients' age ranged from 16 to 79 years and average age was 47,6.

Table 1: Layout/Distribution of the Coincidental Lesions

Coincidental Lesions	Patient Number	%
Vertebral Hemangioma	35	5.65
Tarlov Cyst	22	3.55
Renal Cyst	14	2.26
Schmourl Nodule	9	1.45
Liver Cyst	2	0.32
Vertebral Hemangioma+ Tarlov Cyst	4	0.65
Vertebral Hemangiom+ Renal Cyst	3	0.48
Lesion, Undetected	531	85.65
Total	620	100.00

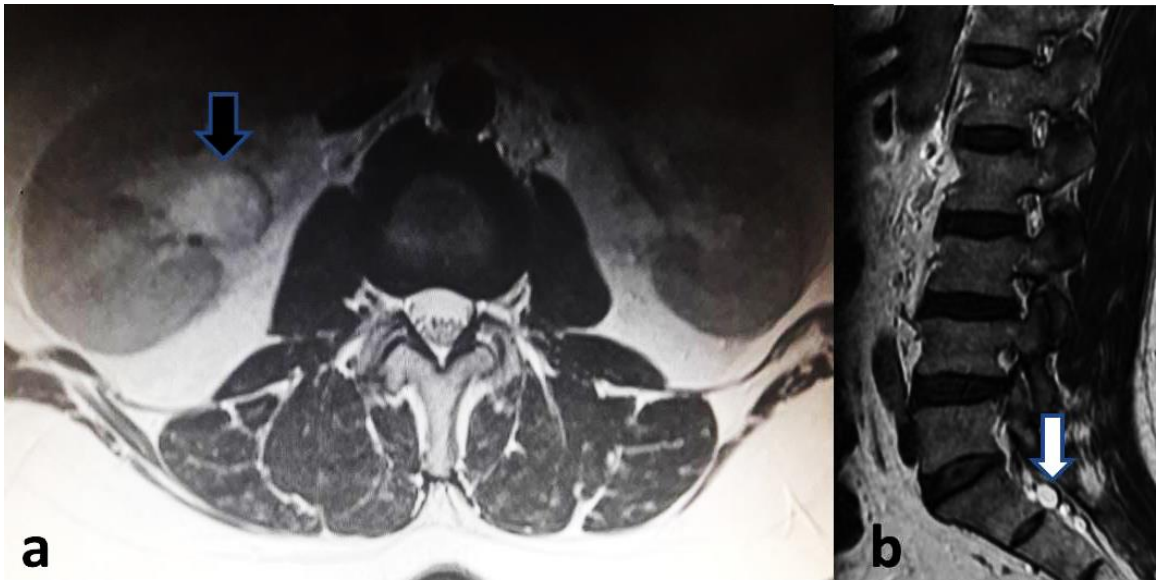

Figure 1: (a) Lumbar MRI (T2) at weighted axial section, right calyx cystic lesion detected (black arrow), (b) Lumbar MRI (T2) at weighted sagittal section sacral region, arachnoid cyst (tarlov cyst) detected (white arrow)

Discussion

In the evaluation of patients considered to be lumbar disc hernia, lumbar MRI is widely used technique for collecting primary data. In the most health centers after commissioning into operation of image archiving and communication system set up in order to scrutinize image assessment, higher number of findings have been observed in Lumbar MRIs (1,4). In daily practices of radiologists it has been reported that coincidental lesions detected at the scrutiny of Lumbar MRI were too much (3,5).

Coincidental findings have been considered as the asymptomatic findings detected in patients with the pre-diagnosis of lumbar discopathy, who was undergone Lumbar MRI (1). The great majority of these coincidental findings are benign (1). Even if the lesions which are thought to be benign have been usually ignored, their effects on human health are not known clearly (4, 5). Some of these lesions may have been the initial stage lesions of some diseases and therefore they should be assessed systematically. Even if the findings such as hemangioma, tarlov cyst, etc remain as asymptomatic at the next period, it has been reported that renal and liver cysts may require monitoring, and what's more they may lead to serious health problems (6, 7).

Studies, which have been carried out in relation with the coincidental findings located at the examinations of Lumbar, exist in literature. Wagner et al. (5), in 2500 MRI reports which were examined by them, have come across with 202 coincidental findings in 183 patients; Park et al. (1) have located 107 coincidental findings in 1268 patients who were thought to have been suffered with lumbar disc hernia. Green et al. however have examined 300 MRI reports and stated that they have spotted 25 coincidental findings (8). In examining of MRI of 613 patients there were 82 (13,3%) coincidental findings in our Study. When it is compared with other studies we can see that the rate of coincidental lesion was somewhat high, which, we think it was because our average patient age (average age: 47,6) was high.

Vertebra hemangiomas are benign, which consist 4% of all spinal tumors (9). Vertebral hemangiomas are benign vascular tumors of the body and are seen too often on the radiological imaging (10). Although it is a most frequent lesion, less than 1% of it, gives neurological findings (11, 12). In the study carried out by Barzin and Maleki in the autopsy reports the frequency of vertebra hemangioma has been determined as 9.5% (9). In our present study we have determined it at the rate of 5.7% in lumbar MRG Reports.

Schmorl nodules among other lesions that we have detected coincidentally were defined in 1930 by Christian George Schmorl. Schmorl nodules develop with the hernia of vertebra, nucleus pulposus from cracks on the cartilage plaques towards the section of spongiosa. It becomes visible by development of reactive sclerosis around it. It may be either congenital, or may develop as the result of passing the disc pressure to the cartilage structure migrating towards the vertebra corpus depending on the degeneration (13). Since Schmorl nodules expanded to the disc volume towards the vertebra corpus, there are some views that the risk of disc hernia was decreased (14).

In our Study, tarlov cysts which we determined them at the 2nd frequency and called them also as sacral per-neural cysts after hemangiomas have been located at the sacral region, and appeared coincidentally. Tarlov cysts are originated from the junction point of dorsal root ganglion and the nerve root, and it is the meningeal dilatation of the sheath of vertebra's dorsal base depending on subarachnoid space (15). They are accepted generally as congenital. They are usually asymptomatic and they do not lead to any neurological findings (16). Nevertheless, in the literature, although it is seen rarely in some cases, tarlov cysts may cause clinical findings such as radiculopathy due to the fact that tarlov cyst puts pressure onto the rooted nerve toot or neighboring nerve roots (16). Nabors et al. (17) determined the frequency/density of sacral peri-neural cyst as the 1%. Paulsen et al. (18) reported that the rate which is less than 1% of sacral peri-neural cysts was symptomatic. The rate of appearance of tarlov cysts in our study was 3.5% and all of them were asymptomatic.

Liver cysts are benign tumors liquid content in liver, generally formed as single, and defined as a simple cyst. Although etiology has not been revealed clearly, it is thought that great majority of them is congenital (19). They are detected generally during check-ups or in any way at the time of radiological tests. The simple cysts do not give much symptom. But cyst tending to enlarge may cause complaints of jaundice depending on right upper stomach-ache, distension (bloating) and biliary obstruction (20). Tuncel et al. reported that frequency of these cysts was 0.15% (21). In the study carried out by Quattrocchi et al. frequency of liver cysts was found as the 0.2% (6). In our present Study the rate of liver cyst is 0.3% and both cases are also asymptomatic.

The simple renal cysts are lesions which are most frequently seen in kidney. Although its frequency rises at older ages, it has seen less in the population of young group (22). The simple cysts which are not give clinical findings generally have been detected coincidentally as the result of radiological tests such as ultrasonography, computerized tomography and MRI, etc. They rarely require treatment. Some patients suffer, be it rare, such symptoms as pain, hypertension, hematuria, cyst rapture, etc. (23). Its rate of appearance at below 18 years of age is 0.10% to

0.45%, when the age goes up the rate has been rising up to 20% (24, 25). In the study carried out by Ciezanowski et al. the prevalence of renal cyst has been found as the 2.9%; the renal cyst prevalence has been determined as 6.4% in the study carried out by Tuncel et al. (21). In our present study however this rate was 2.2%. Some of the renal cysts which have been detected coincidentally are clinically important because of their pressure onto kidney and leading to such findings as hydronephrosis and requires immediate treatment in order to prevent long term damage of kidney (3, 22). Konnak et al. (26) reported that in patients with renal carcinoma detected coincidentally, their rate of surviving patients who applied symptoms and diagnosis of renal carcinoma were higher than the former. This shows that coincidental renal lesions perhaps that renal carcinoma may be early stage and therefore we thought that rate of surviving have increased due to early stage diagnosis.

The coincidentally detected lesions in Lumbar MRI, even if they were independent from the main complaint, may bear importance from the clinical point of view. Therefore, systematical assessment of spinal and non-spinal structures in Lumbar MRI is important in daily practical. We have been thinking that to get information on the frequency of the coincidental lesions, to manage them and their effects on the life of patients and to provide information to patients about this issue is necessary.

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Compensation of MRI findings in asymptomatic patients with chronic low back pain

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Abstract

Objective: Chronic low back pain can originate from a number of constructs. It has a range of pathologies depending on multifactorial causes. In this study, we aimed to investigate in asymptomatic patients who compensation complaint of chronic low back pain in our outpatient clinic and demonstrate its for functionality in treatment planning.

Method: MRI results of 78 asymptomatic patients (46 males, 32 females) who complained of low back pain for at least 12 weeks between March 2016 - January 2017 were examined. During Magnetic Resonance Image (MRI) assessments, T1 and T2 weighted sagittal plane and transaxial images of the lumbar region (L1-S1) and radiology reports of these images were obtained for all patients. Degenerative disc disease, Bulging protrusion, Spinal canal stenosis and Nerve root compression re-evaluated and patients findings were assessed.

Results: There was no abnormality in the MRI results of 16 patients (20%) examined within the study criteria. Nerve root compression was detected in 17 patients (22%), spinal stenosis in 24 patients (30%) and disc degeneration or bulging in 57 patients (78%). There was no statistically significant difference in the incidence of pathologies by asymptomatic patients findings.

Conclusion: Chronic back pain is a disease that involves a wide range of pathologies. MRI scan provides detailed images to the clinician, it is difficult to make a specific diagnosis in the majority of patients with low back pain. Difficulty should be taken into account that the findings obtained by the clinician during assessment can also be seen in asymptomatic individuals.

Keywords: Low back pain, MRI, Asymptomatic

Introduction

Chronic low back pain is a health condition affecting most of the world population, most commonly between the ages of 30-50, which causes social and economic losses, and it affects about 23% of people in a certain time of their lives (1,2). Chronic low back pain can originate from a number of constructs such as nerve roots, muscles, intervertebral discs, and abdominal organs. It has a range of pathologies depending on multifactorial causes, including structural, somatic and psychological factors (3,4), Treatment aiming at biomechanical factors may be inadequate in some cases. Non-specific low back pain is diagnosed when the causes of pain could not be detected by currently available assessment and diagnostic tools and is defined as chronic back pain when the duration of low back pain is 12 weeks or more (5). The knowledge that the correlation of imaging with symptoms is poor in patients with chronic low back pain is based on many studies. In many studies, magnetic resonance imaging revealed disc herniation and spinal stenosis in patients, with degenerative disc or bulging findings noted in more than 90% of patients (6,7,8). When clinical symptoms of these pathologies are examined, asymptomatic examination findings or findings caused by a number of intertwined problems are observed. In a study evaluating the results of magnetic resonance imaging (MRI) in patients without low back pain, Greenberg JO et al. reported 39% degenerative disc disorder with bulging, 18% disc protrusion or herniation as well as spinal stenosis, nerve root canal stenosis, osteophyte localized in vertebra corpus (9).

