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ORIGINAL RESEARCH PAPER

Depression and Anxiety in Patients with Multiple Sclerosis: A Retrospective Study on the Impact of Glatiramer Acetate

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Ali Ulvi UCA[1a*], Faruk Ömer ODABAŞ[2b], Mustafa ALTAŞ[1c], Faruk UĞUZ[1d], Osman Serhat TOKGÖZ[1e]

[1.] Department of Neurology, Meram Faculty of Medicine, Necmettin Erbakan University, Konya, Turkey.

[2.] University of Health Sciences, Department of Neurology- Konya Education and Research Hospital, Konya, Turkey.

Orcid ID: [a]0000-0002-5783-8061[b]0000-0001-9136-9388 [c]0000-0003-3011-1062 [d]0000-0002-6876-5005 [e]0000-0002-4919-0285

Abstract

Objective: *It has been reported that of disease-modifying therapies used in treatment of relapsing-remitting MS (RRMS) may affect mood of the patients. This study aims to investigate the impact of glatiramer acetate (GA) on depressive and anxiety symptoms in patients with RRMS.*

Methods: *The study included 31 patients who were admitted to the neurology clinic, and who were diagnosed with RRMS. To assess depressive and anxiety symptoms in the patients before and after the treatment with GA was used the Center Epidemiologic Studies Depression Scale (CES-D) and the Hospital Anxiety and Depression Scale (HAD), respectively.*

Results: *Before the treatment, based on the scales CES-D and HAD-Depression scores, 18 (58.1%) and 17 (54.8%) patients had depression, respectively and based on HAD-Anxiety 15 (48.4%) patients had anxiety. After the treatment, the same numbers were 8 (25.8%), 9 (29.0%), and 7 (22.6%), respectively. The statistical analyses indicated that the mean scores of CES-D (t=4.51, P=0.000), HAD-Depression (t=2.91, P=0.007), HAD-Anxiety (t=2.78, P=0.009) and HAD-Total (t=3.15, P=0.004) significantly decreased from the onset of treatment to the end of treatment.*

Conclusion: *Results of the present study suggest that GA may be useful effects on depressive and anxiety symptoms rather than negative effects in RRMS patients.*

Keywords: Multiple sclerosis, glatiramer acetate, depression, anxiety

[*] Corresponding author: E-mail: aulviuca@hotmail.com

Introduction

Multiple sclerosis (MS) is a chronic, inflammatory and demyelinating disorder of the central nervous system that is frequently observed in young adults between the ages of 20–45 and is characterized by episodic neurologic dysfunction[1]. MS causes not only physical disability but also fatigue, gait disorders, bladder and bowel dysfunction, cognitive dysfunction, nociceptive or neuropathic pain, depression, and anxiety.

Over the last decade, several studies have shown that comorbidity is common in MS, even at diagnosis, and its prevalence increases with age[2,3]. It has been reported that the prevalence of psychiatric disorders is 72% in MS, 54% of which is constituted by depressive disorders[4]. Prevalence of depression is 2–3-fold higher in MS patients than in the general population, while the lifetime prevalence is around 50% [5]. However, estimates regarding the prevalence of depression (4.98%–58.9%) and anxiety (1.2%–43.6%) in the MS population show significant differences[6]. Although depression is the leading psychiatric disorder associated with MS, prevalence of anxiety disorders also increases in MS.

Studies have shown that depression is not just an emotional disorder in MS patients; it can be a biological-based symptom[7]. In other words, many factors such as structural brain changes, immune-inflammatory, genetic and psychosocial factors can cause this. Depression and anxiety in MS are important because they frequently accompany the clinical presentation of MS, in addition to being major determinants of the quality of life, affecting cognitive functions, causing suicidal thoughts and suicide attempts, and affecting social relationships and adherence to disease-modifying treatments (DMTs) [8].

The most commonly used DMTs for the treatment of MS are interferon beta (IFNβ) −1a, IFNβ-1b and glatiramer acetate (GA). According to reports, prevalence of depression increased after IFNβ was introduced for the treatment of relapsing-remitting MS (RRMS) in the 1990s[9]. However, it is not possible to draw a definite conclusion from these studies that were conducted as case reviews. Although it is believed that IFNβ causes secondary depression due to the inhibition of serotonin, Patten and Metz reported that there was no such relationship in their study aiming to reveal the relationship between depression and IFNβ treatments[10]. Numerous controlled and uncontrolled clinical studies data on IFN-βwere evaluated in a common pool and there was no association with suicide attempts or with the increase in depression rating scale scores[7]. Long-term data have also failed to confirm the hypothesis that IFNβ treatment for RRMS causes depression.

The mechanism of action of GA, which has an approved safety and efficacy profile in the first-line treatment for RRMS, is different than that of IFNβ. GA is synthesized by a copolymer polypeptide structure that consists of glutamic acid, lysine, alanine, and tyrosine [11]. The drug was produced to compete with and mimic myelin basic protein. Although its mechanism of action is not entirely known, it was reported to induce suppressor T cells in animal studies [12]. Briefly, GA is a first-line therapeutic against the RRMS, in which it acts by immune modulatory mechanisms, which also touch T and B cells, interfering with the disease course. Glatiramer acetate is generally well tolerated by the patients. The most common side effects observed with GA are mild local injection site reactions, which can include pain, erythema, inflammation and induration. Systemic adverse event related to GA is rarely seen, but postinjection transient flushing, chest tightness, palpitations, and dyspnea can be observed. While IFNβ package insert information warns of depression and suicide, the GA package insert information does not carry such a warning. No adverse events associated with depression were reported in placebo-controlled or open-label studies with GA. In a study, the incidence of depression has been investigated in a clinical randomized trial involving patients receiving IFN-β or GA and no obvious differences were detected between the treatment groups in terms of Beck Depression Inventory scores[13]. However, Ziemssen et al. demonstrated that patients who were on GA had less severe depression and improved quality of life [14].

An ideal pharmacological agent should have a dual therapeutic action of being effective in the treatment for RRMS and reducing comorbid psychiatric symptoms. This study aims to investigate the effects of GA on depression and anxiety symptoms in RRMS patients.

Materials and Methods

This study was approved by the ethics committee of our institution, and a written informed consent was obtained from all participants. The present study was conducted under the good clinical practice guidelines of the declaration of Helsinki and its later amendments (Registration number of ethical approval: 2020/2899 by the ethics committee of Meram Medical Faculty, Necmettin Erbakan University).

Study population and data collection

The study data were obtained by retrospectively reviewing medical registers. Therefore, no interference of the natural treatment of the patients occurred because of this study. A total of 65 patients with MS who were examined between January 2016 and December 2019 at the Neurology Outpatient Clinic of a University Hospital were included in the study (Figure 1). Clinically definite

MS patients treated with GA from clinical site was retrospectively selected. Demographic characteristics (i.e. age, age at disease onset, gender, education status, employment status, marital status) and clinical characteristics (i.e. duration of disorder, number of previous MS attack, Expanded Disability Status Scale (EDSS) score) were obtained from hospital Enlil HBYS software (Table 1).

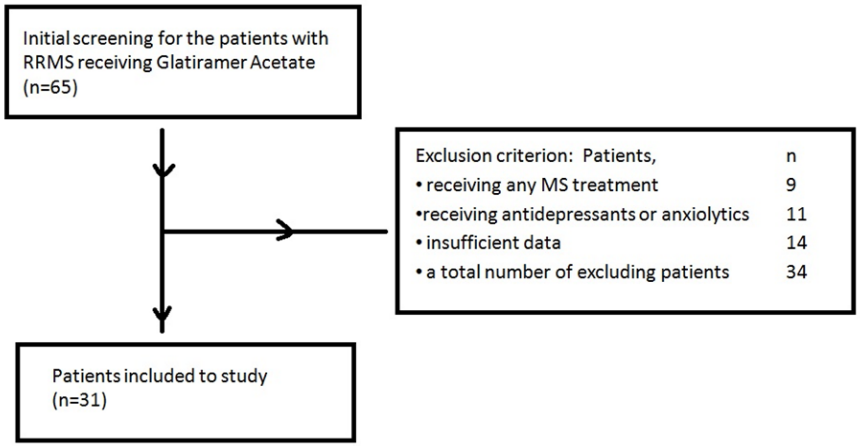

Figure 1. The flow chart of the patients

RRMS: Relapsing-Remitting Multiple Sclerosis

Table 1. Sociodemographic and clinical characteristics of the sample

Age at the assessment, mean±SD, years	33.90±7.15
Age at the onset, mean±SD, years	29.83±7.07
Duration of disorder, mean±SD, years	4.04±3.68
Number of previous MS attack, mean±SD	3.35±1.74
Gender, n(%)	
Female	25 (80.6)
Education, n (%)	
Primary school	14 (45.2)
Secondary school	8 (25.8)
University	9 (29.0)
Employment status, n (%)	
Unemployed	24 (77.4)
Marital status, n (%)	
Married	23 (74.2)
EDSS score, mean±SD	1.33 ± 0.75

SD: Standard Deviation - MS: Multiple Sclerosis -EDSS: Expanded Disability Status Scale

In our clinic, there is no specific protocol regarding which drug therapy will be selected for patients meeting MS diagnostic criteria. The choice of medication is determined according to accessibility, the experience of the physician and the characteristics of the patient. In addition, the Center for Epidemiologic Studies Depression Scale (CES-D) and Hospital Anxiety and Depression Scale (HADS) are used in our clinic before the injection treatments and during the 2nd month controls, as far as the polyclinic facilities allow. In subsequent controls, scales are applied in case of psychiatric complaints, although not periodically.

Methods

The inclusion and exclusion criteria were as follows:

Inclusion criteria

• Patients diagnosed according to McDonald criteria

• To have a relapsing–remitting course

• Patients treated with GA (subcutaneously once daily 20 mg/mL solution)

• Those who did not receive DMTs before GA (naïve patients)

• Those that were evaluated in terms of depression and anxiety symptoms before the GA treatment and 2 month after starting the treatment using CES-D and HADS

Exclusion criteria

• Incomplete medical history and data (n=14)

• Those who received any MS treatment prior to GA treatment (n = 9)

• Those who used antidepressants or anxiolytics (n = 11) for any reason

On the basis of the exclusion criteria, 34 patients were excluded from the study. As a result, the study data include the results of 31 patients.

Center for Epidemiologic Studies Depression Scale

The CES-D is a self-report questionnaire that has been developed to measure depression symptoms and to identify people at risk of having a depressive disorder[15]. The Turkish version of the CES-D, developed by Spijker et al., was used in this study. CES-D contains 20 items that can be responded to on a four-point Likert scale, with response categories ranging from “rarely or none of the time” (0 points) to “most or all of the time” (3 points). These items are then summed to obtain a total score, with higher scores indicating more severe depression symptoms. A cut-off score of ≥16 is generally accepted as an indicator for clinically significant depression [16].

Hospital Anxiety and Depression Scale

HADS is used to determine a patient's risk of developing anxiety and depression, and to also measure its severity and the resulting change in the severity. It has two sub-scales that separately evaluate anxiety and depression. Cut-off scores used in the Turkish version of the scale are 10 and 7 for the anxiety and depression sub-scales, respectively [17].