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MRI has been used for a long time in diagnosis of lumbar region pain. MRI shows not only pathological changes but also physiological changes caused by aging (10,11,12). Degenerative changes also describe physiological changes developing over time, rather than pathological changes in asymptomatic people. Previous studies in the literature reported a high percentage of disk degeneration in asymptomatic patients and a few studies focused on changes in the lumbar region, and there is no study investigating the changes in patients with chronic low back pain. In this study, we aimed to investigate existing changes in asymptomatic patients who had undergone lumbar MRI assessment at least once with the complaint of chronic low back pain in our outpatient clinic and demonstrate its functionality in treatment planning.

Material and method

MRI results of 78 asymptomatic patients (46 males, 32 females) who complained of low back pain for at least 12 weeks between March 2016 - January 2017 were examined. All patients included in the study were assessed and their findings deemed as normal examination findings are given in Table 1. Patients who did not meet normal lumbar examination findings as a result of physical examination were not included in the study. Also patients with a past medical history of fracture, surgical intervention in lumbar region, metabolic diseases that may lead to systemic disorder or genetic diseases (chronic renal failure, osteoporosis, achondroplasia, osteogenesis imperfecta, osteopetrosis, etc.) and those with a history of malignancy with potential for metastasis were not included in the study.

During MRI assessments, T1 and T2 weighted sagittal plane and transaxial images of the lumbar region (L1-S1) and radiology reports of these images were obtained for all patients. An orthopedist and a radiologist who participated in the study re-evaluated the lumbar zone 5 level intervertebral disc structure and neural foramina and classified all MRI results as those with no abnormality, those with nerve root compression, those with spinal canal stenosis and those with disc degeneration and bulging.

Degenerative disc disease diagnosis was made according to modified Pfirrmann criteria in T2 weighted section in midsagittal plane (Table-2) (13). Patients with Grade 2 - 6 disc degeneration change were deemed to have degeneration. Grade 7,8 disc degeneration was not observed in the patient group included in the study so it could not be evaluated.

Bulging diagnosis was made according to MRI assessments, Glenn et al.'s classification (Table-3) (14) . Grade 1-3 was deemed as the presence of bulging symptom and included in the study.

Spinal canal stenosis or nerve root compression is caused by the central canal, lateral recess, or foramen. Diameter of normal lumbar spinal canal is 15-27 mm. An anteroposterior area of the canal less than 70 mm2 indicates central spinal stenosis. In our study, those with a central canal diameter less than 11.5 mm were regarded as spinal canal stenosis. Normal foraminal height is 20-23 mm at lumbar region. In our study, a foraminal height of 15 mm or less was associated with foraminal stenosis.

Statistical analysis

Descriptive statistics were used to define continuous variables. (mean, standard deviation, minimum, median, maximum)

Student's t test was used to compare two continuous independent and normally distributed variables, and Mann Whitney u test was used to compare two independent variables not showing normal distribution for age comparison by pathologies.

Chi-Square (or Fisher Exact test where applicable) was used to examine the relationship between categorical variables for statistical evaluation among the pathologic findings according to sex.

Statistical significance level was set to 0.05. Analyses were performed using MedCalc Statistical Software version 12.7.7 (MedCalc Software bvba, Ostend, Belgium; http://www.medcalc.org; 2013).

Results

Lumbar MRI results of 78 asymptomatic patients who received medical treatment due to low back pain that age and gender distribution at Table 4 and Table 5.

There was no abnormality in the MRI results of 16 patients (20%) examined within the study criteria. Nerve root compression was detected in 17 patients (22%), spinal stenosis in 24 patients (30%) and disc degeneration or bulging in 57 patients (78%). (p> 0.05). Table 6.

Age distribution by disk degeneration was 32,6+5,8 /35 (20-40) (p<0,05). Age distribution by Spinal stenosis was 31,5+6,5/31 (21-40), Herniated Nucleus 32,6+5,8/35 (20-40) and Bulging 32,1+6,1/32,5(21-41) (P>0,05) (Table 7).

In addition to this, there was flattening due to lumbar lordosis loss in 27(%34) patients, osteophyte in 13(%16) patients, hemangioma in 7(%1) patients, simple cyst forming bone islet in 2(%0,2) patients and enchondroma in 1 (%0,1) patient.

Table 1: Asymptomatic patient assesment scheme.

Anamnesis and Physical Examination
Inspection
-Lomber Lordoz
-Dorsal spine muscle weakness
-Posture
Palpation
-Spinous bulge
-Individual range
-Tenderness
-Mass
Joint movement range
-Extention
-Lateral flexion
-Rotation
Lower extremity examination
-Hip, Knee Ankle
Neurological view
-L4, L5, S1 neurological level test
-Patella reflex
Spesific Tests
-Straight leg lift test
-Femoral nerve stretch test

Table 2. T2 weighted section in midsagittal plane according to modified Pfirrmann criteria

Grade 1	Normal disc no disc degeneration
Grade 2,3	There is a signal change in disc nucleus and annulus fibers
Grade 4	The border between inner and outer fibers of annulus is indistinct in posterior edge
Grade 5	Disc is hypointense and there is no loss of disc height
Grade 6,7	Disc height loss progressive decrease
Grade 8	Final stage disc structure is completely distorted and disc height has disappeared

Table 3. T2 weighted section in midsagittal plane according to Glenn et al.'s classification

Grade 1	Mild bulging symptom, bulging from the edge is minimal
Grade 2	Mild bulging symptom
Grade 3	Intermediate protrusion
Grade 4	Protrusion
Grade 5	Herniation

Table 4. Distribution of patients by gender

Gender	N	%
Male	46	59.0
Female	32	41.0
Total	78	100.0

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Table 5. Mean age range.

	N	Mean	Median	St. Deviation	Min.	Max.
Age	78	31.2	30.5	6.1	20	41

Table 6. Gender distribution of asymptomatic patient findings with *Fisher's Exact p* analysis.

		Male N (%)	Female N (%)	p
Herniated Nucleus	**No**	34 (73.9)	27 (84.4)	0.404
	Yes	12 (26.1)	5 (15.6)	
Spinal stenosis	**No**	35 (76.1)	19 (59.4)	0.139
	Yes	11 (23.9)	13 (40.6)	
Disc Degeneration	**No**	30 (65.2)	17 (53.1)	0.349
	Yes	16 (34.8)	15 (46.9)	
Bulging	**No**	18 (39.1)	8 (25.0)	0.229
	Yes	28 (60.9)	24 (75.0)	

Table 7. Age distribution of asymptomatic patient findings with *Mann-Whitney U p* analysis.

		Age Mean+Std. Deviation Med. (Min.-Max.)	P
Herniated Nucleus	**No**	30.8±6.2 30 (21-41)	0.332
	Yes	32.6±5.8 35 (20-40)	
Spinal Stenosis	**No**	31.07±6.03 30 (20-41)	0.765
	Yes	31.5±6.5 31 (21-40)	
Disc Degeneration	**No**	29.7±5.6 29 (21-40)	**0.016**
	Yes	33.4±6.4 36 (20-41)	
Bulging	**No**	29.3±5.8 29 (20-40)	0.053
	Yes	32.1±6.1 32.5 (21-41)	

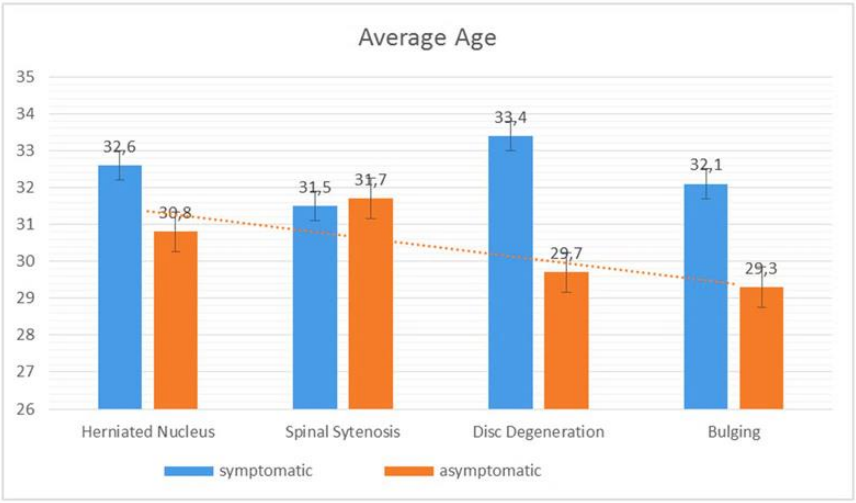

Figure 1: Asymptomatic patient findings distribution with age.

Discussion

Chronic back pain is a disease that involves a wide range of pathologies depending on the anatomical structures from which the pain originates, the severity of the pain, and whether it is of mechanical or inflammatory character. Main causes include lumbar muscle spasm, lumbar degeneration, disc herniation, and lumbar canal pathologies. In clinical examination and imaging assessments, 85% of patients do not have a specific diagnostic outcome or pathology and are considered as nonspecific low back pain (2,15,16). In our study, only 20% of the patients who had normal examination findings on the physical examination had completely normal MRI findings. Although the distribution of patients with normal MRI findings was found to be higher in the age range of 20-30 years, gender did not result in a significant difference. Powell et al. reported a linear increase in disc degeneration with age in a series of 302 cases in which the rate of intervertebral disc degeneration was assessed by MRI in asymptomatic women between the ages of 16-80 years, and more than one third of the patients with disc degeneration were in the range of 21-40 years of age (17). Disc degeneration and bulging were the most common findings in our study with a percentage of 78%. Disc degeneration and bulging are associated with inflammation, dehydration of nucleus pulposus, reduced disc height, annular tears, disc protrusion and deterioration of mechanical function as a result of deterioration of normal anatomy and biochemistry of disc upon changes emerging over time and the onset of degenerative process. Disc degeneration starts with aging and is the most prominent between 25 and 35 years of age. There is some disc degeneration in everybody after fifty years of age, and it mostly concerns L5-S1 and L4-L5 ranges (18,19). Our study showed that disc degeneration caused a statistical difference in age distribution.The distribution of findings by age groups is given in and bulging disc finding was more common in lower age range compared to other findings, whereas degenerative disc disorder was observed to be minimum. Figure 1. Nerve root compression, spinal canal stenosis were identified in all age ranges included in the study. All cases with disk degeneration had several grades of bulging symptoms, with the minimum being grade 1. These changes are known to lead to periodic pain attacks in the active age group with high labor force, resulting in labor loss. In patients with intact peripheral disc structure and no evidence of nerve root compression, chronic low back pain may arise from disruption of internal architecture of disc.(20) Possible mechanism related to degenerative disc involves growth of nociceptive nerve into intervertebral disc upon degeneration, causing pain by stimulation of these nerve endings by inflammatory mediators. Decreased disc height due to biomechanical changes upon degeneration manifests itself with annular bulging, herniation and early osteophyte formation. Cartilage thinning associated with degenerative disc, capsule looseness, instability and increased range of motion increase osteophyte formation (15,19,21). These MRI changes not causing pathology indicate that the degenerative process proceeds from all directions. In our study, there was no patient showing grade 7,8 disc degeneration according to Pfirrmann classification. The reason for this gives us an idea about the detection of examination finding in these patients. Degeneration grades in the study group were similar in most patients, which was ascribed to the fact that the age range was similar so no assessment was made in that respect.

Central spinal stenosis is usually associated with facet joint hypertrophy and ligamentum flavum hypertrophy at the disc level. It is a degenerative process developing slowly in the lumbar region so the onset of complaints is generally insidious and slow. Neurogenic symptoms, which are conventional findings of spinal stenosis, are particularly manifested by pain, numbness and tingling in the lower extremities, particularly in calf. A canal diameter in the range of 10-13 mm is considered as relative spinal stenosis and a canal diameter less than 10 mm as significant spinal stenosis. In our study, the patients with measurements less than 11.5mm and thus spinal stenosis and grade 5 disc herniation did not cause any difference by age and gender. It has been reported that complaints related to disc herniation may decrease over time and that even MRI findings showing extruded disc herniation can completely resolve and pain-causing symptoms completely resolve. In a study of 3 subjects conducted by Kara et al., patients with severe clinical examination findings and extruded disc herniation, to whom surgical treatment was recommended, rejected surgical treatment and during their follow-ups, their complaints completely resolved and their MRI findings completely disappeared (22). In our study, 21% of patients without any clinical complaints had disc herniation findings. In a study investigating abnormal MRI findings in 102 normal healthy Korean subjects conducted by Sang et al., 36% of subjects had annular fissure, 38% nucleus degeneration, 11.9% disc protrusion, and 7% extruded disc, and it was suggested that lifestyle and cultural habits may be effective in percentages of these abnormal MRI findings being different from those obtained for other populations (10). MRI specificity in lumbar disc hernia ranges from 76% to 96%. In healthy individuals with no low back problem, abnormal MRI findings have reached values higher than 20%. Although an MRI scan provides detailed non-invasive anatomical images to the clinician, it is difficult to make a specific diagnosis in the majority of patients with low back pain (17,20). We believe that the evaluation of these data with physical examination will further increase diagnostic

specificity and that the specific findings obtained by MRI and their reflection on the patient with physical examination may be investigated in another study.

Conclusion

In magnetic resonance imaging performed due to low back pain, pathological changes in lumbar vertebrae are interwoven with physiological process, and it should be taken into account that the findings obtained by the clinician during assessment can also be seen in asymptomatic individuals.

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Should the chronic form of tularemia be defined? Should the treatment of the chronic form be managed differently?

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Abstract

Background: Tularemia is a bacterial, zoonotic disease caused by Francisella tularensis. Although the ulceroglandular form is the most common form in the world, oropharyngeal tularemia is the most common form in Turkey. Lymph node suppuration is the most common complication. F. tularensis causes granulomatous and suppurative lesions in the lymph nodes and other organs.

Methods: Seventeen suspected oropharyngeal form tularemia cases complicated with suppurated lymphadenitis have been examined in this study. All of the patients (17, 100%) had cervical lymphadenopathies and had a history of beta-lactam antibiotic use with the diagnosis of tonsillitis. Tularemia cases were diagnosed according to the case definition of World Health Organization (WHO).

Results: All of the patients (17, 100%) had cervical lymphadenopathies ranging in size from 2-8 cm and unilateral lymphadenopathy, while 12 (71%) patients had right-sided lymphadenopathy. The rate of fever was 41% and the rate of pharyngitis or tonsillitis was 52% at presentation. All patients had a history of beta-lactam antibiotic use with the diagnosis of tonsillitis. Seven patients recovered with first-line monotherapy. In the remaining 10 patients, treatment was rearranged, and these patients were switched to combination treatment or another anti-infective. Surgical drainage was performed on all but two of the patients.

Conclusions: The diagnosis of tularemia is often delayed. It may take a significant length of time to diagnose the condition and the disease may become complicated. As it is understood from our study and other studies, the types and duration of treatment can vary and differences can be observed in cases that are past the acute stage. Although the guideline has included a classical treatment approach for the tularemia, there is no standard approach to cases with delayed diagnosis, complicated cases and those refractory to conventional regimens. These observations and other examinations have raised the question whether the chronic form of tularemia should be defined, and whether the treatment options and durations should be re-standardized according to the 'chronic tularemia' definition as a 'chronic granulomatous disease'.

Keywords: Tularemia, Orofarengeal Form, Chronic, Granulomatous infection, Treatment

Introduction

Tularemia is a bacterial, zoonotic disease, especially seen in the northern hemisphere (1). However, in recent years, tularemia cases have been reported from Turkey, Yugoslavia, Spain, Kosovo, and Switzerland (2). Turkey represents 13% of the reported cases of tularemia in Europe between the years 1992 and 2012 (3). In recent years, outbreaks that are particularly associated with water have been observed in Turkey. *F. tularensis* is a bacteria that is highly resistant to environmental conditions and the ability of *F. tularensis* to survive in free-living water amoeba (*Acanthamoeba castellani*) is considered to be important for the regional persistence of the disease and in the waterborne epidemics (4).

F. tularensis is transmitted to humans via dermal, oral, conjunctival or respiratory routes by direct contact with infected animals, ingesting contaminated food or water, inhalation of contaminated aerosols, or arthropod bites (5).

F. tularensis causes granulomatous and suppurative lesions in the lymph nodes and other organs (6).

The bacterium locally replicates at the entry site from where it spreads to the regional lymph nodes. Since it is a facultative intracellular microorganism, it can continue to replicate inside endothelial cells and macrophages (7).

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Rapid proliferation of the bacterium in lymphoid tissues causes follicular hyperplasia leading to focal suppurative necrosis, which in turn results in the formation of granulomas. Histopathologically, it is characterized by characterized by granulomatous lesions containing focal caseous and necrotic areas. Differential diagnosis should include infectious and non-infectious causes due to the development of granulomatous and suppurative lymphadenitis. Granulomatous lymphadenitis is often confused with tuberculosis (2,4,6,8).

There are six main clinical forms of tularemia: ulceroglandular, glandular, oculoglandular, oropharyngeal, typhoidal, and pneumonic forms (6). Although the ulceroglandular form of the disease is the most common form in the world, oropharyngeal tularemia is the most common form in Turkey. This clinical form involves direct invasion of oropharynx by the bacteria. It is transmitted by the consumption of contaminated water and food. Lymph node suppuration is the most common complication (9).

Oropharyngeal tularemia may be easily confused with other diseases affecting the cervical lymph nodes, such as streptococcal tonsillitis, tuberculosis, infectious mononucleosis and lymphoma (10).

The majority of the patients have a history of tonsillopharyngitis prior to beta-lactam antibiotic use and unresponsiveness to treatment. It may take a significant length of time to diagnose the condition and the disease may become complicated. Delays in the use of the appropriate antibiotics result in failure to respond to treatment.

Oropharyngeal form tularemia cases complicated with suppurated lymphadenitis have been examined in this study.

Material and Method

Seventeen suspected tularemia cases were admitted to the Department of Infectious Diseases and Clinical Microbiology at Balıkesir University Faculty of Medicine between January 2015 and September 2017. The data were retrospectively retrieved from the medical records. Data included demographic characteristics of the patients, history of illness, symptoms, clinical findings, laboratory test results, treatment characteristics and therapeutic responses. Detailed information about patient's occupation, the site of infection, day of onset, insect bites, contact with animals, living in rural areas, clinical symptoms, and so on was obtained using an applied questionnaire. Tularemia cases were diagnosed according to the case definition of World Health Organization, suspected tularemia case was defined as the presence of fever, membranous pharyngitis or tonsillitis and cervical lymphadenopathy. Suspected cases may be coming from the epidemic region and unresponsive to beta-lactam antibiotics. Suspected case with a positive serological laboratory result (serological titer ≥1/160 for micro-agglutination test) and positive polymerase chain reaction (PCR) for *F. tularensis* was considered to be diagnosed with disease (6).

Blood samples were collected from patients having clinical findings consistent with tularemia. Serum samples were separated and sent to National Central Laboratory, where the micro-agglutination test was used for serological diagnosis. Confirmed tularemia cases were patients with compatible clinical findings and with positive serological titer (titer≥160 for MAT). Brucella, salmonella, toxoplasma serology, rubella, Epstein-barr virus, cytomegalovirus, hepatitis A/B/C, HIV serologic tests, PCR and bacterial culture of tuberculosis (lymph node drainage material) tests were requested for differential diagnosis.

Results

Seventeen tularemia cases were included in the study; demographic characteristics, clinical and laboratory findings, and treatments were evaluated. The mean age of the patients was 47 (18-76); 12 (71%) were female and 5 (29%) were male. All patients were rural inhabitants living in endemic regions, using tap water and in contact with animals. All patients had oropharyngeal form of tularemia complicated with suppurated lymphadenitis. Ulcerative skin lesions were not found in any patient.

All of the patients were patients with treatment experience who had previously applied to a health facility more than once. The average time from disease onset to admission to our clinic was 113 days (20-220). All of the patients (17, 100%) had cervical lymphadenopathies ranging in size from 2-8 cm. All patients had unilateral lymphadenopathy, while 12 (71%) patients had right-sided lymphadenopathy. Two patients had preauricular lymphadenopathy in addition to cervical lymphadenopathy. Patients with large lesion size had painful and limited neck movements. In the medical history of the patients, it was found that all patients had symptoms such as fever, tremor, myalgia, sore throat, and fatigue during the onset of the disease. The rate of fever was 41% and the rate of pharyngitis or tonsillitis was 52% at presentation. All patients had a history of beta-lactam antibiotic use with the diagnosis of tonsillitis. Demographic data, clinical and laboratory findings are presented in table1. Seven patients recovered with first-line monotherapy. In the remaining 10 patients, treatment was rearranged, and these patients were switched to combination treatment or another anti-infective. One patient was unresponsive to four-week course of therapy, and response was achieved after the patient was switched to third-line therapy. No treatment failure was observed in patients who used quinolone in monotherapy or combinations. Surgical drainage was performed on all but two of the patients. Details of the treatments are given in table 2.