Statistical analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS), version 16.0, for Windows (SPSS Inc., Chicago, IL). For sociodemographic data of the sample was used descriptive analyses. The scores of CES-D, HAD-depression and HAD-anxiety before and after the treatment were compared with t test for dependent variables. Correleations between CES-D and HAD subscales and EDSS scores were assessed with Pearson's correlation test.

Result

Mean age of the patients (n = 31) was 33.90 ± 7.15. Patients were mostly female (n = 25, 80.6%), married (n = 23, 74.2%), and unemployed (n = 24, 77.4%). Nearly half of the sample (n = 14, 45.2%) included elementary school graduates. Average duration of the disease was 4.04 ± 3.68 years (range = 0.5–16 years), the mean number of MS attacks was 3.35 ± 1.74 (range = 2–10), and the mean EDSS score was 1.33 ± 0.75 (range = 0–3).

According to the pretreatment CES-D and HADS-Depression scores, 18 (58.1%) and 17 (54.8%) patients had depression, respectively. In addition, HADS-Anxiety scores showed that 15 (48.4%) patients had anxiety. The same numbers were 8 (25.8%), 9 (29.0%), and 7 (22.6%), respectively, 2 month after the treatment.

Statistical analyses show that CES-D (t = 4.51, p = 0.000), HADS-Depression (t = 2.91, p = 0.007), HADS-Anxiety (t = 2.78, p = 0.009), and HADS-Total (t = 3.15, p = 0.004) scores exhibited a significant decrease in the second month of treatment (Table 2). In addition, EDSS score was not associated with baseline scores of CES-D (r=0.077, p=0.685), HADS-Depression (r=0.137, p=0.470), HADS-Anxiety (r=0.048, p=0.800) and HADS-Total (r=0.096, p=0.614) scales.

Table 2. Anxiety and depression symptom levels before and after glatiramer acetate in patients with multiple sclerosis

	Before treatment, mean ± SD	***After treatment, mean ± SD***	***t***	***P***
HADS-Depression	7.74±4.87	5.42±4.23	2,91	0.007
HADS-Anxiety	9.81±5.72	7.16±4.36	2,78	0.002
HADS-Total	17.55±9.60	12.58±7.88	3,15	0.003
CES-Depression	17.03±12.37	9.19±11.03	4,51	0.000

HADS: Hospital Anxiety and Depression Scale, CES: Center Epidemiologic Studies, SD: Standard Deviation

Discussion

MS is a disorder that can significantly impact physical, mental, and social wellbeing. There are several reasons for MS affecting the psychological state of the patients. They are as follows: MS has direct effects on the central nervous system; there is no clear diagnosis and prognosis in MS; it has an episodic and unpredictable clinical course; it affects work and family life; there are several concomitant symptoms and other chronic diseases that accompany it; and the most important thing there is no cure for MS. In addition, prolonged use of drugs in the treatment and protection against attacks also has many psychiatric side effects.

Estimates regarding the prevalence of depression (4.98%–58.9%) and anxiety (1.2%–43.6%) in the MS population show significant differences[4]. According to the CES-D and HADS-Depression scores in our study, 18 (58.1%) and 17 (54.8%) patients had depression, respectively. In addition, HADS-Anxiety scores showed that 15 (48.4%) patients had anxiety. The fact that nearly half of these 31 patients showed symptoms of depression and anxiety underlines the necessity and importance of investigating psychiatric comorbidities in MS patients. The presence of depression and anxiety in a majority of MS patients also increases the importance of DMTs that will be administered. Thus, the treatment of choice should not elicit symptoms of depression and anxiety or increase existing psychiatric symptoms, and should, at the very least, have no impact on these symptoms. When starting MS treatment, most neurologists believe that IFNβ will increase depression more in the course of the disease than GA. For this reason, newly diagnosed patients with signs of depression or psychiatric history are usually given GA treatment from the beginning of MS treatment. This approach clearly shows itself in the treatment preferences of the patient group included in the study. Thus, we think that GA treatment is preferred more because approximately half of MS patients have depression and anxiety symptoms.

CES-D, HADS-Depression, HADS-Anxiety, and HADS-Total scores displayed a considerable decrease in the second month of treatment, which was also statistically significant. Therefore, it was shown that such a GA treatment modality not only prevented an increase in the symptoms of depression and anxiety in RRMS but was also may be effective in reducing psychiatric symptoms. The results obtained are interesting when it is considered that the efficacy of GA in MS treatment occurs at the earliest 2nd month, mean 4th and / or 6th month. Despite the uncertainty of the future caused by the disease, the difficulty of daily self-administered injection treatment, side effects of treatment and fear of injection, the decrease in psychiatric symptoms after 2 months of treatment makes the success of GA treatment even more interesting. According to the results of the study, considering that GA treatment was preferred in a patient group more prone to depression and

anxiety, it can be said that the positive effect of GA on psychiatric symptoms started earlier than its effect on MS. Since a 4-6 week waiting period is predicted for the onset of efficacy in an antidepressant drug, the application of clinical scales at the second month control visits seems appropriate to evaluate psychiatric symptoms. Similar to our findings in a study by Nagy et al., it was found that GA treatment reduced depression and improved the quality of life[18]. Additionally, in a 2016 study[14] involving more than 750 patients, 96% of whom were RRMS, patients had either did not receive disease-modifying therapy (de novo, n = 481) or previously treated with subcutaneous 20mg / mL GA once daily (n=237). In this study, patients have been evaluated in terms of disease progression, relapse rate, general functionality, quality of life (QoL), cognition, fatigue, and depression for 2 years. MS Inventory Cognition Scale scores showed a significant improvement between previously treated patients and de novo cohorts. In the same study, General Depression Scale scores also decreased significantly. These data show that MS patients benefit from GA treatment in QoL parameters beyond relapse and disease severity measures. In contrast, two different studies that compared patients who were on IFNβ-1b and GA found no difference in terms of depression. According to a retrospective study by Kirzenger et al., patients who were on GA and IFNβ had similar antidepressant use and depression scores[19]. In another study by Schippling et al., it was reported that IFNβ-1b and GA did not provide different results in terms of depression[20]. EDSS score was not correlated with baseline scores of CES-D, HADS-Depression, HADS-Anxiety, and HADS-Total. The most important reason for this result was thought to be that the patient group consisted of individuals with low EDSS scores and suitable for first line MS treatment. Such a patient group is an advantage for our study. Because, we think that determining and evaluating the positive effects of GA on depression and anxiety will be more difficult due to additional problems in the patient group with high EDSS scores.

Both preclinical and clinical studies have shown that peripheral GA administration can increase central brain-derived neurotrophic factor (BDNF) activity or serum BDNF levels[21]. GA possibly exhibits antidepressant effects by increasing central BDNF either by stimulating neurogenesis or by exhibiting anti-inflammatory effects[21]. The anti-inflammatory effect of GA has also been demonstrated by its ability to induce Th2 cells that cross the blood–brain barrier, accumulate in the brain, and increase IL-10 and BDNF expression. Considering all its aspects, GA is, in addition to its efficacy in MS treatment, also effective in the first-line treatment of RRMS due to its positive impact on the comorbid depression and anxiety symptoms. Thus, it can be safely used in RRMS patients who exhibit comorbid depression and anxiety symptoms.

There are some inherent limitations of the present study. First, the sample size of our study population is small. Secondly, due to the retrospective nature of our study, the fact that it did not evaluate common conditions in MS such as fatigue, pain and cognitive dysfunction that coincide with depression and anxiety is an important limitation. Furthermore, there were a few limitations of this study, including the fact that one-to-one psychiatric interviews were not conducted to evaluate the psychiatric state of the patients, and the CES-D and HAD scales were not periodically used during the treatment period. Considering these features in prospective study planning will be beneficial in revealing the positive effects of GA on psychiatric symptoms.

Conclusion

Neither IFNβ nor GA treatment appears to exacerbate depression and anxiety symptoms in patients with RRMS. However, the results of this study suggest that RRMS patients can benefit from GA in terms of their depression and anxiety symptoms. While depression and anxiety are the most prevalent psychiatric disorders in MS patients, GA can show dual therapeutic effect in RRMS patients with depression and anxiety.

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ORIGINAL RESEARCH PAPER

An Investigation on The Clinical Characteristics of Cases with Lung Cancer in The South-eastern Anatolian Region

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Abdullah KARAKUŞ[1a], Vehbi DEMIRCAN[1b*], Abdurrahman IŞIKDOĞAN[2c]

[1]Dicle University, Faculty of Medicine, Department of Hematology, Diyarbakır, Turkey
[2]Dicle University, Faculty of Medicine, Department of Medical Oncology, Diyarbakır, Turkey

Orcid ID: [a]0000-0003-2090-4392 [b]0000--0002-0378-8687 [c]0000-0002-7451-7286

Abstract

Objective: *The present study aimed to retrospectively determine the demographic, epidemiological, and clinical characteristics of the patients with lung cancer monitored in our clinic.*

Material and Method: *The study retrospectively investigated 865 patients with lung cancer diagnosed, treated, and monitored between 2000 and 2011 in the Medical Oncology*

Result: *Of the 865 patients with lung cancer, 691 (79.5%) had Non-small Cell Lung Cancer (NSCLC), and 174 (20.5%) had Small Cell Lung Cancer (SCLC). Of the patients with NSCLC, 12.3% were in the local stage, 34.7% in the locally advanced stage, and 53% in the metastatic stage.*

The mean survival time of the patients was 31 months in the local stage, 17 months in the locally advanced group, and 9 months in the metastatic period. The smoking rates of patients were 93.8% in patients with squamous cell cancer, 72.5% in those with adenocarcinoma, and 91.4% in those with SCLC.

Conclusion: *Regarding the histopathological subgroups of the patients in our study, we have observed that adenocarcinoma patients rate was higher compared with the average data observed in our country. The smoking rate in patients with adenocarcinoma was less than the average tendency in our country.*

Keywords: Lung cancer, smoking, metastasis

* Corresponding author: E-mail: vehbi_dmrcn@hotmail.com

Introduction

İnvestigations suggest that lung cancer is the most common cause of death from cancer in men and women[1]. Research also reports that lung cancer incidence and mortality are closely related to smoking. Despite the decrease in the incidence and mortality in developed countries with smoking control initiatives in recent times, it is one of the leading cancer-related deaths due to the high rate of smoking in developing countries[2]. Globally, lung cancer cases and deaths have been on the rise in recent years. It is the third most common cancer type in women and the second most common cause in men, and the most common cause of cancer deaths (18.4%) worldwide. Lung cancer is a preventable disease. Smoking is responsible for lung cancer development in 90% of the cases[3]. Other etiological factors such as age, race, gender, occupation, air pollution, radiation, previous pulmonary disease sequela, diet, viral infections, genetic and immunological factors also play a role at a rate of 6%. Of the lung cancer cases, 90% are symptomatic due to local, regional, metastatic or systemic effects of the tumor[4]. The related symptoms are cough, hemoptysis, dyspnea, fever, hoarseness, bone pain, weight loss, anorexia, confusion, neuropathic pain, weakness, headache, ataxia, etc. Physical examination findings can be completely normal, but findings regarding supraclavicular lymphadenopathy, Horner's syndrome, pleural fluid accumulation, localized rhonchus, hepatomegaly, cachexia, localized bone sensitivity as well as peripheral motor and/or sensory neuropathy findings and neurological findings can also emerge[5]. The stage of the disease is the most important prognostic factor. Unfortunately, more than 80% of NSCLC cases turn out to be at the locally advanced or advanced stage at the time of diagnosis. On the other hand, 60% of SCLC cases are metastatic at the time of diagnosis[6]. The present study aimed at retrospectively determining the demographic, epidemiological, and clinical characteristics of a series of lung cancer cases monitored in our clinic for a long period.