Table 1: Demographic data, clinical and laboratory findings of Tularemia patients

Age (Mean) years	47 (18-76)
Gender	12 (71%) female, 5 (29%) male
Living in rural areas, n (%)	100%
Onset of symptoms (days)	113 days (20-220 days)
Fever, n (%)	41%
Sore throat, n (%)	52%
Lymphadenopathy, n (%)	17 (100%)
WBC (mm^3)	9500 (5300-13500)
ESR (mm/hr)	27 (4-74)
CRP (mg/L)	18 (3-49)
AST (U/L)	19 (13-24)
ALT (U/L)	20 (6-47)
Tularemia micro-agglutination test titers (range)	1/160- 1/1280
Brucella Agglutination test positivity	None
Salmonella Agglutination test positivity	None
Positive serology of Toxoplasmosis	None
Positive serology of Rubella	None
Positive serology of Epstein Barr virus	None
Cytomegalovirus positivity	None
Hepatitis A/B/C, HIV positivity	None
Bacterial culture (lymph node drainage material)	None
Tuberculosis PCR (lymph node drainage material) (positivity)	None

Table 2: Treatment management of cases

Case	First-line Therapy (2 weeks)	Second-line Therapy (2 weeks)	Third-line Therapy (2 weeks)	Drainage
1	Streptomycin+doxycycline	Doxycycline+ciprofloxacin	-	+
2	Doxycycline	Streptomycin	Ciprofloxacin+gentamicin	+
3	Streptomycin	Doxycycline+ciprofloxacin	-	-
4	Doxycycline	-	-	+
5	Streptomycin+doxycycline	-	-	+
6	Streptomycin	-	-	+
7	Doxycycline	Ciprofloxacin	-	+
8	Doxycycline+ciprofloxacin	-	-	+
9	Doxycycline	Ciprofloxacin	-	+
10	Doxycycline	Doxycycline+ciprofloxacin	-	+
11	Doxycycline	-	-	+
12	Ciprofloxacin	-	-	+
13	Streptomycin	-	-	-
14	Doxycycline	Doxycycline+ciprofloxacin	-	+
15	Doxycycline	Doxycycline+ciprofloxacin	-	+
16	Doxycycline	-	-	+
17	Doxycycline	-	-	+

Discussion

In Tularemia cases, the severity of the disease can range from asymptomatic or mild disease to rapidly progressive and fatal clinical course, depending on the bacterial virulence, the mode of entry to the host, the number of inocula, and the immunological status of the host (8,9,11). The clinical picture is characterized by sudden-onset high fever, tremor, headache, fatigue, myalgia, and arthralgia. Fever is usually present in the early phase of the disease and may not be present in patients presenting in the late term (12).

The majority of the cases in this study were patients who presented to our clinic during the later stages of the disease, with unresponsiveness to previous antibiotherapy. At the time of admission, only 7 (41%) patients had fever. In these cases, fever was accompanied by fatigue, myalgia, sore throat, and headache. Swelling in the neck was observed in all cases. The most common complaints in cases of oropharyngeal tularemia are swelling in the neck, sore throat, and fever. In cases occurring in Turkey, swelling in the neck is observed at a rate of 92-100%, fever is observed at a rate of 66-90%, and sore throat is observed at a rate of 58-92% (13,14,15,16). In a multi-center study conducted in Turkey, oropharyngeal form of tularemia was observed in 85.3% of the cases. Lymphadenopathy was observed in 95%, fever in 85%, sore throat in 84%, and headache in 4% of the cases, and the mean time to admission was 21 days (1-135) (17). In our cases, the mean duration of disease was 113 days (20-220). This was due to the fact that the patients in this study were previously monitored and treated in primary and secondary healthcare services, but referred to tertiary healthcare services due to unresponsiveness to treatment.

In our cases, lymphadenopathy was localized to the right cervical region in 71% of the cases. There was no bilateral involvement. In the study by Tezer et al. (18), right lymphadenopathy was observed in 11 out of 16 cases (68.7%), and in the study of Şencan et al., cervical lymphadenopathy was observed in the left side in 66.7% of 19 oropharyngeal tularemia cases (19). Lymph node suppuration is the most common complication of oropharyngeal tularemia. Delayed initiation of tularemia treatment increases the likelihood of developing suppuration, if the treatment is not started in a few days delays may occur, and suppuration may progress despite effective treatment (20,21). In a tularemia case series in Turkey, suppuration in the lymph nodes was observed in 40% of the cases with delayed diagnosis (> 3 weeks). It has been reported that if the treatment is started within the first three weeks of the disease, suppuration of the lymph nodes can be prevented [16]. In another study, it has been shown that early treatment increases the success chance and prevents lymph node suppuration (22).

In our study, lymph node suppuration was observed in all of the cases and surgical drainage was performed in 88% of the cases. This was associated with the fact that the cases in our study are comprised of those who previously received therapy with the diagnosis of pharyngitis or tonsillitis, who remained undiagnosed for a long period of time, and those who were admitted to the tertiary healthcare facility after being admitted to several primary or secondary healthcare facilities.

In biochemical tests of patients, leukocyte count, erythrocyte sedimentation rate, and C-reactive protein (CRP) levels were not found to be related to disease diagnosis or disease course. The tube agglutination test was used as a diagnostic test. Although several tests can be used for serologic diagnosis, microagglutination test is still the most widely used method (23). Although there are authors who claim that while agglutination assays are useful for early and specific diagnosis of tularemia, they may fail to detect antibodies late period on life; there are also those who state that these assays have a high reliability (23,24). In the study by Bevanger et al., seropositivity was found in 64% of cases in microagglutination tests performed eight years after tularemia treatment (25). Test results of our cases were observed at a rate between 1/160 and 1/1280.

Natural resistance against aminoglycosides, tetracyclines, chloramphenicol and quinolones in F. tularensis strains has not been reported. Streptomycin- and tetracycline-resistant strains have been developed for experimental purposes.

Erythromycin resistance is widespread in northern Europe (especially Scandinavia), in the endemic regions of Russia, and in Turkey (14,26,27). It was reported that erythromycin resistance could be used as an epidemiological indicator (2,28).

Doxycycline, streptomycin and quinolone preparations have been used as a monotherapy or combination therapy in the treatment of our cases. Response to treatment was achieved in 41% of the cases with the first-line therapy, while 59% of the patients required rearrangement of the treatment. Response to treatment was achieved in all cases with quinolone-containing regimens. No treatment failure was observed in patients using quinolones as a monotherapy or as a part of the combination therapy. In the study by Kılıç et al. (7). comparing treatment options in tularemia, similar results were obtained in the group treated with quinolones compared to the group treated with aminoglycosides in terms of treatment failure and relapse, whereas the failure and relapse rates were lower than in the doxycycline group. In the study in which 39 F. tularensis strains were evaluated by E-test method; MIC values for aminoglycoside, tetracycline, fluoroquinolone,

macrolide, penicillin, cephalosporin, imipenem, clindamycin, linezolid, chloramphenicol and rifampicin were examined. All strains were susceptible to conventional antibiotics commonly used in tularemia treatment. Fluoroquinolones were found to have the lowest MIC (50) and MIC (90) values. The lowest MIC values were emphasized in terms of their advantages compared to aminoglycosides due to oral use and lower toxicity, and it was emphasized that quinolones have the potential to be an effective first-line treatment for tularemia (29).

In a study where 145 tularemia cases were evaluated, treatment failure was reported in 38% of the cases and the most successful results were reported in the quinolone group, whereas moxifloxacin and ciprofloxacin were reported as new alternative agents in the treatment of oropharyngeal tularemia (30).

In a study in which 1034 cases were evaluated, 48% of the cases did not respond to first-line therapy, and response was achieved with modifications in the treatments and treatment courses of 2-6 weeks. In the Gölcük epidemic, it was found that when the treatment was started after the 14th day, the clinical failure rate doubled and the recovery time was three times longer than in patients receiving early treatment (31). In the study by Çelebi et al., it was reported that doxycycline, fluoroquinolone, streptomycin, or combination therapies are administered to cases in a tularemia epidemics, and suppuration of lymphadenopathies or surgical excision were considered to be a treatment failure (14).

The cases in this study were patients who presented to our clinic long after the disease onset, complicated with suppurative lymphadenopathy, some of which failed in first-line treatment and were later treated with alternative options or combined treatments. The majority of the cases required surgical drainage.

Tularemia is a disease characterized by granulomatous, suppurative lymphadenitis and focal caseous necrosis. In our cases, similar findings were obtained in the histopathological examination. In a series in which 17 cases of lymph node resection were evaluated, granulomas, necrosis, and suppurative inflammation extending to extracapsular regions, epithelial histiocytes and rare phagocytosed bacillus-like microorganisms were observed in histopathology (30).

The diagnosis of tularemia is often delayed. It is highly important that tularemia should be considered in differential diagnosis. Delayed diagnosis is accepted as the most important factor leading to the development of complications. As it is understood from our study and other studies, the types and duration of treatment can vary and differences can be observed in cases that are past the acute stage. In our case series, treatment success was achieved with surgical treatment, treatment changes, and combined regimens with average treatment duration of 4 weeks in patients who presented in the late period 3 months after symptom onset.

In line with other studies, treatment success is higher with quinolones and quinolone-based combination therapies. Although the guideline has included a classical treatment approach for the tularemia, there is no standard approach to cases with delayed diagnosis, complicated cases and those refractory to conventional regimens.

Conclusion

These observations and other examinations have raised the question whether the chronic form of tularemia should be defined, and whether the treatment options and durations should be re-standardized according to the ‘chronic tularemia’ definition as a ‘chronic granulomatous disease’. Further studies are required on a larger number of cases on this subject.

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Analysis of the patients with lichenoid drug reactions: a retrospective study

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Abstract

Objective: Lichenoid drug reactions (LDR) are a rarely known type of drug reaction that resembles lichen planus. The exact etiology of LDR is not known but it is thought to be caused by the triggering of all kinds of chemical substances. In this study; we aimed to investigate the clinical and demographic characteristics of the patients who were diagnosed with LDR.

Material and Method: The files of 56 LDR patients who were followed in our outpatient clinic among 2011 - 2016 have been reviewed retrospectively. The demographic characteristics, the drugs considered to cause reaction, the presence of multiple drug usage, the duration between drug intake and appearance of the initial skin eruption, clinical findings, lesion locations, laboratory findings and associated diseases have been recorded.

Results: Out of the 56 LDR patients, who were clinically and histopathologically diagnosed and followed, 36 were female and 20 were male. The average age was 52.8 (19-86 years of age). The duration of the symptoms was between 1-3 months in 58.9% of the patients, between 3-12 months in % 17.8, between 1 to 30 days in % 14.2 (n=8) and more than 1 year in 8.9% of the patients.48.2% (n = 27) of the lesions were on the extremities, 37.5 % were generalized, 7.1% were invers type. The most frequently accused drug groups were nonsteroidal anti-inflammatory drugs (NSAID) and antihypertensive.

Conclusions: It has been found that the use of NSAID, and cardiovascular drugs on their own and / or in combination with other medications often led to lichenoid drug reactions.

Keywords: Lichenoid, drug, reaction, nonsteroidal, anti-inflammatory, antihypertensive

Introduction

Drugs are chemical substances that are used in the diagnosis, treatment and prevention of diseases. On the other hand, drugs frequently have unwanted side effects(1). With the advancement of science and technology, the discovery of new medication and the increase of their usage, undesirable drug reactions have been a major problem and a current issue (2-4). It has been suggested that approximately 2% of the patients develop a drug-induced skin reaction (1).

Drug allergies have a different range of symptoms including a slight color change up to alife-threatening picture. While exanthematous, morbiliform, maculopapular, urticarial, and generalized pruritus are the most common skin reactions. The lichenoid drug reactions (LDR) are rarely seen (1). As indicated in various studies the ratio varies between 1.9 to 6% (5-10).

LDR can show up with various medications around the world (2-4).

The information about epidemiology is very limited and the frequency varies according to the population studied (5,11).

It may be due to the fact that the same group of medicines are not preferred in all populations. It has been found that LDR generally appear at the end of very long periods of drug intake and they are seen less frequently when compared with other drug reactions (3, 12).

These have been reported in domestic and foreign literature mostly case reports of patients who were hospitalized (4, 13-28). We did not come across in the literature with any study that investigates only LDR.

For that reason, we aimed to research the clinical and demographical characteristics of the patients who are suffering with LDR, uncommon disease disturbing patients for a long period of time.

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Material and Method

Our study project was approved by local ethics committee (IRB (Institutions review board) number: 11/ 02/2015 date and number 26379996/65). In this study we retrospectively reviewed the medical records of 56 adult patients who were admitted to our outpatient clinic between January 2011 and December 2016 with a diagnosis of LDR. All patients were diagnosed with biopsy and histopathological examination. Data obtained from the records included the demographic characteristics such as age, sex, clinical findings, lesion location, coexisting diseases, the drugs used by the patient continuously and the duration of the skin eruption.

In all patients detailed history was taken in regard to drug intake. In addition, care was taken to select cases whose symptoms were improved or declined when suspected drug was stopped. The laboratory findings of the patients were also recorded. The drug groups were mostly nonsteroidal anti-inflammatory drugs (NSAID), antihypertensive (beta-blockers, angiotensin converting enzyme (ACE) inhibitors), antiarrhythmic, antidiabetic and neuropsychiatric drugs, vitamins, antacids, antiepileptics, antibiotics and combined drugs. The duration between the intake of the suspicious drug (s) and the development of the skin eruption was divided into groups of 1 to 30 days, 1-3 months, 3 months - 1 year and more than 1 year.

All these findings were evaluated and compared with general literature.

Statistical Analysis

A detailed statistical analysis was made based on the acquired retrospective data. Statistical analysis was performed using SPSS software, Version 20 (SPSS Inc., Chicago IL, USA). Frequencies were calculated for variables related to demographic and clinical patient characteristics. Qualitative variables were expressed as percentage. Quantitative variables were expressed as mean.

Results

There were 56 LDR patients who were diagnosed and followed clinically and histopathologically in our outpatient clinic. 36 of these patients were female and 20 of them were male. The female / male ratio was 1.8. The average age was confirmed as 52.8 (between 19-86 years). The average age was 56 for women and 46.6 for men. The most common age range was 50-70 (58.9%, n =27). The percentage of the patients according to age and gender has been shown in Table1.

The time elapsed from the first intake of the medication / drug until the beginning of the skin eruption ranged from 10 days to 15 years. The time elapsed from the drug ingestion to the eruption of the lesion was at most at the rate 58.9(n=33) between 1-3 months. 17.8 % was between 3-12 months (n=10),%. 14.2 was between 1-30 days (n = 8), 8.9% (n=5) complained more than 1 year. When evaluated in terms of symptoms only 9 patients (16 %) had itching. When evaluated in terms of localization, the extremities were the most frequent localization with a ratio 48.2% (Figure 1,2).LDR was generalized in 37.5% (n=21) of the patients, invers in 7.1% (n = 4) and localized in 5.3% (n = 3) of the patients in which lesions were only on the face and hands. In one patient it had a scapular zosteriform shape (% 1.7) (Figure 3).

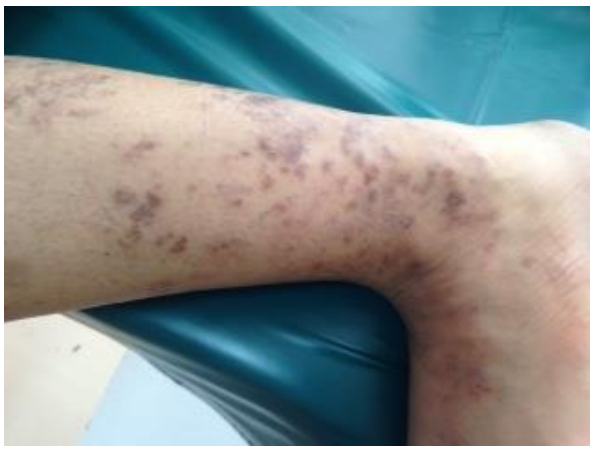

Figure 1: Hyperpigmented lichenoid lesions located on leg.

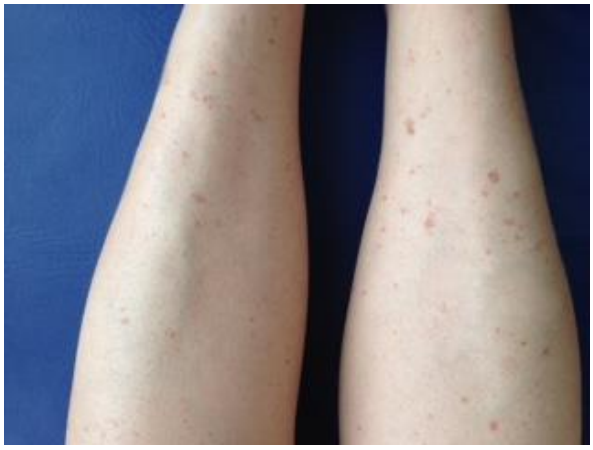

Figure 2: Bilateral lichenoid lesions.

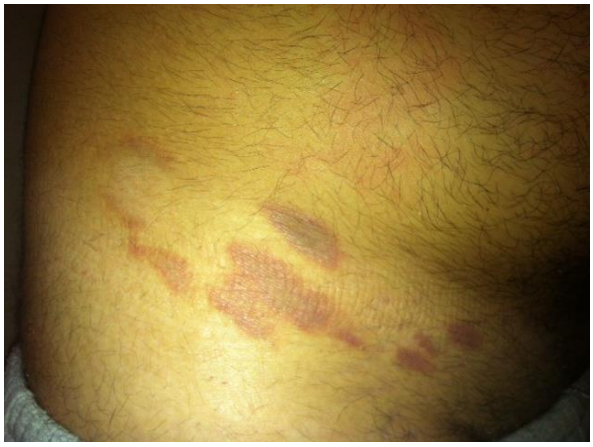

Figure 3: Zosteriform lichenoid lesions on the trunk.

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Table 1: The percentage of the patients according to age and gender

Age	Med age	Male	Female	Total	Rate(%)
19-29	22.8	6	1	7	12.5
30-39	34.3	2	4	6	10.7
40-49	45.6	3	6	9	16.2
50-59	55.4	2	8	10	17.8
60-69	63.7	4	10	14	25
70-79	72.2	2	5	7	12.5
80-89	84	1	2	3	5.3
Total	52.8	20	36	56	100

Table 2: The time elapsed from drug ingestion until the skin eruption

Time	Patient no (n)	Patient rate (%)
1-30days	8	14.2
1-3months	33	58.9
3-12months	10	17.8
>1 year	5	8.9

Table 3: Lesion localization and rates

Lesion location	Patient no (n)	Patient rate (%)
Extremities	27	48.2
Generalized	21	37.5
Invers	4	7.1
Face and hands	3	8.9
Zosteriform	1	1.7
Genital and oral mucosa	-	-
Hair and nail	-	-

Table 4: Accompanying diseases and rates

Concomitantdiseases	Patient no (n)	Patient rate (%)
Hypertension and coronary artery diseases	21	37.2
Anemia	11	19.6
Diabetes mellitus	8	14.2
Neuropsychiatric diseases	7	12.5
Gastrointestinal complaints	6	10.7
Thyroid diseases	5	8.9
Elevation of liver enzymes	4	7.1
Fungal infections/Polyarthritis,/Myalgia	3	5.3
Astma/Menstruel irrgularity	2	3,5
Lichen planus pigmentosus(LPP)/Psoriasis	2	3.5
Osteoporosis/Epilepy/Renal impairment /Pelvic inf /Allergic rhinitis /Venous insufficiency/Migraine/Cerebro vascular disease/Pneumonia/ Irritable bowel syndrome	1	1.7
Presence of multiple illnesses	25	46.6

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Table 5: Drugs causing lichenoid reaction and rates

Drugs	Patient (n)	Patient Rate (%)
NSAID; DiclofenacPotassium (1), AcidSalicylicAcid (ASA)(3),NaproxenSodium (1), Flupirofen(1),Dexketoprofen (1),Meloxicam (1), DeksketoprofenTrometamol(1), Unknown (18)	27	48.2
Antihypertensive + Antiaritmicdrugs; Amliyodipin(6), IsosorbideDinitrat (1) ,Trimetazon(1),Propranolol(1), Metoprolol(2), BenipinHydroclorur(1), CandisartanHydroclorur(1), Dihydropiridin(1), Atenolol(1),ValsartanHydrochlorothiazide(1), Ramipril(2), LosartanPotassium(1), Telmisartan(1)	21	37.5
Antidepressans; Sertraline (2), 5-Hydroxytryptamine (1), Sitalopram (1), Risperidone (1), Essentialopram (1), Amitriptyline (1)	7	12.5
Antidiabetics ;Metformin (4), Glycidase (1), Insulin (1)	6	10.7
Gastrointestinaldrugs; Lansoprol (2), Pantoprazole Hydrotalcite (1), Esomeprazole (2), Famotidine(1), Sodiumalginate + Potassiumbicarbonate (2), Dihydroxyaliminium(1)	6	10.7
Diuretics;Furasamide (1), Indapamide (2), Perindopril (1)	4	7.1
AntithromboticDrugs ;ClopidogrelhydrogenSulfate(4)	4	7.1
Antifungal;Terbinafine (1),Griseofulvin (1),Fluconazole (1)	3	5.3
Antiastmadrugs **;**Fluticasonepropionate (3)	3	5.3
Antityroiddrugs; Levothyroxine (3)	3	5.3
Acetaminophen/paracetamol;(3)	3	5.3
Antibiotics;Quinolone (1), Ornidazole (1), Metranidazole + Imidazole (1)	3	5.3
Mylelorelaksan;Thiocolchicine (2), Tizanidine) (1),Cyanocobalamin (2), Piracetam(1)	3	5.3
Vit B12;Cyanocobalamin (2)	2	3.5
Iron preperats;IronOxide (2**)**	2	3.5
Hormone ; OralContraceptive (2)	2	3.5
Anti Lipidemics;Simvastatin (2)	2	3.5
Serebrovaskulerregulator; Piracetam(1),	1	1.7
Antiosteolitic ;AlendronicAcid(1)	1	1.7
Other drugs; Acetylcysteine (1), Betamethasone dipropionate (1), 1.25 Cholecalciferol (1), Leflumid, Entekavir = Baraclude (1), MonteclastSodium (1)	5	8.9

There was no patient with hair, nail, oral and genital mucosa involvement. Lesion localization and rates are shown in Table 3.

The percentage of concomitant diseases are shown Table 4 . The others received medication because of pain, fever, etc. No hepatitis B and C were detected in any of the cases.

It has been found that the most accused drug groups were NSAID and drugs for the cardiovascular system (anti-hypertensive, cardiac drugs, diuretics, anticoagulants). The 48.2 % (n=27) of the patients were using NSAID.

This was followed by the patients who were using antihypertensive and cardiac drugs with 37.5% (n=21).