Materials and Methods

The study retrospectively investigated 865 patients with lung cancer diagnosed, treated, and monitored between 2000 and 2011 in the Medical Oncology

Statistical Evaluation

A standard form was created with the pre-determined data of the cases, the files were assesment, and the data were recorded on the computer. The SSPS 16.0 programme was used for statistical analysis. The student's t-test was used to compare parametric variables for two groups, and analysis of variance was used for more than two groups (histopathological subtypes). Pearson's chi-square (x2) test was used to compare categorical variables. Survival analyses were performed using the

Kaplan-Meier method. Overall survival was defined as the period from the date of diagnosis to death.

Result

Of the cases, 691 (79.5%) had NSCLC, and 174 (20.5%) had SCLC.As for the gender of the cases, 780 (90.1%) were men and 85 (9.9%) were women, all with an average age of 59.7. According to histopathological subtypes, the results based on the gender of NSCLC cases show that 98.3% of patients with squamous cell carcinoma were male and 1.7% female. On the other hand, in the cases with adenocarcinoma, 77.5% of the cases were male and 22.5% female.

The classification of the cases by age groups has revealed that 31 (3.5%) of the cases were under 40 years of age, 583 (67.3%) in the age group of 40 to 65, and 251 (37.2%) over the age of 65 years.

The study also evaluated the relationship between lung cancer and smoking, one of the most important etiological factors in developing the disease. Of the patients with NSCLC, while 587 (85.2%) were smokers, 104 (14.8%) reported being non-smokers. Of the patients who reported being a smoker, 577 (93%) were men and 10 (14.5%) women. Based on the smoking rates calculated according to the histopathological subtype of cases with NSCLC, the study found that the smoking rate was 93.8% in 241 cases with squamous cell cancer and 72.5% in 193 adenocarcinoma cases.

The most frequent complaint that stimulated the patients to present in our clinic was cough in 514 cases (59.4%), followed by other symptoms such as hemoptysis (208 patients / 24%), dyspnea (315 patients / 36.4%), chest pain (344 patients / 39.7%) and weight loss (270 patients / 31.2%).

The patients presented to our clinic were grouped according to the NSCLC staging system as local, locally advanced, and metastatic stage. While 85 (12.3%) of the cases were in the local stage, the number of locally advanced cases was 240 (34.7%). The majority of the cases (366 patients / 53%), on the other hand, were in the metastatic stage.

The study also investigated the average survival times of the patients diagnosed with NSCLC based on the disease stage. The related results show that, while the mean survival time was found to be 31 (1-72) months in patients in the local period, it was 17 (1-72) months in the locally advanced group and only 9 (1-42) months in the metastatic period (Table 1).

The patients presented to our clinic were identified as patients at a limited stage and those at the disseminated stage based on the SCLC staging system. In the initial phase, while the number of the patients with SCLC at the limited stage was 73 (42%), 101 patients (58%) were diagnosed with one at the disseminated stage. While the average survival time of the patients with SCLC at the limited

stage was calculated to be 14 months, it was 8 months in those with one at the disseminated stage (Table 2).

Table 1. SCLC demographic and clinical characteristics

SCLC 174(%20)	
Gender	
Men	**158(90.8)**
Women	**16(9.2)**
Age (average)	**57.7±10.2**
Men	**57,9±9.9**
Women	**56,6±13.2**
Smoker	
Yes	**159(%91.4)**
Men	**152(%96.2)**
Women	**7(%43.7)**
No	**15(%8.6)**
Men	**6(%3.8)**
Women	**9(%56.3)**
Symptoms	
Cough	**101(%58)**
Haemoptysis	**35(%20.1)**
Chest Pain	**51(%29.3)**
Dyspnoea	**55(%31.6)**
Weight Loss	**64(%36.7)**
Stage	
Limited Disease	**73(%42)**
Disseminated Disease	**101(%58)**

Table 2. NSCLC demographic and clinical characteristics

NSCLC691(%80)	
Gender	
Men	**622(%90)**
Women	**69(%10)**
Age (average)	**59.8±10.8**
Men	**60.4±10.1**
Women	**55±13.7**
Smoker	
Yes	**587 (%85.2)**
Men	**577 (%93)**
Women	**10(%14,5)**
No	**104 (%14.8)**
Men	**45(%7)**
Women	**59(%85.5)**
Symptoms	
Cough	**413(%59.7)**
Haemoptysis	**173(%25)**
Chest Pain	**293(%42.4)**
Dyspnoea	**260(%37.6)**
Weight Loss	**206(%29.6)**
Stage	
Local	**85(%12.3)**
Locally advanced	**240(%34.7)**
Metastatic	**366(%53)**
Histopatologic sub-type	
Adenocancer	**193(%22)**
Squamous cancer	**242(%28)**
Others	**256(%30)**

Discussion

Although lung cancer cases are divided into subtypes histopathologically, SCLC has an aggressive clinical course, with a shorter doubling time and a much greater tendency for regional or distant metastases than other major lung cancer types. SCLC accounts for 14% of all lung cancers[7], a rate which is 16.1% in Turkey according to the cancer statistics for 2015. Of the 865 cases investigated in our study, 174 (20%) were diagnosed with SCLC, a rate which was slightly higher than the ones observed in previous research performed in our country and around the world.

Age, a factor effective in lung cancer development, is one of the most important determinants of risk. Research reports that lung cancer incidence increases with age and peaks in decades 6 and 7. A study conducted by Wells CK et al. reported a mean age of 61.2 years[8]. In a study conducted in our country, on the other hand, the mean age was found to be 58.4 years[9]. Another study performed in our country investigating 7303 cases with lung cancer reported that 90.5% of all cases were men, and the remaining 9.5% were women[10]. In our study, 90.2% of the cases were male and 9.8% female. These data are compatible with the overall data observed in our country.

Lung cancer risk in smokers is 24-36 times higher than non-smokers. Passive smoking, on the other hand, accounts for 3.5% of all cases. While the prevalence of smoking in developed countries is 20-40% in women and 30-40% in men, it is 2-10% and 40-60%, respectively, in developing countries[11]. In Turkey, on the other hand, evidence indicates a smoking prevalence of 24% in women and 63% in men. A study performed in our country on 7303 cases with lung cancer reports that 91.5% of the cases reported being a smoker[10]. The smoking rate varies according to the histopathological subgroup. In the present study, 91.4% of the cases were smokers, a result similar to the ones observed in past research in our country. On the other hand, 93.8% of the patients with squamous cell carcinoma were smokers. Our study results indicate that 72.5% of the patients with adenocarcinoma lung cancer, which is the histopathological subgroup likely to have the least relation with smoking, were smokers.

The most frequent symptom of lung cancer is cough. Previous research reports an incidence rate of cough between 50 and 75 % on average[12]. In the present study, 514 (59.4%) of the 864 cases presented to the clinic with cough, an incidence similar to the one observed in previous studies. On the other hand, 188 cases (%21.7) had hemoptysis, 315 (% 36.4) respiratory disorders, and 344 (% 39.7) chest pain. SCLC is one of the most aggressive tumours and has been grouped as a limited and disseminated disease since the possibility of surgical removal of the tumour is very low. Research reports that 60% of the patients had metastasis at the time of diagnosis, a rate that is consistent with the results observed in studies previously performed in our country[13]. In our study, 101 (58%) of the 174 SCLC cases already had metastasis at the date of diagnosis.

Since the symptoms are noticed, and the findings are detected late in NSCLC, the diagnosis is also established in the late period. The cases with NSCLC are mostly detected in advanced (Stage IV) or locally advanced stage (Stage IIIA and IIIB). Generally, 70% of the cases do not have the chance of surgery used as a radical treatment method at the time of diagnosis[14]. In our country, the cancer statistics for 2015 reveal that 14.8% of patients with NSCLC have been identified in the local stage. In our study, NSCLC was diagnosed in the late period, and the disease was already at the local stage

in 85 (12.3%) of the patients. While the studies conducted in our country in 2001 found an incidence of 16.9%, the statistics for 2015 show that it was the most common subtype with a rate of 47.1%. Adenocarcinoma accounted for 22% of the cases in our study. Since SCLC patients do not have a surgical chance, radiotherapy and chemotherapy are given limited disease periods. In the present study, the median survival time of the patients was 14 months. Metastasis was detected in 60% of the patients with SCLC at the time of diagnosis. The average survival time of the cases in our study was 8 months.

Although curative surgery is the only chance in cases with NSCLC at the local stage, very few lung cancer cases are diagnosed in the local stage. The average survival time of the patients diagnosed at the local stage in our study was 31 months. On the other hand, the mean survival time for locally advanced patients was 17 months, and it was 12 months for metastatic patients.

Conclusion

İn the present study we found a significant difference between the mean ages of the cases according to histopathological subtypes. Another result indicates that adenocarcinoma and SCLC emerged at an earlier age than cases with squamous cell cancer. Analysing smoking, one of the etiological factors of lung cancer, based on the gender of cases, showed significantly higher smoking behaviour in men than women. On the other hand, the smoking rate was significantly lower in cases with adenocarcinoma. Another result is that the most frequent smokers were those diagnosed with squamous cell cancer.

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ORIGINAL RESEARCH PAPER

Evaluation of Knowledge About HIV/Aids Patients Among Dental Students: Findings from Eastern Turkey*

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Zehra SUSGUN YILDIRIM[1a], Onur NACAKGEDIGI[2b], Candan AYDIN HOS[3c], Elif Pinar BAKIR[3d], Emrullah BAHSI[3e]**

[1]Faculty of Dentistry, Department of Restorative Dentistry, Cukurova University, Adana, Turkey.
[2]Department of Public Health Sciences, UC Davis School of Medicine, Davis, California, United States.
[3]Faculty of Dentistry, Department of Restorative Dentistry, Dicle University, Diyarbakir, Turkey.