This was then followed by antidepressants, antidiabetics, gastrointestinal drugs, antibiotics and antifungals respectively.18 of 27 cases used NSAID the name of which they did not know for pain or fever reasons.

The time periods from drug uptake until the appearance of skin eruption has shown in Table 2.

When the drugs that are considered to be responsible for LDR in patients were examined; In 21 patients (37.5%) antihypertensives, ACE inhibitors / cardiac drugs, in 27 patients (48.2%) NSAID, in 7 patients (12.5%) neuropsychiatric drugs, in 6 patients (10.7%) H1 receptor antagonists and antidiabetics were found. In 4 cases (5.3 %), diuretics, anticoagulants; in 3 cases antibiotics, vitamins, muscle relaxants, antithyroid drugs, antifungal agents, paracetamol in 2 cases iron

deficiency drugs and antiacids, in one patient (3.5%), antiosteolytic, cerebrovascular regulator (1.7%), simvastatin (antihyperlipidemic) and antiepileptic drugs were used.

In 31 (55.4%) of the cases followed at our outpatient with LDR diagnosis, the use of single agent was responsible for the drug reaction, whereas in 25 patients (44.6%), the use of combined drugs was responsible for the eruption.

The most frequently observed combination was antihypertensive, anticardiac drugs and diuretics with a frequency of 14%.

Drugs causing lichenoid reaction and rates is shown in Table 5.

Discussion

Nowadays, the discovery of new medicines, the increasing usage of medicines and the prolonged usage of the drugs and together with the increased life span have increased the effect of drugs on humans(1). Up to now, numerous medications have been reported to cause LDRs and a new one is added at every passing day (29,3). The first data belonging to LDR were the cases that include arsenic which was used for the syphilis treatment in year 1929 and the gold and antimalarial usage for rheumatoid arthritis that was reported in 1940 (10,29-31). Afterwards it has been reported that too many drugs caused this eruption (25,28-33). But LDR mostly caused by and NSAID and antihypertensive drugs (25,28 -33).

The rate of incidence of LDR in cutaneous drug reactions is very low (10). While Puavilai detected 1.2 % case LDR in 80 disease cases series in 1998, Qayoom detected 4% in year 2015 (6,34). As the drug diversity increases, the possibility of LDR appears to increase. In our country this ratio varies between 1.9 % and 6 % (4,7-9,26,33,34).

In general, the main drugs that cause to a drug reaction are NSAID and cardiac drug groups. It has been found that the chances they cause LDR are also high (31,33). The NSAID that can be obtained without prescription and thus frequently used in complaints such as pain, fever, etc. are easily accessible at all times are causing the most frequent LDR (35). In our country, Ozkan et al. carried out a research with 92 patients with lichen planus and found out that the most frequent triggering drug for lichen planus is NSAID and they have the potential to cause lichen planus like skin eruption (36). In the foreign literature, different studies have also shown these drugs are causing LDR (6,19,37,38). We have obtained similar results in our study. Even though some studies have reported that the NSAID would cause oral lichenoid reactions, in our study even though there were many patients with skin lesions. Interestingly there were no cases of oral lesions (37).

Another group of drugs that is reported to be the most common cause of LDR is ACE inhibitors, beta-blockers, cardiovascular drugs including thiazide group diuretics (10,14,20-24,27,39-42). Upadhayai et al. found that atenolol and amlodipine were the main drugs causing LDR in their studies where they used antihypertensive agents (39). In our study, similar to the literature, LDR developed secondary due to antihypertensive drugs. 21 of our patients were taking antihypertensive drugs. We observed that amlodipine was the cause in 6 of these cases. Fessa et al. claimed that LDR was the result of the suppression of the adrenergic system in the skin or the result of the drug cross adrenergic (40).

The neuropsychiatric drugs may trigger LDR (43,44). Akpinar et al. reported in their study with 106 cases that the 3 patients with LDR were using neurologic drugs (8). In our study, there were 6 patients who were receiving antidepressant medication.

Sulfonylurea and anti-hypoglycemic drugs may cause LDR, especially in elderly patients (45). We had 6 patients using antihyperglycemic agents.

The main problem in diagnosis and treatment of LDR is the ability to describe the offending drug responsible for patients who are taking more than one drug. Because while drugs can make LDR alone, sometimes they can potentialize the lichenoid effects of other drugs (10) .

In our study when we observe generally, while the use of single drug was observed in 55.4% cases, the rate of the combined agents was determined as 44.6 %. Among these treatments, the use of the NSAID or together with acid salicylic acid (ASA) or with the cardiac drugs (frequently beta blockers and ACE inhibitors) was taking a place on the forefront.

We have found out as a result of our studies that the cutaneous drug reactions are more frequent in females than males and in adults than in children (33,46). The fact that females have more autoimmune diseases, tendency to hypersensitivity and the use of more medications may facilitate this (10,46). In our study we also had a 61% female superiority and were have also found that LDR are more frequently seen over 30 years of age.

The time that elapsed after the development of LDR, until the patient's application can take months (33).This duration of time can vary from a few months to years. This is especially specific when taking multiple medicines. This time may vary according to the dosage of the drug, the response of the site, the presence of previous exposure and the intake of different drugs at the same time. Apart from that, there may also be a delay in the diagnosis due to different skin findings such as psoriasiform or eczematous lesions (12). The time to emergence of the lesions was reported to be 2 months to 3 years for penicilamine, 1 years for beta blockers, 3 to 6 months for ACE

inhibitors, and 4-6 weeks for quinacrine (3,31,33). Upadhayai et al. have determined the time of formation for LDR as 19.6 months on an average (39). In our study, the duration of the lesion appearance was between 1 month and 3 months in 58.9% (33 cases) of the patients. Only at 5 cases it took more than a year. In one of these cases, the medication taken by the patient for 15 years had reacted. As in our cases, the lesion receded within months by stopping the responsible agent. No latent period could be determined because the NSAID were being taken every now and again.

Lichenoid rashes were observed in the photosensitive regions of the thiazide group diuretics, diltiazem, quinine, quinidine tetracycline, etambutol, and chlorpromazine group drugs (3,22,23,30). Puavilai et al. determined photo lichenoid eruption in a patient using thiazide group drug (34). In our study, we observed a photosensitized lichenoid drug reaction in the face and hands of three patients using thiazide group diuretic and antihypertensive combination of drugs.

LDR is known to be a rare disease (31) . In our study that we have conducted, we have seen that this disease is actually not a very rare disease. The reasons for under diagnosis of LDR are appearing after a very long period after the intake of the drug, being eczematous apart from the lichenoid appearance, having papular, plaques or desquamation shape. Thus LDR is generally overlooked and the main diagnosis is delayed (33). Therefore, the definitive diagnosis may also be difficult. Especially it is difficult to distinguish it from classical lichen planus by clinically and histopathologically (31). Also preliminary diagnoses and the histopathologic diagnosis can be incompatible (47).

Even though there are similarities to lichen planus histopathologically, the presence of eosinophils, findings such as focal parakeratosis, lymphoid cell exocytosis into the upper epidermal layers, colloid bodies in the dermoepidermal compartment, cell infiltration around the deep veins are more common in LDR (3,33,47). Clinical manifestation, histopathological findings, drug intake history and the positivity at the drug patch and / or provocation test can guide to the definitive diagnosis. The diagnosis of all the cases in our study was supported by histopathologically. Apart from this, the lesions were improved by stopping the drug which were blamed and the lesions were repeated when the drug was started again.

In LDR, lesions may be limited to a small area in the skin but also it can be generalized throughout the body. Unlike the typical flexural involvement of the lichen planus, it is located more on the extremities and trunk (31). In most of the cases, the lesions were located symmetrically in the upper and lower extremities in 27 cases. In 21 cases, more than one involvement was mentioned. There were inverse localizations in only 5 of our cases. There was a hand and face localization in 3 patients. There was only one zosteriform site in a patient. None of our patients had any hair, oral, genital or nail involvement as in the literature.

It has not been clearly determined by which means the medicines caused LDR. Delayed type 4 hypersensitivity reactions are thought to cause the drug to merge with the epidermal proteins and to transform the epidermis to an antigenic state by acting like a hapten (2,48, 49). The dose of the drug, host reaction, predrug exposure and concomitant drug intake all affect the LDR pathogenesis (2-4). The presence of autoimmune diseases may also facilitate the emergence of LDR. In our study, 2 patients had LPP and 1 patient had psoriasis history. In addition, our patients had associated autoimmune diseases such as arthritis, diabetes, thyroid diseases, vitamin B12 deficiency anemia, etc. Also, medicines used against these diseases could facilitate the emergence of LDR (10).

LDR can be seen in all age groups around the world. While people in middle-age and older age are the high-risk groups for the development of drug reactions, this is very rare in children (11). In patients over 65 years of age, renal and hepatic functions lead to more physiological decline, multiple disease agents and multiple drug use, drug-disease interactions, drug-drug interactions and forgetfulness (46,50). Dilek et al found that in their study which they conducted with people over 55 years of age, that with the increase of age, the drug reactions increase (46). The average age at our study was 52.8 years. However, especially in patients over sixty years of age (which constituted 41% of these cases), skin lesions were both more common and diffuse. In 4 patients, liver enzyme elevation was determined whereas in 1 patient renal insufficiency was detected.

The treatment of LDR is the detection of the drug causing the disease and its interruption. In our cases, the lesions of the patients disappeared after the medication was interrupted. Furthermore, symptomatic treatment such as topical and systemic corticosteroids may also be given (3). We have also provided symptomatic treatment.

Conclusion

The patients with LDR may come across us with various clinical features. It is important that the clinical characteristics of the patients are well known because of the fact that the LDR are identified and that the symptoms and findings are forming a basis.

It has been determined that the drugs containing NSAID which are commonly used due to the fact that they can be purchased without prescription are causing LDR. Care should be taken regarding the possible cutaneous side effects of drugs in patients,

especially in the presence of multiple and long-term drug use and advanced age.

In the elderly population where secondary diseases increase, one should avoid the use of combined drugs.

Dermatological examination as well as the monitoring of the drugs at regular intervals will be effective in reducing the side effects of the drugs. Cessation of the stimulant drugs that are determined by the detailed drug anamnesis interrogation is important in terms of increasing the success of the treatment and preventing recurrences. And this will increase the quality of life of the patient.

The feedback on drug side effects is important all over the world. For this purpose, in year 1985, TUFAM (Pharmacovigilance Center of Turkey) was established in our country (4). However, this center is not very effective in reporting the LDR due to its longterm appearance and sometimes due to the misdiagnosis.

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Ethical issues: All Authors declare that Originality of research/article etc... and ethical approval of research, and responsibilities of research against local ethics commission are under the Authors responsibilities. The study was conducted due to defined rules by the Local Ethics Commission guidelines and audits.

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Stereotactic Radiotherapy For Patients Withs Metallic Implants On Vertebral Body: A dosimetric comparison

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Abstract

Objective: Metallic implants have impacts on dose distribution of radiotherapy. Our purpose is evaluating impact of metallic implants with different dose calculation algorithms on dose distribution.