Orcid ID: [a]0000-0002-1717-8214 [b]0000-0002-6347-8613 [c]0000-0002-6473-0905 [d]0000-0003-4011-5091 [e]0000-0001-7649-9459

Abstract

Objective: *It is important that all dentists should have sufficient knowledge of HIV/AIDS patients, and their attitude should meet professional expectations. The purpose of this study was to evaluate Dicle University Dentistry students' knowledge levels and attitudes about HIV/AIDS.*

Methods: *353 students (353/561X 100= 63%) students that were divided into two groups as clinical (4th and 5th grades) and preclinical (1st, 2nd and 3rd grade) cohorts. The assessment was done using questionnaires consisting of four main topics voluntarily between the 2016-2017 academic years. Data analysis was performed using SPSS version 21 (SPSS Inc., Chicago, USA). When applicable, the data were assessed by t-test and Pearson correlation coefficient.*

Results*: The overall response rate to the questionnaire was 62.9 percent. It was noted that 89.99% of students knew HIV/AIDS could infect dental workers while 95.42% were well aware of the mode of transmission of HIV/AIDS. Despite their awareness that HIV patients may infect them, they were poorly informed about the procedure of protection. Also, the information about the oral manifestations of the patient was limited.*

Conclusion: *This study showed that dental students' knowledge in the east part of Turkey about HIV infection and prevention was not adequate.*

Keywords: AIDS, Attitudes, Dental students, HIV, Knowledge.

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** Corresponding author: E-mail: susgunzehra@gmail.com

Introduction

HIV/AIDS (Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome) is transmitted by body fluids (blood, semen, vaginal secretions, breast milk) is a serious health problem in the world.[1] According to Progress Report 2016 of The World Health Organization (WHO), while the average 36.7 (34.0-39.8) million people infected with HIV are living in the world, 1.1 million people died due to this disease in only 2015. While more than 95% of all HIV-infected cases are seen in developing countries, 80% of cases are seen in sub-Saharan Africa, South and South-east Asia.[2]

In Turkey, following the first HIV (+) case reported in 1985, HIV/AIDS notification was put on the list of notifiable diseases. In 1986, the circular on the screening of all blood and blood products for HIV was put into action, followed by serological tests that have begun in 1987. In 1994, HIV/AIDS notifications were systematized, and in 1996 the National AIDS Commission was established. While 3 cases were reported in 1985, the case number has increased to 21.520 by 31 December 2018. According to the Ministry of Health statement, from 1 January to 31 December 2018, 3.356 newly diagnosed cases included 83,6% males, and most of them 25 - 29 years. It was also noted that 15,8% of cases were foreigners. When the route of transmission is examined, it is known that 49.4% of the cases are sexually transmitted, and 70.8% of the reported cases of sexual transmission are heterosexual.[3]

Dental treatment operations often include blood and saliva that may contain a variety of bloodborne pathogens and microorganisms such as HIV. All dental health care specialists and staff in oral and dental health services fall into the high-risk category in terms of infection. During dental treatment operations, for ensuring effective clinical management against infections, increasing awareness of dental students (as dentists of the future) about infection control and transmission routes of HIV-AIDS is very important.[4-6]

In 1988, the obligation to treat HIV (+) patients by all dentists was declared by the World Health Organization (WHO).[7] According to this obligation, dentists cannot legally refuse to take these patients. Ethical responsibility, lack of knowledge, and concern about being infected with HIV are the most likely reasons to refuse to treat patients infected with HIV.[8] Therefore, it is important that all dental professionals should have adequate knowledge of HIV infection and patient management.[9,10]

HIV virus leading the host vulnerable to diverse types of antigens from bacteria, virus, fungi and protozoa. People suffering from HIV / AIDS exhibit clinically oral manifestations during the early stages of the disease. Therefore, these signs of oral cavity are extremely important for the

presumption for HIV infection. In fact, dentist may be the first health professionals to suspect of positivity. People living with HIV virus may have oral pathognomonic manifestations of AIDS, including oral candidiasis, hairy leucoplakia, Kaposi sarcoma, linear gingival erythema, necrotizing ulcerative gingivitis, necrotizing ulcerative periodontitis, and non-Hodgkin lymphoma. However, the most commonly diagnosed oral lesions are oral candidiasis and hairy leucoplakia, which most important indicators of infection by HIV.[2,9,10]

The purpose of this study was to evaluate and to compare Dicle University Dentistry Faculty clinical and preclinical students' knowledge of HIV/AIDS and its transmission and attitudes about related issues such as infection control regulations, ethical obligations, willingness to treat HIV-positive patients, fear of contracting HIV, and perceptions about HIV-positive patients.

Materials and Methods

The Ethics Committee of Dicle University approved the study protocol with numbers 2015-34 and dated 30 December 2015. This cross-sectional survey was carried out in Faculty of Dentistry, Dicle University, Diyarbakir, between the 2016-2017 academic year. A modified version of a self-administered anonymous questionnaire was used. This tool has been successfully tested.[11,12]

The dental curriculum in Turkey is five years. The total population of Faculty of Dentistry is 561 persons as clinical (4^{th} and 5^{th} grades = 215 students) and preclinical (1^{st}, $2^{nd,}$ and 3^{rd} graders = 346 students). Because our questionnaire was held on a voluntary basis, only 353 students (199 preclinical and 154 clinical) of the total 561 students participated as a volunteer in the survey study. The study population's expected number was a minimum of 229 (N: 561, Confidence level: 95%, with confidence interval +/- 5). The response rate was 62,92 %.

The questionnaire occurred from four main topics.

Section 1; Demographic information, which includes age, gender, and school year.

Section 2; Knowledge of HIV infection, transmission routes, and adequacy of their knowledge about HIV-positive patients (Table 1). The eighteen knowledge questions were answered using the options "Correct" and "Incorrect". Each correct answer was scored 2 points. Maximum score 36 (18 x 2 = 36) was translated as 100 percent. Scores were classified into four groups according to the mean percentage of correct answers: less than 25 percent (weak), between 25 and 50 percent (moderate), between 50 and 75 percent (good), and more than 75 percent (excellent).

Table 1. *Dental students who gave correct responses to knowledge statements about HIV/AIDS, by percentage of total respondents.*

HIV/AIDS patients can contaminate dental workers. (True)	**89.99**
HIV/AIDS patients can be diagnosed with oral manifestations. (True)	**60.85**
HIV infection can be transmitted through; blood or tissue transplantation, needle stinging or open wounds, sexual intercourse and from mother to fetus and with mother's milk. (True)	**95.42**
Saliva can be a vehicle for the transmission of AIDS. (False)	**31.99**
HIV is a virus that is extremely weak. Virus within blood, sperm, and vaginal fluid can remain viable up to 1 hour in the external environment. (True)	**24.92**
For the destruction of the virus in the infected items, it is sufficient that wait within diluted sodium carbonate (1:10) for 10 minutes. (True)	**21.99**
Western blot is a definite test for HIV/AIDS diagnosis. (True)	**29.71**
ELISA is a screening test for HIV infection. (True)	**52.14**
Hepatitis B is more communicable than HIV/AIDS. (True)	**75.13**
Infection control methods for hepatitis B provide adequate protection against the transmission of HIV. (True)	**30.07**
There is a lot of HIV in the saliva of HIV/AIDS patients. (False)	**25.49**
CPR in patients with AIDS can transmit HIV infection. (False)	**29.42**
All sterilization methods have cidal effects against HIV. (True)	**54.88**
HIV can transmit through sweating; skin touching; someone else's towel; shaking hands; kissing cheeks; food and beverage; sharing dish; pool and toilet use; to share the same house; to wear someone else's clothes. (False)	**48.7**
HIV can be transmitted through aerosols by handpieces. (False)	**33.9**
If the needle of HIV / AIDS patient sank into my hand, it is beneficial that immediately washing my hands with soap and water at least 20s, then alcohol-riding. (True)	**55.14**

Section 3; Oral manifestations of HIV / AIDS patients (Table 2). The answer section of these fifteen questions was 'yes' or 'no'.

Table 2. Dental students' knowledge about oral manifestations of AIDS, by percentage of total respondents

Oral manifestations	**Percentage**
Oral candidiasis	48.43
Major aphthous	10.54
Kaposi's sarcoma	33.9
Acute necrotizing ulcerative gingivitis	23.01
Severe periodontitis	39.82
Cytomegalovirus	5.12
Gingivitis	34.47
Xerostomia	22.22
Hairy leukoplakia	27.35
Salivary gland infection	28.69
Herpes zoster	10.82
Herpes simplex	18.85
Lichen planus	20.17
Condyloma	7.97
Papilloma	11.96

Section 4; Behaviors related to the treatment of HIV-positive patients, legal responsibilities, and willingness to treatment were asked (Table 3). Answers were taken according to the Likert scale (strongly agree, agree, neutral, disagree, and strongly disagree). The maximum score is 85 (17x5=85). Scores were classified into three groups: more than 75 percent (positive), between 50 and 75 percent (passive), and less than 50 percent (negative).

In the literature, many researchers confirmed the validity of this questionnaire.[1,4,7,8,10,11] This questionnaire was translated to Turkish, because it is a major education language in Turkey. Data analysis was performed using SPSS version 21. When applicable, the data were assessed by *t*-test and Pearson correlation coefficient. A p-value of <0.05 was considered statistically significant with the level of 95 percent confidence.

Table 3. Responses of dental students to questions about their attitudes toward HIV/AIDS patients, by the percentage of total respondents Attitudes Statement

	Strongly Agree	Agree	Neutral	Disagree	Strongly Disagree
Treatment of HIV/AIDS patients means wasting national resources.	4.91	6.64	8.38	30.92	49.13
All dental patients should be considered potentially infectious.	35.36	43.47	6.37	11.3	3.47
If I know that my friend has HIV infection, I end the friendship.	4.04	5.78	16.47	34.1	39.59
Supporting HIV/AIDS patients improves community health.	41.9	41.04	9.24	4.91	2.89
Dentists with HIV/AIDS should not be allowed to treat patients.	8.4	13.33	20.57	31.3	26.37
HIV/AIDS patients should be treated in a separate ward.	34.39	42.77	10.11	9.82	2.89
A blood test should be taken for diagnosis of HIV infection in all dental patients.	23.69	43.93	19.07	11.84	1.44
I am morally responsible to treat HIV/AIDS patients.	32.36	43.64	14.73	6.06	3.17
HIV/AIDS patients can live with others in the same place.	19.94	47.39	18.78	10.69	3.17
I am not obligated to treat HIV/AIDS patients.	6.64	15.31	13.87	40.17	23.98
HIV/AIDS patients can lead a normal life.	26.08	51.59	12.46	8.4	1.44
I can safely treat HIV/AIDS patients.	17.34	39.59	32.65	8.09	2.31
I will treat HIV/AIDS patients.	20.8	44.5	25.14	5.78	3.75
My knowledge about infection control is enough to treat HIV/AIDS patients.	5.49	19.94	28.61	34.39	11.56
I worry about being infected with HIV by my patients.	15.02	51.44	19.65	10.98	2.89
I will do CPR if HIV/AIDS patients need it.	17.63	43.64	29.47	7.22	2.02
It is my right to know if my patients are infected by HIV.	66.86	25.58	4.36	2.61	0.58

Result

The overall response rate to the questionnaire was 62.9 % (353 from 561students). The results indicated that 56.4 % of the students were in preclinic. 43.6 % of the respondents of the surveys were female. The total mean knowledge score was 56.26 % (good knowledge), as 56.91 % for males and 55.44 % for females.