Material and Methods: Two patients with metallic implants on vertebral body were included in this study. They were treated with stereotactic radiotherapy. The data of the patients were retrospectively re-calculated with different TPSs and calculation algorithms. Ray-Tracing (Ry-Tc), Monte-Carlo (MC), Acuros XB (AXB) and analytical anisotropic algorithms (AAA) were compared.

Results: Ry-Tc, AAA and AXB underestimated minimum and maximum doses of target volumes and critical organs compared with MC.

Conclusion: MC seems more reliable for dose calculations in patients with metallic implants but more studies with more number of patients should be done to identify the best dose calculation algorithm for patients with metallic implants.

Keywords: Prostheses and Implants, Stereotactic Body Radiotherapy, Monte-Carlo method, Acuros XB

Introduction

Various metallic spinal implants have been used for bone stability on patients with spinal metastases or primary spinal tumors. The radiation therapy has been widely used to treat metastatic or primary spinal tumours.

Recently, spine stereotactic radiotherapy (SRT) is frequently used in the management of spinal tumors. SRT offers a highly conformal and high dose per fraction. The tolerance dose of spinal cord is a limitation factor for prescription dose.

To deliver ablative radiotherapy CyberKnife® (CK)-based SRT is an effective method. Ray Tracing (RyTc) and Monte Carlo (MC) algorithms are dose calculation algorithms which are used by Multi Plan (MP), Cyberknife® Accuray treatment planning system.

In the lung cancer, RyTc algorithm has been shown to be less accurate than MC algorithm in terms of dose calculation due to the inhomogeneus tissue density at the lung-tumor interface and the small fields employed (1-3). Because of these limitations RTOG advises MC calculations for lung cancer cases.

However it is not known that how other sites are affected by different calculations of different algorithms.

The effects of metallic implants on dose calculation have been studied by the several authors. One analysis of dose profiles using metallic rods showed that the TPS overestimated the attenuation effect (4). These data were from relatively simple experimental model or an old TPS such as analytical anisotropic algorithm (AAA) (5).

Acuros XB, a new dose calculation algorithm based on photon and electron transport, has been installed in Eclipse TPS.

AXB uses a technique to solve the linear Boltzmann transport equation (LTBE) and directly accounts for the effects of heterogeneities on dose calculations (6-8).

The purpose of this study was to evaluate the dose calculation accuracies of AXB, AAA, MC and RyTc on two patients with metallic spinal implants.

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Material and Method

Patients

This is a retrospective study which was conducted on CT data sets, collected from two patients who underwent spine SBRT at Ankara Oncology Training and Research Hospital. First patient had renal cell carcinoma with bone metastasis and metallic implant was inserted on 11th and 12th thoracal, 1st and 2nd lumbar vertebra. Second patient had recurrent schwannoma and metallic implant was inserted on 11th and 12th thoracal and 1st lumbar vertebra. The implants were consisted of the corpus and the roots. These parts were contoured separately as corpus and the root. The corpus of the implants included a titanium alloy which composed of 6.09 % Aluminium, 0.2% Iron, 0.1% Oxygen and 4.17 % Vanadium. The roots of the implants included a titanium alloy which composed of 6.12 % Aluminium, 0.18% Iron, 0.12% Oxygen, 4.19% Vanadium. The relative electron dansities of implants were calculated.

Gross tumor volumes (GTV) were deliniated as the T1 contrast enhancement lesion on MRI. The planning target volume (PTV) was obtained by an isotropic expansion of the GTV by 2 mm. Spinal cord was contoured from the T2 flair as offered by RTOG 0631. Planning organ at risk volume (PRV) was defined as the spinal cord plus a 2 mm expansion to account for set-up errors. The PTV volume was 432.5 cm^3 for the first patient and 470,7 cm^3 for the second patient.

Treatment Planning

The prescription dose was 22.5 Gy over 5 fractions for first patient and 25 Gy over 5 fractions for second patient with a goal at least 80 % of PTV received the prescription dose. Treatment plans were produced using RyTc algorithm.

The patients were treated with these plans and the data was retrospectively analyzed with different TPSs and calculation algorithms. Multi Plan Treatment Planning System V3.5 with RyTc, Monte-Carlo dose calculation algorithms and Eclipse. Treatment Planning System V.13.0 with Acuros XB, AAA dose calculation algorithms were used for to create new plans. All doses of targets volumes and critical structures which were individually calculated from these TPSs and these dose calculation algorithms were compared and recorded.

Results

In this study different calculation algorithms were compared retrospectively on the patients with metallic spinal implants. Minimum and maximum doses on target volumes and on critical structures were underestimated at Ry-Tc algorithm compared to MC algorithm. Minimum doses of PTVs were 1% underestimated for both patients. Maximum doses of PTV were underestimated 2% for the first patient and 8% for the second patient. Maximum dose of PRV spinal cord was underestimated 2% for the first patient and 3% for the second patient. Minimum and maximum doses of target volumes and critical structures were underestimated at AAA algorithm compared to AXB algorithm. Minimum doses of PTV were underestimated 3,7% for the first patient and 1,7% for the second patient. The maximum doses of PTV were underestimated 1,8% for the first patient and 2,8% for the second patient. The maximum dose of PRV spinal cord was underestimated 1,9% for the first patient and 2% for the second patient. The isodoses were calculated by the AAA and AXB algorithms on Eclipse TPS are shown in figures 1 and 2 respectively. The PTV coverages and critical organ doses that were obtained from each TPS and calculation algorithm are presented in table 1 and 2.

Table 1: Results of VARIAN Eclipse TPS AXB13 and AAA algorithms

		Patient 1		Patient 2	
		Acuros XB	AAA	Acuros XB	AAA
PTV	Dmin %	74.3	70.6	81.7	80
	Dmax %	121.5	119.7	124,8	122
	Dmean(Gy)	24.2 Gy	24.2 Gy	27.7 Gy	27.4 Gy
PRV spinal cord	Dmax (Gy)	21.5 Gy	21.1 Gy	23.6 Gy	23.1 Gy

Eclipse TPS: Eclipse Treatment planning system, **AXB13:** Acuros algorithm, **AAA:** Analytical anisotropic algorithm

Table 2: Results of Cyberknife® Accuray TPS MC and RyTc

		Patient 1		Patient 2	
		MC	RyTc	MC	RyTc
PTV	Dmin %	94	93	80	79
	Dmax %	122	120	136	128
	Dmean(Gy)	24.1 Gy	24 Gy	28.1 Gy	27.1 Gy
PRV spinal cord	Dmax (Gy)	24.6 Gy	24.2 Gy	23 Gy	23.9 Gy

Accuray TPS: Accuray Treatment planning system, **MC:** Monte Carlo algorithm, **RyTc:** Ray- Tracing algorithm

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Figure 1: The isodose curve for first patient calculated both by AXB and AAA algorithms

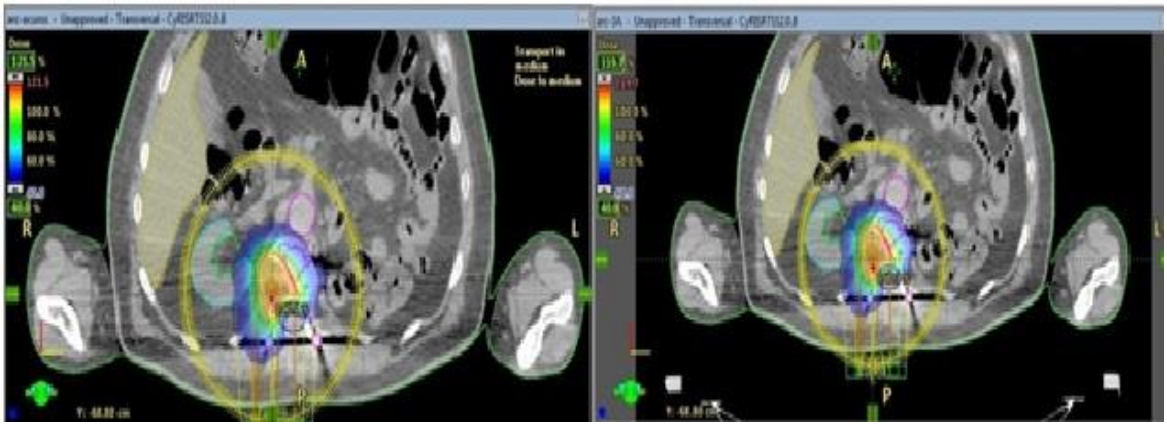
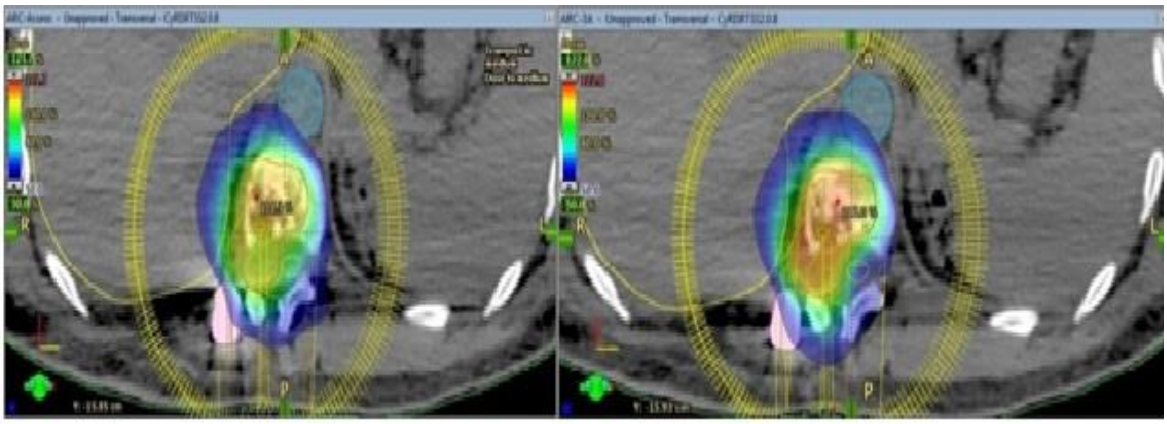


Figure 2: The isodose curve for second patient calculated both by AXB and AAA algorithms



Discussion

This study shows that the differences of the dose distributions between different calculation algorithms on patients with metallic spinal implants.

There are some problems that must be taken into account for the dose calculation on patients with metallic spinal implants. The electron densities of metallic implants are different from the tissue and computed tomography and the radiotherapy planning systems cannot identify them. Metallic implants cause artifacts on CT scans. It is difficult to deliniate the target volume and critical structures on these artifacted CT scans. It also causes dose distribution inaccuracies on TPSs.

The pencil-beam algorithm has the limitation for accurately calculating the dose contribution of the 3-D scatter doses from the metal. Various authors have investigated the effect of metallic implants on radiation therapy, and efforts have been made to reduce these effects. Newhauser et al. suggested a method to reassign HU values in the regions containing artifacts to the HU values in artifact-free regions of tissue (10).

The calculation of dose with TPS mainly depends on relative electron density, which is derived from CT value. A large artifact may occur when scanning a metal implant with high density, which will result in error in CT calculation. We contoured the roots and the corpus of the metallic implants separately and reassign the HU values of them for AAA and AXB. In the other hand we inserted the relative electron densities of the metallic implants in Accuray TPS for RyTc and MC calculations. So we aimed to reduce the scattering effects of the metallic implants.