The knowledge scores of 5.3 %, 20.7 %, 62.6 %, and 11.4 % of the students were excellent, good, moderate, and weak, respectively. There was no statistically significant difference between male and female students (p-value > 0.05). The total rate of correct responses ranged from 2 to 28. The maximum value for the question "HIV infection can be transmitted through; blood or tissue transplantation, needle stinging or open wounds, sexual intercourse and from mother to fetus and with mother's milk" was 95.42 %; and the minimum value for the question "For the destruction of the virus in the infected items, it is sufficient to soak with diluted sodium carbonate (1:10) for 10 minutes" was 21.99 %.

Regarding oral manifestations, 48.43 % correctly identified oral candidiasis, 39.82 % severe periodontitis, and 34.47 % gingivitis (Table II). There were no significant differences between attitude scores by gender.

The results showed the overall mean attitude score was 50.91 % (passive attitudes; 50.95 % for males and 50.86 % for females), with the following distribution: 35.8 % positive, 61.8 % passive, and 2.6 % negative attitudes. In other words, only 2.6 % had professional attitudes. The attitudes score ranged from 0 to 80. The statement "It is my right to know if my patients are infected by HIV" obtained the higher positive attitude score, and the statement "Treatment of HIV/AIDS patients means wasting national resources" obtained the higher negative attitude score.

There were no significant differences (p-value > 0.05) between attitude scores by gender (Table III). According to the Pearson correlation coefficient, students with higher knowledge scores had more positive attitudes towards HIV/AIDS patients ($r=0.257$, $p<0.0005$). Our findings showed that there a significant correlation between the school year of the students and their level of basic knowledge ($r=0.368$, $p<0.0005$). It means that the more advanced students had a higher basic knowledge.

Discussion

The overall response number to this cross-sectional questionnaire was 353 dental students in our study, similar to the number of students participating in studies in a previous survey that was published by Alsamghan[12] (363 students), and Fotedar *et al.*[13], (164 students). 199 dental students in the preclinical years and 154 dental students in the clinical years responded to this survey.

Due to the increase in cases of HIV-infected patients, medical and dental care of these patients will increase[1,7,14], thus dental students and dentists will be required to improve their management ability of HIV.[15] The total mean knowledge (56.26 percent good) is less than the study of Sadeghi *et al.* (82.1 percent).[11] Also, Alsamghan reported a slightly higher score (62.7) than our findings.[12]

The findings showed that there a significant correlation between the school year of the students and their level of basic knowledge ($r=0.368$, $p<0.0005$). It means that the more advanced students had a higher basic knowledge.

In the current study, the statement "HIV infection can be transmitted through; blood or tissue transplantation, needle stinging or open wounds, sexual intercourse and from mother to fetus and with mother's milk" had the highest percentage of correct responses (95.42 percent). Sadeghi *et al.*[11], and Fotedar[13] also reported one of the highest percentages of correct responses to this knowledge question. Al- Salihy *et al.*[16] showed health care workers in Iraq have a good level of knowledge about vertical transmission of disease. Also, the statement "For the destruction of the virus in the infected items, it is sufficient that wait within diluted sodium carbonate (1:10) for 10 minutes" had the lowest percentage of correct responses (21.99 percent) by dental students. This indicated that students know that HIV / AIDS patients may contaminate themselves, and unfortunately, they do not know how to protect from it.

31.99 percent of students stated that "Saliva can be a mode for the transmission of AIDS"; 25.49 percent of students thought that "There is a lot of HIV in the saliva of infected patients". 29.42 percent believed that "CPR in patients with AIDS can transmit HIV infection". In the literature, there is no report of transmission with saliva in the clinic due to the infectivity of HIV is inhibited by glandular saliva function.[17] But almost half of the students believe that saliva may transmit the virus, and most of them do not know that it is a weak virus and sensitive to sterilization and disinfection processes. Therefore, most of the students (66.46%) worry about being infected with HIV by patients.

Oral manifestations are important indicators of some systemic diseases. One of them is HIV infection. Therefore, dentists have a critical responsibility to detect HIV infection. The most common oral manifestations are Kaposi's sarcoma, oral candidiasis, and oral hairy leukoplakia.[18-20] Relationships of HIV and oral candidiasis, severe periodontitis, and gingivitis were known by the students; 48.3 percent, 39.82 percent, 34.47 percent, respectively. Although it is one of the most common oral manifestations of the HIV, only 33.9 percent of the students were aware of the relationships between HIV and Kaposi's sarcoma. In this study, the dental students' knowledge of

oral manifestations of HIV infection is less compared to Iranian, Indian, and Saudi Arabia dental students' knowledge, as reported by Sadeghi *et al.*[11], Awad[12] and Fotedar *at el.*[13].

In our study, the overall attitude score was 50.91 percent, which is comparable to the study reported by Sadeghi *et al*. (57.4 percent)[11] and Fotedar *et al*. (65.6)[13]; however, it was less than the results of Seacat *et al.*[21] (81.1 percent). According to the results of Albujeer *et al.*[22], the level of attitude of Iraqi dentistry students was 21.4%, which was also intermediate, and none of them occupied the "good" attitude category. Al- Salihy *et al.*[16] also showed the same result among Iraqi health care workers. This result was well below the data of our study.

In the current study, 77.16% of students stated that "HIV/AIDS patients should be treated at a separate ward"; 56.93 percent of students stated that "I can safely treat HIV/AIDS patients". 65.3 percent responded that "I will treat HIV/AIDS patients" in this study, but Sadeghi *et al*. (11) reported only 11.6 percent and one previous study.[23] However, at Albujeer *et al*.' s[22] study; the appropriate attitude rates to given the questions by Iraq dentistry students respectively are; 89% "Treatment of HIV/AIDS patients requires special dental clinics", 33% "One can safely treat HIV/AIDS patients", and 50% "I will be treating HIV/AIDS patients for elective treatment". According to these results, about half of Iraq dentistry students stated that they would treat HIV/AIDS patients, but they said that separate clinics are needed because they think they cannot safely treat HIV/AIDS patients. The current students, too, are afraid of cross-infection, they prefer to treat HIV/AIDS patients in a separate place; but most of them (65.3) are more willing to treat them.

In this study, 78.83% of students stated that each patient should be considered potentially infectious in this survey. This result was less than the results reported by Sadeghi *et al.*[11] (65.7 percent); although these findings are comparable to Fotedar *et al.*[13] (about one-third of the students). Some HIV/AIDS patients hide their illness from dental professionals due to fear of rejection of dental care, so this result is acceptable.[11] According to this statement, the Centers for Disease Control and Prevention declared that standard infection control preventions must be strictly followed with every patient for infection control.[24]

In this study, 21.95 % of the students stated that "I am not obligated to treat HIV/AIDS patients," which is less than the results of Sadeghi *et al*. (49.7 percent).[11] In 1988, the obligation to treat HIV-positive patients by all dentists was declared by the World Health Organization (WHO).[7] According to this obligation, dentists cannot legally refuse to take these patients. Also, 76 percent of the students stated that "I am morally responsible to treat HIV/AIDS patients". In this context, students

are aware of the ethical and moral responsibility of treating these patients; therefore, they only need to know more about the transmission of the disease, prevention methods, and oral manifestations.

In this survey, it was understood that students with higher knowledge scores had significantly more positive attitudes towards HIV/AIDS patients by Pearson correlation coefficient ($r=0.257$, $p<0.0005$). The findings of the present study were in line with the studies performed by several investigators who found that higher knowledge scores about HIV/AIDS among students were significantly associated with a more positive attitude to treat HIV-infected patients.[11,16,25] However, a previous study reported that there is no correlation between knowledge and attitude scores about HIV infection among students.[26] it was observed that there was no clear correlation between knowledge of HIV infection and the education year of the students. The expectation from this result was higher knowledge in the clinical group than preclinical group. This result was different than most of the other previous studies.[11,13,23] In our study, the reasons for this situation may be due to Turkey have a conservative society, and emotional reactions could play a significant role when answered the questionnaire.

Conclusion

This study showed that the knowledge of Eastern Turkey's dental students about HIV infection and prevention was not high. Especially, lack of some basic information such as Kaposi's sarcoma and transmission routes of HIV were some of the significant findings.

According to these findings regarding HIV-infected patients' management, they need to complete their knowledge and improve their attitudes. For example, students are well aware of how the HIV virus is transmitted but lacks knowledge of cleaning from contact surfaces. Also, lecturers should improve the dental school curriculum to prepare them for future dentists about HIV/AIDS patient management. Because this study showed that students with higher knowledge scores had more positive attitudes towards HIV/AIDS patients. The current study population did not represent the entire country. Fortunately, Diyarbakir is a developing and receiving heavily immigration city. For better results of knowledge and attitudes towards HIV/AIDS of dental students, similar further studies are needed in other dental schools in Turkey.

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Declaration of Interest

The authors have no conflicts of interest relevant to this article.

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ORIGINAL RESEARCH PAPER

Evaluation of Cancer and Non-Cancer Patients Receiving Palliative Care Service in Terms of Hospitalization Times and Overall Survival During Hospitalization

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Ziya KALKAN[1a*], Senar EBİNÇ[1b], Tuğba TEZER KALKAN[2c], Zuhat URAKÇI[1d], Zeynep ORUÇ[1e]

1. Department of Medical Oncology, Dicle University Medical Faculty, Diyarbakır, Turkey.

2. University of Health Scıences Diyarbakır Gazi Yasargil Training and Research Hospital Department of Internal Medicine, Diyarbakır, Turkey.

Orcid ID: [a]0000-0001-7858-8180 [b]0000-0002-0878-6525 [c]0000-0002-5971-998X [d]0000-0003-3878-988X [e]0000-0002-7931-2941

Abstract

Objective: *In the last 20 years, palliative care has gained a place within the health system worldwide. Our aim is to review the demographic characteristics of patients hospitalized in palliative care centers, to investigate the factors influencing hospitalization times of patients with cancer and non-cancer diagnoses and the median in-hospital survival.*

Results: *A total of 428 patients, comprising 237 (55.4%) males and 191 (44.6%) females were included in the study. Median patient age was 75 (18-105) years. In terms of hospitalization times, there were no significant differences between genders (p=0.79) and diagnoses (malignant/non-malignant); however, there was a statistically significant difference between survival statuses (died/discharged) and patients who died had longer hospitalization times (16 days versus 12 days) (p=0.008). When age, gender, hospitalization type and diagnosis were compared with regard to median in-hospital survival in multivariate analysis, the diagnosis (non-malignant/malignant) was an independent factor indicating median in-hospital survival (HR:2.08, 95% CI:(1.47-2.94), p<0.001).*

Conclusion: *Among the patients receiving inpatient treatment in the palliative care center, those who died had a longer hospitalization time compared with those who were discharged. Also, patients with a malignant diagnosis had a shorter overall survival during hospitalization compared with those with non-malignant disease.*

Keywords: Palliative care, cancer, hospitalization time, survival

* Corresponding author: E-mail: zyklkn7221@gmail.com

Introduction

Palliative care (PC) is an approach that aims to effectively prevent or correct the life-quality, physical and psychosocial problems of patients who encountered problems stemming from life-threatening diseases and their relatives through early detection.[1] The goal of PC is to help the patient live as well as possible in this period before their death, increase the quality of the death process and, particularly, to provide the best care during death. This process is the most difficult and intense aspect of palliative care in cancer patients.[2] While PC is a form of basic care that should be offered since the diagnosis for the quality of life, it is needed more for terminal stage cancer patients during the final days of life.[3] Cancer was reported to be the second most common cause of death after cardiovascular diseases in Turkey and worldwide. Every year, 7.9 million individuals die because of cancer and it is estimated that 12 million individuals will lose their lives in the year 2030.[4] Reviewing the literature, there exist numerous factors that influence hospitalization times and median in-hospital survival in palliative care centers (PCC) such as decubitus ulcers, cerebrovascular disease, diabetes mellitus, hypertension, nutritional state, systemic infections and malignancy. Our aim in this study is to review the demographic characteristics of the patients hospitalized in a tertiary PCC, to investigate the factors influencing hospitalization times and the median in-hospital survival.

Materials and Methods

Patients aged 18 years or older who received inpatient supportive treatment in the palliative care service of Health Sciences University, Gazi Yasargil Training and Research Hospital between August 2018-July 2019 were included in the study. In this retrospective, descriptive study, last hospitalizations of patients with repetitive hospitalizations were considered. Sociodemographic characteristics, hospitalization diagnoses, hospitalization times, discharge statuses, hospitalization dates, discharge dates and dates of death of the 428 patients who met the inclusion criteria were obtained from patient records. The study was approved by the Health Sciences University, Gazi Yasargil Training and Research Hospital Ethics Committee (05.03.2021-692). All of the ethical considerations had been strictly followed in accordance with the Helsinki declaration.

Data were analyzed using Statistical Package for the Social Sciences 18.0 (SPSS Inc, Chicago, IL, USA). As descriptive statistics; number of units (n), percentage (%), mean ± standard deviation ($\bar{x}\pm ss$), minimum value (min), maximum value (max), median were provided. Descriptive statistics were used in order to evaluate patient characteristics and the frequency of parameters, Student's t-

test for normally distributed variables, Mann-Whitney-U test for the analysis of non-parametric variables. Survival analysis (OS) was conducted using Kaplan-Meier analysis. The Cox regression test was used for multivariate analyses. A p-value below 0.05 was considered statistically significant.

Results

A total of 428 patients receiving inpatient treatment in our palliative care center, comprising 237 (55.4%) males and 191 (44.6%) females were included in the study. Median patient age was 75 (18-105) years [77 (18-105) years in females, 74 (25-95) years in males]. There were 207 (48.4%) patients hospitalized due to a non-malignant disease diagnosis and 221 (51.6%) patients hospitalized due to malignant disease. At hospitalization, median age of patients with non-malignant disease was 79 (27-101) years, median age of patients with malignant disease was 70 (18-105) years. The diagnoses of the 211 patients with malignant disease and their frequencies were as follows: lung cancer 43 (10%), colorectal cancer 40(9.3%), gastric cancer 35(8.2%), pancreatic cancer 21(4.9%). Other cancer frequencies are listed in Table 1.

Of the patients, 344 (80.4%) were hospitalized from the emergency service polyclinic and 84 (19.6%) from normal polyclinics. Of the patients, 265 (61.9%) were discharged, 163 (38.1%) died during hospitalization.

Median hospitalization time was 9 (1-78) days in males and 8(1-110) days in females. Hospitalization times were 9 days (1-78) in those with non-malignant disease, 7 (1-110) days in those with malignant disease. Hospitalization times in those with malignant diseases were median 6 (1-52) days in lung cancer, median 9 (1-81) days in colorectal cancer, median 5 (1-64) days in gastric cancer, median 7 (1-53) days in pancreatic cancer, median 6 (2-49) days in hepatobiliary cancer, median 10 (3-50) days in malignant neoplasm of the brain, median 12.5 (6-38) days in head-neck cancers, median 11.5 (4-38) days in mesothelioma, median 12.5 days (6-45) in renal cell cancer, median 11.5 (2-84) in breast cancer, median 10 (3-39) days in bladder cancer, median 6 (1-17) days in prostate cancer, median 2 (1-7) days in skin cancers, median 30 (29-42) days in ovarian cancer, median 82 (54-110) days in cervical cancer, median 9 (1-25) days in other cancers.

Median hospitalization times were 8 (1-84) days for patients hospitalized from the emergency service, 10 (1-110) days for patients hospitalized from the polyclinic. Discharged patients had a median hospitalization time of 8 (1-81) days, patients who died during hospitalization had a median hospitalization time of 10 (1-110) days. Basic characteristics of the patients are specified in Table 1.

When the patients were compared with regard to hospitalization times based on gender (male/female) and diagnosis (malignant/non-malignant), there were no significant differences across the groups. Male patients had a median hospitalization time of 13 days and females had a median hospitalization time of 14 days (p=0.79). Patients with a malignant diagnosis had a median hospitalization time of 13 days and patients with a non-malignant diagnosis had a median hospitalization time of 14 days (p=0.29). When those who were discharged during hospitalization and patients who died during hospitalization were compared, the hospitalization time of those who died was found to be higher at a statistically significant level (16 days versus 12 days) (p=0.008).

When the survival times of the patients during hospitalization were evaluated according to clinical parameters; no statistically significant differences were found based on age (p=0.49), gender (p=0.53) and hospitalization type (emergency department/polyclinic) (p=0.74). Median survival time during hospitalization was 34 days in patients hospitalized due to non-malignant disease and 20 days in patients hospitalized due to malignant disease, with a statistically significant difference [Hazard ratio (HR):1.94, 95% CI: 1.40-2.68, p<0.001].

When the patients were compared in Cox regression analysis with regard to the median survival time during hospitalization based on age, gender, diagnosis, type of hospitalization; only the primary diagnosis (malignant/ non-malignant) was found to be an independent prognostic factor indicating median in-hospital survival [HR:2.08, 95% CI: 1.47-2.94, p<0.001]. Univariate and multivariate analysis results are specified in Table 2.

Table1*: Baseline characteristics of patients*

	n (range vs %)	**Length of stay (median days/rance)**
	n=428	
Age	75 (18-105)	
Female	77 (18-105)	
Male	74 (25-95)	
Gender		
Female	191 (44,6)	8 (1-110)
Male	237 (55,4)	9 (1-78)
Diagnosis		
Non-malignant diseases	207 (48,4)	9 (1-78)
Malignant diseases	221 (51,6)	7 (1-110)
Lung cancer	43 (10)	6 (1-52)
Colorectal cancer	40 (9,3)	9 (1-81)
Stomach cancer	35 (8,2)	5 (1-64)
Pancreatic cancer	21 (4,9)	7 (1-53)
Hepatobiliary cancer	16 (3,7)	6 (2-49)
Brain malign neoplasia	11 (2,6)	10 (3-50)
Head and neck cancer	8 (1,9)	12,5 (6-38)
Mesothelioma	6 (1,4)	11,5 (4-38)
Renal cell cancer	6 (1,4)	12,5 (6-45)
Breast cancer	6 (1,4)	11,5 (2-84)
Bladder cancer	5 (1,2)	10 (3-39)
Prostate cancer	5 (1,2)	6 (1-17)
Skin cancer	3 (0,7)	2 (1-7)
Ovarian cancer	3 (0,7)	30 (29-42)
Cervical cancer	2 (0,5)	82 (54-110)
Other cancers	11 (2,6)	9 (1-25)
Hospitalization Type		
Emergency department	344 (80,4)	8 (1-84)
Polyclinic	84 (19,6)	10 (1-110)
Final situation		
Discharged	265 (61,9)	8 (1-81)
Died	163 (38,1)	10 (1-110)

Table 2: Factors affecting survival during hospitalization - results of univariate and multivariate analysis

	Univariate Analysis			Multivariate Analysis		
	HR	**95% CI**	**P value**	**HR**	**95% CI**	**P value**
Age	0.99	0.98-1.00	0.49	1.00	0.99-1.01	0.41
Gender	0.90	0.66-1.23	0.53	0.82	0.60-1.13	0.23
Type of hospitalization (Emergency department /Polyclinic)	1.06	0.73-1.55	0.74	0.95	0.65-1.39	0.82
Diagnosis (Non-malignant /Malignant)	1.94	1.40-2.68	**<0.001**	2.08	1.47-2.94	**<0.001**

Discussion and Conclusion

In our study, the median age of the 428 patients hospitalized in a tertiary palliative care center over a 1-year period was determined to be 75; the median age of our patients with non-malignant disease was 79 years and the median age of the patients with malignant disease was 70 years. In a study performed by Munch and colleagues, the mean age was found to be 60 years.[5] In a study conducted by Senel Ozalp and colleagues on cancer patients, the mean age of the patients was reported as 61 years.[6] In a similar study done by Yuruyen and colleagues, the mean age of the patients was reported as 71,0±15.8 years.[7] The mean age was 74.55±16.71 years in a study by H. Cinar and colleagues[8], the mean age of the patients diagnosed with cancer in a palliative care study performed by Lee HS. and colleagues was 62 years.[9] The age of the patients in our study was similar to some studies in the literature and differed from some others.

In a study by Ozalp and colleagues, the patients hospitalized in the PCC the most commonly were patients diagnosed with cancer and within this patient group, patients with gastrointestinal cancers were found to be the most frequent.[6] Similarly, in a study conducted by Menezes VH. and colleagues with 502 patients, patients diagnosed with cancer were hospitalized in the PCC most commonly.[10] In a study by Uysal and colleagues, the three cancers hospitalized the most commonly in the PCC were gastrointestinal tract cancers, lung cancer and hepatobiliary/pancreatic cancers.[11] In our study, the patients hospitalized the most commonly in the PCC were patients diagnosed with cancer. In particular, patients diagnosed with gastrointestinal cancer ranked first, in compliance with the literature. The likely cause of this situation is that patients with gastrointestinal cancer frequently show nutritional problems, which we reason increases the need for palliative care.