In Roberts et al study it has been showed that the accuracy of dose calculation varied with errors up to 20% because the TPS, in which the pencil-beam algorithm was used, overestimated the attenuation for a titanium prosthesis (11).In addition same relationship was found between MC and Acuros XB, that differences up to 12% in DVH analysis were seen (12).We observed dose calculations varied up to 8%.

But in this study the TPSs of the MC and AXB13 that we have used were different so the difference observed between MC and AXB may not reflect the accurate results.

In clinical, Monte Carlo method is the unique method able to calculate the dose accurately near a high-Z inhomogeneity (13). There are various papers that showed the different dose distribution between the calculation algorithms in TPS. Xiao et al. recalculated the plans with a heterogeneity corrections algorithm and showed that the PTV V60 decreased on average by 10.1% (14). Wu et al. also compared the RyTc plans and re-calculated MC plans. They showed the PTV D95% decreased from 50.0 Gy to 42.9 Gy in MC plans and in small peripheral tumors incline to be greater (15). All of these dosimetric studies showed that the actually delivered dose to the target was 10 to 14% lower in the RyTc plans. We also observed that RyTc underestimated the doses of target volume and critical organs compared to MC. The underestimated doses of the critical organs especially like in spinal cord may cause unexpected side effects.

In Ojala et al. study the authors declined that the AXB algorithm is a reliable dose calculation algorithm for patient plans with hip implants that contain beams traversing the implant, but the use of AAA is not encouraged (12). In this study we could not observe significant difference between the doses of metallic implant corpus and roots when calculated with AAA and AXB 13. So we cannot say that AAA is not encouraged for the patients with metallic implants.

In this study, original plan was calculated with RyTc and recalculated with the MC model, AAA and AXB13 algorithm. RyTc, AAA and AXB underestimated the doses of target volumes and critical organs compared to MC. AXB was very close to MC. Comparison of the isodose curves in the implant and elsewhere confirms that the deviations between the MC model and the AXB algorithm were small, while the MC model producing higher doses.

The results of our study indicate that metallic implants nearby the target volume have a negative impact on dose distribution of radiotherapy. It is especially important when metallic implant is inserted to vertebra in terms of spinal cord dose. However, there is still controversy regarding the best method to determine correct radiation dose distribution. Future studies should focus on ways to avoid the scattering effects of metallic implants on dose distributions.

Conclusion

In our study we show that MC algorithm and Acuros XB algorithm give more reliable results on the patients with metallic spinal implants, so both could be used for the stereotactic radiotherapy plans of patients with the metallic implants. But more studies with more number of patients should be done to identify the acceptable calculation algorithm.

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Ethical issues: All Authors declare that Originality of research/article etc... and ethical approval of research, and responsibilities of research against local ethics commission are under the Authors responsibilities. The study was conducted due to defined rules by the Local Ethics Commission guidelines and audits.

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Gastrointestinal stromal tumor mimicking such as incarcerated inguinal hernia

Murat Ferhat Ferhatoglu[1], Abdulcabbar Kartal[1*], Taner Kivilcim[1]

Abstract

Gastrointestinal stromal tumors, are most common sarcoma of the gastrointestinal tract, originate from Cajal cells which are responsible for the motility of the gastrointestinal tract. This sarcoma is most commonly observed in stomach and small intestines, can rarely be located in omentum, mesentery or retroperitoneum. Herein, we aimed to present a case of gastrointestinal stromal tumor presented as incarcerated inguinal hernia.

Key words: Gastrointestinal stromal tumor, GIST, hernia, inguinal hernia, incarceration

Introduction

Gastrointestinal stromal tumor (GIST) is a mesenchymal tumor originating from Cajal cells responsible for the motility of the gastrointestinal tract (1). GISTs are most commonly located in stomach (60-70%), small intestines (20-30%), colon and rectum (5%)(2), but it may be localized anywhere from esophagus to anus. Rarely, they can localize in retroperitoneum, omentum and mesentery(3). Primary treatment is surgical removal of the mass.

The most common structures found in the inguinal hernia are omentum and small intestines. More rarely, however, the appendix, sigmoid colon, bladder can be found in the inguinal hernia sac. It is an extremely rare case that an gastrointestinal system originated tumoral mass to be found in the inguinal hernia sac. We aimed to present a case of GIST presenting in the form of left incarcerated inguinal hernia in this case.

Case

A 67 year-old male patient was admitted to the emergency department with left groin pain and mass swelling in the left groin. An irreducible, hard, painful mass was palpated in the left groin area. He had subfebrile fever and in the blood tests leukocyte count was 11400/mm3 (4000-10400/mm3), all other test result were normal. He was operated with the diagnosis of left incarcerated inguinal hernia. A necrotic mass filling up the hernia sac with a size of 13x4 cm with hemorrhage on the surface was observed during surgery. (Figure 1) The mass was isolated from the spermatic cord and the testis and excised.

When intraabdominal site was palpated from the hernia incision during surgery, it was determined that there were widespread implants on the peritoneal surfaces. As a result of the pathologic examination, the patient was reported having GIST mass, postoperative radiological examination revealed extensive GIST metastases in the abdomen and on the peritoneal surfaces and imatinib mesylate treatment was initiated for the patient by a medical oncologist.

Discussion

GISTs are the most common sarcomas of the gastrointestinal tract. Rarely, they may be located in the abdominal peritoneum or mesentery. However GISTs located in these localizations are often presented as metastasis of the primary disease originating from the gastrointestinal tract (5).

Since they usually give symptoms in the late period, more than 50% of patients have locally advanced or metastatic disease at the time of admission (2).

Surgical removal of the mass as a whole constitutes is the basis for treatment. However, even after a complete surgical resection, 50-65% of patients have a 5 year survival chance. In advanced stage and metastatic disease, this rate is reduced to 35% (2).

Although there are publications in the literature about positivity of lymph node metastasis (6,7), nodal metastasis is very rare in GIST, and thus surgical consensus is that a lymph node dissection is not necessary (8).

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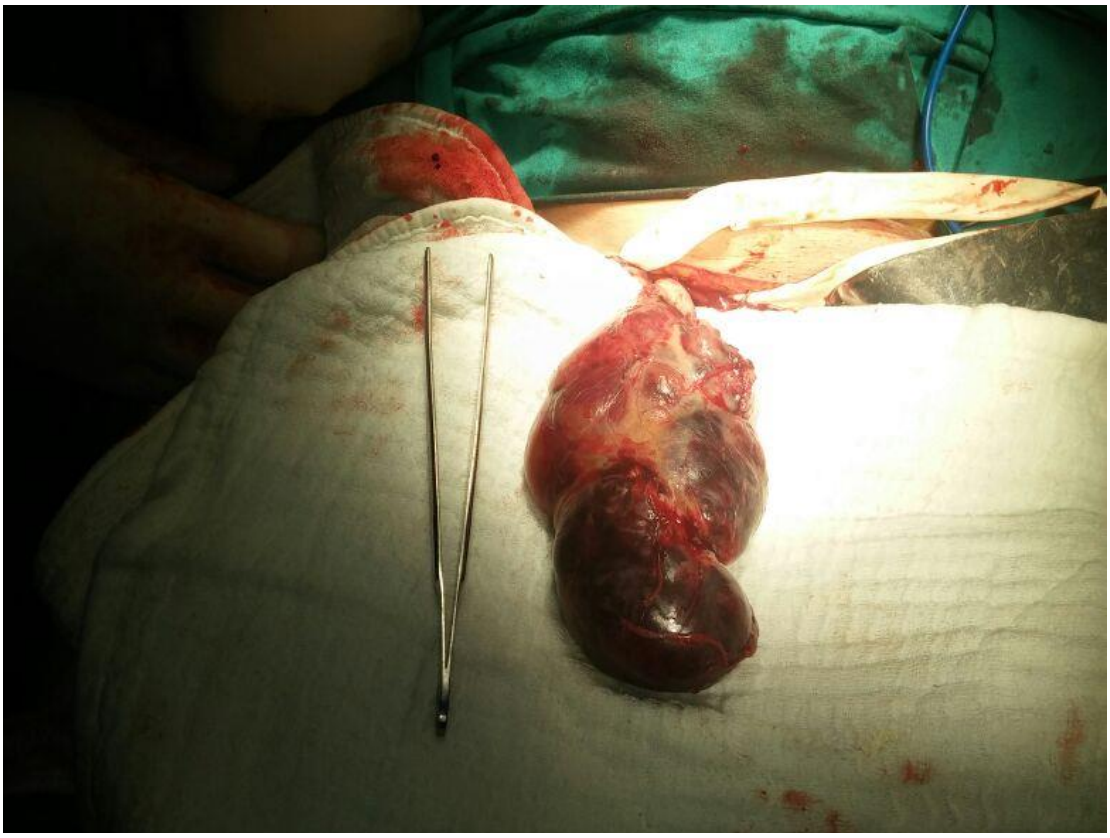

Figure 1: Hemorrhagic fragile mass taken out from the hernia sac

Table 1. Assessment of clinical aggression of GIST in accordance with the American National Institutes of Health guidelines (10)

Aggressiveness	Tumor size (cm)	Mitotic index (HPF)
Very low	<2	<5/50
Low	2-5	<5/50
Moderate	≤5	6-10/50
	5-10	<5/50
High	>5	>5/50
	>10	>10/50

Table 2. Poor prognostic factors for GIST (1)

✓	Tumor size > 10 cm
✓	High mitotic index (≥5/50 HPF)
✓	Non-gastric localization
✓	Distant metastasis
✓	Damage to the integrity of the tumor during surgery
✓	Perforation
✓	Multifocal tumor
✓	Advanced age
✓	Widespread tumors

In 95% of the cases c-kit (CD117) (4), in 70% CD34 (1), in 5% □- platelet derived growth factor gene mutations are observed (9). In post-operative adjuvant treatment imatinib mesylate, a specific c-kit inhibitör is used. It has been shown that this treatment reduces or stops progression of the tumor in more than 50% of patients (10).

In patients with high-risk tumors (Table 1) and poor prognostic factors (Table 2), the recurrence can be reduced by routine follow-up after surgery and adjuvant chemotherapy.

A sudden, irreducible, painful mass in the inguinal region is called an incarcerated inguinal hernia. This situation is one of the few classical emergency surgical indications. The absence of inguinal hernia history, description of non-specific gastrointestinal symptoms and history of GIST surgery should make the surgeon suspect that it may be an additional pathology, and additional radiological examinations such as ultrasonography can be used to diagnose unusual pathologies preoperatively. In our case, the surgeon considered the patient as having an incarcerated inguinal hernia and during surgery, noticed that the palpated mass within the hernia sac was a tumoral mass.

Conclusion

Incidental tumor finding in the inguinal hernia sac is an extremely rare condition. Very few cases have been reported in the literature regarding this situation. Advanced technological imaging methods such as ultrasonography should be used to detect cases such as this and other rare cases in patients with a long history of gastrointestinal symptoms, especially those with no inguinal hernia history

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Ethical issues: All Authors declare that Originality of research/article etc... and ethical approval of research, and responsibilities of research against local ethics commission are under the Authors responsibilities. The study was conducted due to defined rules by the Local Ethics Commission guidelines and audits.

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