In our study, hospitalization times were median 10 (mean 13 days) days in cancer patients and median 9 (mean 14.6 days) days in non-cancer patients. In a study performed by Yuruyen and colleagues, the mean hospitalization time was determined to be 15.4±15.7 days.[7] In a different study, the mean duration of hospitalization in the PCC was 27.2 days, while in another study, this duration was found as 14.50 ± 12.03 days.[12,13] Reviewing the literature, the hospitalization times of the inpatients in PCCs show variability and this is because the hospitalization time is influenced by a multitude of factors. Although studies investigating the factors that influence hospitalization times in PCCs are scarce, hospitalization times of patients diagnosed with cancer were shorter in two studies performed in Turkey.[14,7] In the research by Allman RM. and colleagues, cancer appeared to be a negative factor for hospitalization in the PCC, while cerebrovascular disease, hypertension and diabetes mellitus were determined to be positive factors. With regard to conditions such as advanced decubitus ulcers, it was described that these could be treated once detected, however, that they certainly influenced the hospitalization time.[15] Again, in the research by Dincer, factors such as age, hypoxic brain, cancer, infection were proven to affect the hospitalization times of inpatients in the PCC.[16]

Meanwhile, in our study, patients with non-malignant diagnoses had a longer hospitalization time compared with patients with malignant diagnoses; however, there was no statistically significant difference between these two groups. When evaluated in terms of survival status (discharged/died), patients who died had longer hospitalization times than discharged patients, with statistical significance [(16 vs 12 days), (p=0.008)]. We reason that this may be because patients at a terminal stage wished to spend their end-of-life period in the hospital. In our study, factors that influenced the duration of hospitalization in the palliative care service were evaluated; no statistically significant differences in hospitalization times were determined across genders (female/male), diagnoses (malignant/ non-malignant), hospitalization types (emergency department/polyclinic).

The limitations of our study include the heterogeneity of the patient population, presence of comorbidities, differences across the patients' diagnoses.

In conclusion; upon evaluating the hospitalization times of patients who received inpatient care in a palliative care center and their survival times during hospitalization, we determined that the patients who died in the hospital had longer hospitalization times and that the median survival time during hospitalization was shorter in patients with malignant diagnoses when compared with patients with non-malignant diagnoses.

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CASE REPORT

Touraine–Solente-Gole Syndrome: A Case Report

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Ayşe Ünal ENGİNAR

Ordu State Hospital, Rheumatology, Ordu, Turkey

ORCID: 0000-0003-0273-6268

Abstract:

Touraine–Solente-Gole Syndrome (TSGS) or pachydermoperiostosis is a rare disorder characterized by pachydermia, periostosis and digital clubbing. It is a clinical variant of primary hypertrophic osteoarthropathy, for which the etiopathogenesis is not fully known. It is seen more often in males and I have not found a female case in the literature. The case presented here is of a female patient who presented with digital clubbing in the hands and feet, periostosis, cutis verticis gyrate, and arthralgia.

Keywords: Touraine Solente Gole syndrome, Pachydermoperiostosis, Hypertrophic osteoarthropathy.

Corresponding author: E-mail: ftrdrayseenginar @gmail.com

Introduction

Touraine–Solente-Gole Syndrome (TSGS) is a rare disorder characterized by pachydermia, periostosis and digital clubbing [1]. The male-female ratio has been reported to be 9:1 [2], and estimated prevalence is approximately 0.16% [3]. TSGS may be idiopathic or inherited. Although autosomal dominant inheritance with incomplete penetration and variable expression has been confirmed, both autosomal recessive and X-linked inheritance have been suggested [1]. It was initially described by Friedreich [4] in1868 and then by Touraine, Solente and Gole [5] in 1935, who recognized its familial nature. Although the etiopathogenesis is not fully known, the 15-hydroxyprostaglandin dehydrogenase gene and the solute carrier organic anion transporter family member 2A1 have been found to be associated with TSGS [6,7]. It is more common in men, and I have not found a female case in the literature. The case presented here is a female patient who presented with arthralgia and was diagnosed with TSGS.

Case

A 51 year old female presented at the polyclinic with complaints of pain in the hands and feet. The complaints had started approximately 30 years ago and joint pains had increased in the last 4-5 years. There was nothing remarkable in the patient's own history or family history. There was nothing determined in the rheumatological investigation. There was no psoriasis. In the physical examination of the patient, deep folds known as cutis verticis gyrata were observed in the scalp (Figure 1).

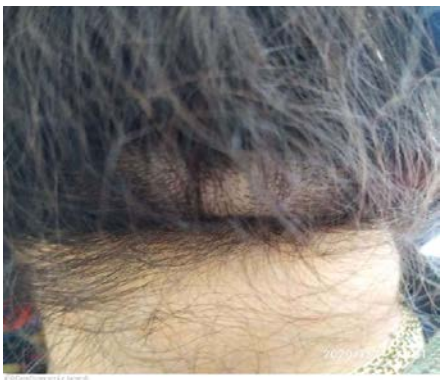

Figure 1. Cutis verticis gyrata

There was mild pachydermia on the forehead. Widening and clubbing was present in the distal of the fingers and toes (Figure 2,3). Joint range of motion was full. There was sensitivity in the joints of the hands and feet but there was no arthritis.

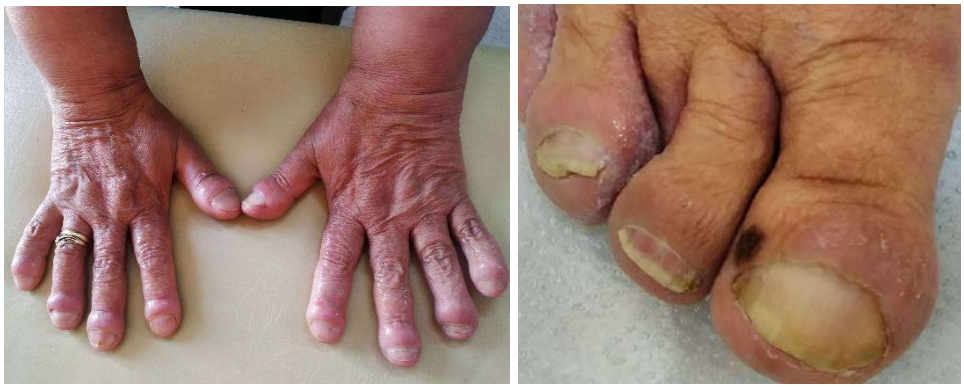

Figure 2,3. Clubbing was present in the distal of the fingers and toes

The blood work up including hemoglobin, hematocrit, red blood cell, white blood cell and blood biochemistry (glucose, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, gamma-glutamyl transferase, serum creatinine, urea) results were in the normal ranges. Erythrocyte sedimentation rate (ESR): 25 mm/h and C-reactive protein (CRP): 3 mg/L(normal <5 mg/L). P-ANCA, C-ANCA, ANA, RF, anti-CCP, cryoglobulins were all negative. Serum iron, ferritin, TSH, T4 (free), growth hormone, immunoglobulins (IgM, IgG, IgA), and complements (C3, C4) were normal. Serology results were negative for viral hepatitis (VDRL, TPHA, HBsAg, anti-HIV, anti-hepatitis C virus), TORCH, antibodies against streptococcus, Epstein-Barr virus and the Write test for brucellosis. Urinalysis revealed no changes.

Abdominal ultrasound, electrocardiogram and chest X-ray examinations revealed no pathology. The plain radiographs of the wrists and feet showed significant metaphyseal and diaphyseal periosteal reactions. Increased cortical thickening was seen in the hand bones and in the tibia (Figure 4,5).

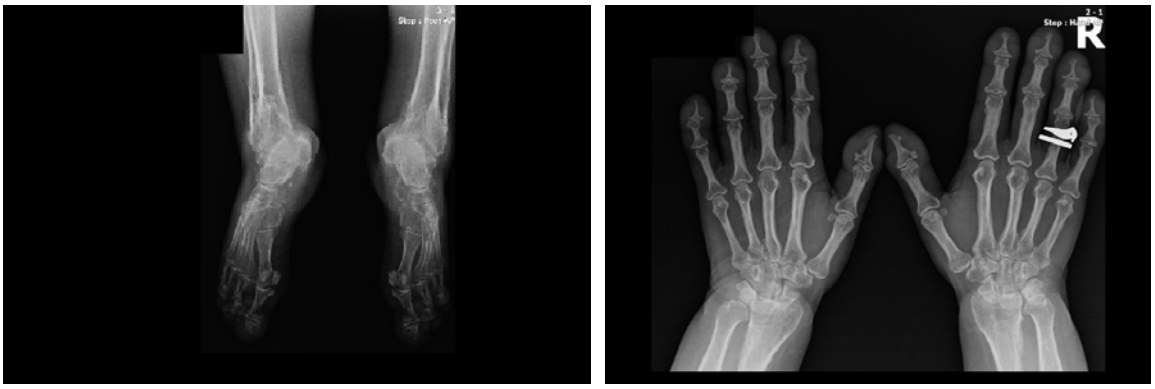

Figure 4,5. Radiographs of the wrists and feet showed periosteal reactions and increased cortical thickening.

A diagnosis of TSGS was made, and treatment was started of non-steroidal anti-inflammatory drugs (NSAID) and colchicine. The pain decreased significantly during follow-up. Written consent was obtained from the patient

Discussion

TSGS is an infrequently seen disease. A previous study over a 17-year period showed TSGS at the rate of 0.03% in rheumatismal diseases in patients presenting at a university hospital [8]. It includes 3-5% of all patients with hypertrophic osteoarthritis, it affects males more than females and phenotypes are more severe in males [9]. There are family clusters in 25%-38% of cases [3]. No differences have been reported between ethnicities [10]. Although the pathogenesis is not fully known, there may be a mutation in the gene encoding the 15-hydroxyprostaglandin dehydrogenase enzyme in TSGS patients, and this leads to an increase in prostaglandin E2 (PGE2) in the blood. By mimicking osteoblast and osteoclast activity, PGE2 can lead to acro-osteolysis and periosteal bone formation [11].

Clinically, the disease is defined in 3 different forms [5].

1. Complete; pachydermia, clubbing and periostitis together
2. Incomplete; skeletal changes are present but no pachydermia
3. Fruste; pachydermia is strongly evident, and mild skeletal changes are seen

The diagnostic criteria of TSGS are classified as major (pachydermia, periostosis, digital clubbing), or minor (hyperhidrosis, cutis verticis gyrate, gastric ulcer, blepharoptosis, arthralgia, joint effusion, column-like legs, edema, seborrhea, acne, hyperhidrosis, flushing) [5].

In the current case, there was clubbing in the fingers and toes, periostosis, cutis verticis gyrate, arthralgia and mild pachydermia. When pachydermia is severe, there may be a lion face appearance [10]. In this patient, the pachydermia was significant on the scalp but mild on the forehead. There is no specific laboratory test for TSGS [10].

Bulbous deformities at the distal fingers, abnormal nail curvature, and soft-tissue swelling can be present on radiographs. Periostosis seen on imaging is characteristic of hypertrophic osteoarthropathy. The shafts of tubular bones are especially affected. Involvement of the epiphysis is more frequent in primary hypertrophic osteoarthropathy [12]. The histopathological findings of pachydermia include dermal edema, mucin deposition, elastic fiber degeneration, dermal fibrosis and adnexal hyperplasia [13].

Secondary hypertrophic osteoarthropathy, thyroid acropachy, acromegaly and syphilitic periostitis are included in the differential diagnosis. There is no specific treatment. NSAIDs, steroids,

pamidronate, risedronate, colchicine, and tamoxifen can be used in treatment [14]. Infliximab has been reported to be of partial benefit in resistant bone pain and arthritis [15]. Surgical interventions are rarely applied [10].

In conclusion, although TSGS is a benign disease, differentiation from secondary causes such as malignancies is important.

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CASE REPORT

A Rare Abnormal Male Karyotype with 46,X,DER(Y)(YQTER→P11.3::2Q2.1→QTER),DEL(2)(2PTER→11.3:)

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Diclehan ORAL[1a], Mahmut BALKAN[1b], Selahattin TEKEŞ[1c], İlyas YÜCEL[1d], Gülbahar Güzel ERDAL[1e], Mahir BINICI[1f], Fikriye Fulya KAVAK[2g*]

[1]Dicle University, Faculty of Medicine, Department of Medical Biology and Genetics, Diyarbakır, Turkey
[2]Izmir Katip Celebi University, Faculty of Medicine, Department of Medical Biology and Genetics, İzmir, Turkey

Orcid ID: [a]0000-0002-0074-0602 [b]0000-0002-0589-9399 [c]0000-0001-6405-1112 [d]0000-0002-4446-0469 [e]0000-0003-0138-6622 [f]0000-0003-1039-9361 [g]0000-0003-0278-7188

Abstract

Objective: *Structural chromosomal abnormalities such as translocation in males and y deletions in the molecular missile cause infertility and related azoospermia. The aim of this study was to perform the karyotype analysis of a 51-year-old male patient who was referred to Dicle University Faculty of Medicine, Department of Medical Biology and Genetics for karyotype analysis due to primary infertility.*

Methods: *Chromosome analysis was performed in peripheral blood culture by applying conventional cytogenetic method and GTG banding technique.*

Results: *Chromosome analysis a rare abnormal karyotype with 46, X, der(Y) (Yqter→p11.3::2q2.1→qter), del(2pte2q 11.3:) chromosomal structure was observed. In thıs study we report a case with balanced translocation between chromosomes 2 and Y.*

Conclusion: *The causes leading to male infertility may be later, and some of them are of genetic origin. While chromosomal abnormalities are seen in 0.5% of the healthy population, this rate increases to 5.8% in infertile men, so it is recommended to genetically investigate all individuals with azoospermia in semen analysis.*

Key Words: balanced translocation, chromosome anomalies, infertility.

* Corresponding author: E-mail: fikriyefulyakavak@gmail.com

Introduction

The rate of numerical and structural chromosomal anomalies in men who have been diagnosed with semen anomalies due to infertility, such as azoospermia and oligospermia, was approximately 20%. The majority of chromosome anomalies associated with infertility include sex chromosomes 1. Among the structural changes, the most common ones are translocations and are seen at 1/500 frequencies 2. The absence of pregnancy despite a regular and unprotected relationship for one year is defined as infertility and occurs in 15% of couples 3. Genetic and non-genetic factors are involved in the etiology of infertility. Half of the cases of infertility are caused by male reproductive insufficiency . Genetic disorders play an important role in the etiology of azoospermic and severe oligospermic patients. When compared to the normal population (0.5%), chromosome anomalies (5.8%) are much higher in infertile men (5%) 4. The most common chromosome anomaly in the presence of azoospermia severe male infertility is 47, XXY (10-20%), but 45, X monosomia and Y chromosome structural anomalies are also seen 4. These stuation are significantly higher in azoospermic men (10-15%) than oligospermic men (5-7%) 5. When the number of sperms drops, the incidence of anomalies increases. Autosomal anomalies (3%) are the most common in the oligospermic group, while sex chromosome anomalies (12.6%) are predominant in azoospermic men 6.

Translocations; is one of the common chromosomal arrangements.Translocations have seen on gonosomes are frequently seen in azoospermic, oligospermic patients. Translocations are divided into two as balanced and unbalanced according to the decrease and increase in the rate of genetic material.When there is loss or gain in the genetic material, translocation it is considered unbalanced. However, if there is no gain or loss in the genetic material, the translocation is considered to be balanced 7,8. Balanced translocations are the most common structural chromosomal anomalies in humans, with an incidence of 1 in 1175 newborns 9. Balanced translocation carriers generally have normal phenotype. However, unbalanced gametes may appear as a result of the pairing between derivative chromosomes and their normal homologs. Genetic disorders associated with azoospermia and severe oligospermia can cause infertility in the male by creating problems in the sperm formation stage or in the sperm transport stage. Y-chromosome microdeletions capable of isolated spermatogenesis defect, cystic fibrosis gene mutations causing congenital vas deferens agenesis, sperm anomalies that disrupt testicular function, genetic factors that directly affect sperm functions are known related to male infertility 10.

Materials and Methods

Case

A 51-year-old male patient was referred to our Dicle University Medical Faculty Medical Biology and Genetics Department for karyotype analysis due to primary infertility from the outer center. The patient has a history of failure to have a child with microinjection therapy.. He was 176 tall and weighed 88 kg. He had the appearance of light gynecomastia. Azospermia was observed as a result of semen analysis of the patient.In ultrasonographic examination, both testicles are in normal size and consistency. The right testicle volume was approximately 22 ml and the left testicle volume was 9 ml. In sperm analysis, no spermatozoa was observed. Blood analysis laboratory values; follicle-stimulating hormone level (FSH) is 20.58 mlU / ml (normal range, 1.5-12.4 mlU / ml) and is high. Plasma luteinizing hormone level (LH) is 7.18 mlU / ml (normal range, 1.7-8.6 mlU / ml) and testosterone hormone level is 3.64 ng / ml (normal range, 2.18-9.05 ng / ml). Glucose level is 207 mg/dl (normal range,70-109 mg/dl).High insulin level was compatible with diabetes mellitus. Growth hormone level was low. The consent of the patient was obtained for this study to be a case.

Cytogenetic analysis

Chromosome analysis was performed in peripheral blood culture by applying conventional cytogenetic method and GTG banding technique. In the chromosome analysis, 50 metaphase plates were examined and karyotypes of 30 metaphase plates were made and reported according to an international system for human cytogenetic nomenclature (ISCN) 2005 (Shaffer & Tommerup, 2005).

In the cytogenetic examination of the case, it was observed that there was 46, X, der (Y) (Yqter → p11.3 :: 2q2.1 → qter), del (2) (2pter →2q11.3:) chromosome structure.

Polymerase chain reaction (PCR) method was applied to detect microdeletions in the Y chromosome. No deletion was found in the patient whose AZFa, AZFb and AZFc gene regions were examined.

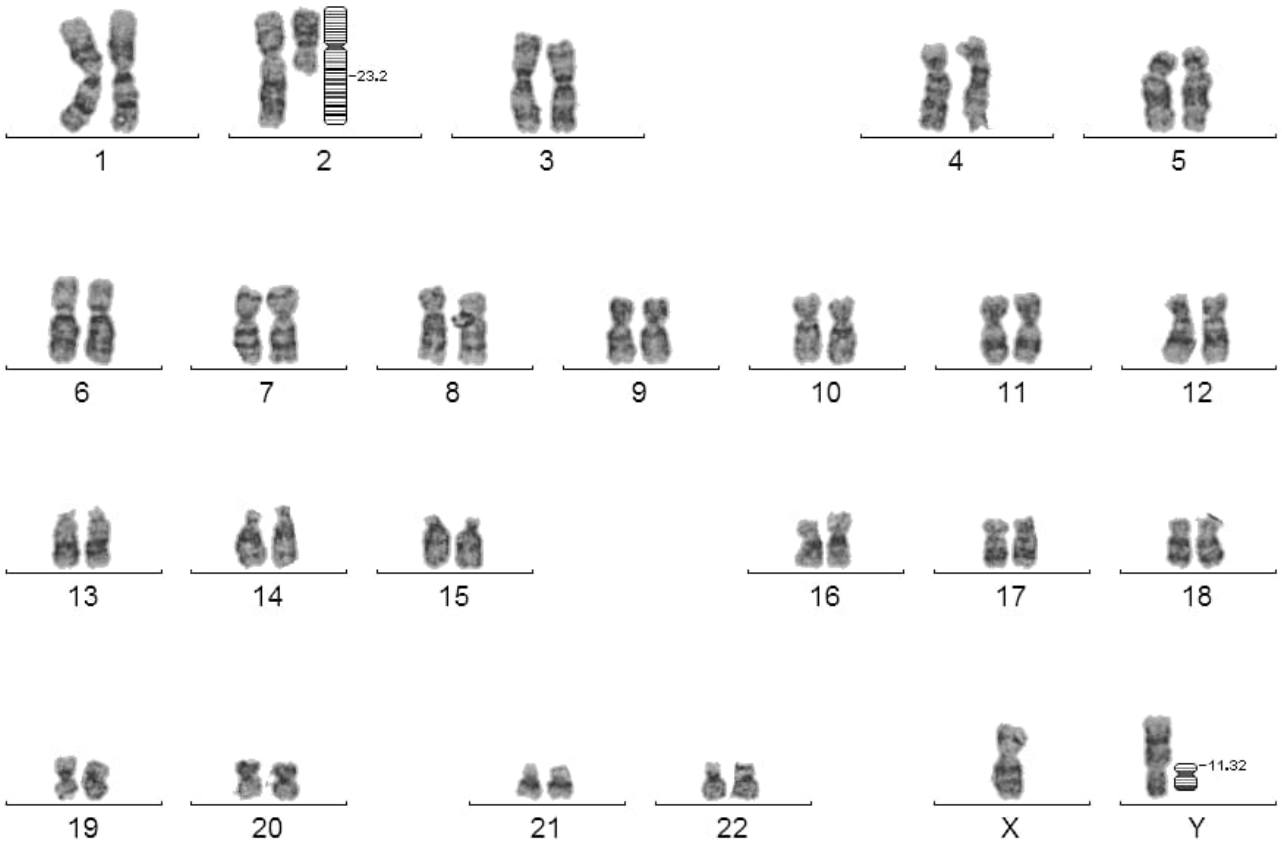

Figure 1. 46,X,der(Y)(Yqter→p11.3::2q2.1→qter), del (2) (2pter→.11.3:)

Discussion

The reasons leading to male infertility may be later, and some are of genetic origin. While chromosome anomalies are observed in 0.5% of healthy population, this rate rises to 5.8% in infertile men, so it is recommended to investigate all individuals with azoospermia in semen analysis 11. Balanced translocation was the cause of infertility in our patient who had azoospermia in semen analysis.

Infertility based on sperm factor can be treated with intracytoplasmic sperm injection (ICSI) technique. However, before ICSI, every couple should be informed about the risk of genetic damage, existing infertility and other changing phenotypic symptoms present to the child. A fetus with unstable chromosomal abnormality resulting in miscarriage was detected in our patient who was treated with ICSI. Balanced chromosal irregularity constitutes an important group among prenatal cytogenetic diagnostic indications, since the risk of fetus with unbalanced chromosal irregularity is 10-15% in parents with this irregularity 12. Sperm anoploidies are frequently seen in

azoospermic patients. Therefore, the risk of transmission of karyotype anomaly is high in pregnancies with ICSI 13. For this reason, amniocentesis or chorionic villus sampling should be recommended for prenatal genetic diagnosis in the genetic counseling given to patients with a numerical or structural chromosomal anomaly prior to ICSI treatment.

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