Pankreasın kistik neoplazileri: Tanı ve tedavi alternatifleri.

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ÖZET

Amaç: Gelişen radyolojik görüntüleme yöntemleri ve abdominal bölgeye yapılan inceleme sayısının artması ile pankreas kistik neoplazileri daha çok tanınmaya başlamıştır. Hem müsinöz kist adenomlar hem de intraduktal papiller müsinöz neoplaziler değişik oranlarda malignite potansiyeli taşıyan lezyonlardır. Benign, premalign ve malign lezyonların tanınması tedaviye yön verir. Bu yazıda, 21 hastanın klinik verileri eşliğinde pankreas kistik neoplazilerinde tanı, tedavi ve takip uygulamaları ile bunların sonuçları tartışılmıştır.
Hastalar ve Yöntem: Kliniğimizde 2000-2008 yılları arasında histolojik ve/veya radyolojik olarak 'pankreas kistik neoplazi' tanısı alan 21 hasta retrospektif olarak incelendi. Hastaların yaş, cinsiyet, tümör özellikleri, klinik ve radyolojik bulguları, doku tanısı için uygulanan girişimler, ek malignite varlığı, takip ve tedavi şekilleri kaydedildi. Malign transformasyon ya da nüks gelişen hastalarda bunun zamanı, tümör tipi ve yerleşimi saptandı.
Bulgular: Onu erkek, 11'i bayan olan hastaların, ortalama yaşı 55.6 (30-77) olarak saptandı. Primer lezyon 12 hastada pankreas başında, 5 hastada gövdede ve 4 hastada kuyrukta yerleşmişti. Ortalama kist boyutu 29,5 mm (10-60 mm) olarak saptandı. Altı hastada tanı başka sebeplerle yapılan tetkikler sırasında insidental olarak konulmuştu. Onyedi hastaya takip kararı verilirken, 4 hastaya tanıdan sonra rezeksiyon uygulanmıştı. Takip kararı alınan 17 hastanın ikisinde, ortalama 15,8 aylık süre içinde malignite geliştiği saptandı.
Sonuç: Pankreasın kistik neoplazilerinin tedavisi konusunda literatürde görüş birliği yoktur. Bu hastaların tedavileri planlanırken, klinik ve radyolojik malignite kriterleri hasta bazında değerlendirilmeli ve cerrahi riskler de göz önünde tutularak karar verilmelidir. Radyolojik olarak şüphede kalınan ve yüksek cerrahi risk taşıyan hastalarda mevcut tanı yöntemlerinin

kombine kullanımı ile tanı netleştirilmeye çalışılmalıdır. Cerrahi girişime karar verilen hastalarda total pankreatektomi en uygun seçim gibi görünmektedir.

Anahtar kelimeler: pankreas, kistik neoplazm, seröz kistadenom, müsinöz kistadenom

Cystic neoplasms of pancreas: Diagnosis and treatment options.

ABSTRACT

Purpose: Cystic neoplasms of pancreas (CNP) are frequently diagnosed with improved radiological imaging. Mucinous cystadenomas and intraductal mucinous papillary neoplasms have malignancy potential. Our aim was to share our experience about the diagnosis, treatment and outcomes during follow-up of patients with CNP.
Patients and Methods: Twenty-one patients with histological and/or radiological diagnosis of CNP between 2000-2008 were evaluated according to patient and tumor characteristics, diagnostic procedures, radiological and clinical findings, retrospectively. Malignant transformation and/or recurrence were also evaluated in accordance with tumor type and localization.
Results: Male/female ratio was 0.9 (10/11). Mean age was 55.6 (range, 30-77). Head of pancreas was the most common site. Mean cyst size was 29,5 mm (range, 10-60 mm). Six patients were diagnosed incidentally during abdominal evaluations for other reasons. Median follow up was 15.8 months. Four patients had been operated and the others were followed-up. Two patients in follow-up group had malign transformation within 21 and 25 months.
Conclusion: CNPs are most frequent in fifth decade and have no gender predominance. It is common in pancreatic head. Malign transformation is rare. Treatment should be indivudialized by taking into account clinical / radiological malignancy criteria and surgical risks. Total pancreatectomy might be an option in selected patients.

Key words: pancreas, cystic neoplasm, serous cystadenoma, musinous cystadenoma

Introduction

The prognosis of pancreatic adenocarcinoma is generally poor. Further investigation is needed for premalign lesions and high risk groups [1]. Improved radiological technics, especially in abdominal imaging and abdominal interventions contribute to detect cystic pancreatic lesions even in asymptomatic patients. Most of the pancreatic cystic lesions are benign inflammatory pseudocysts. Clinical and/or radiological diagnosis of pseudocysts is usually not difficult. Cystic neoplasms of the pancreas (CNP) may represent as benign, borderline or malign (in-situ/ invasive) tumors clinically. CNP are serous, mucinous and intraductal papillary mucinous neoplasms (IPMN) which constitute 10-15% of pancreatic cysts [2-4]. They are all epithelial tumors that originate from different cells with various biological behaviours, and this may affect their clinical outcomes. Mucinous cystic adenomas (MCA) and IPMNs have malign transformation risks at different degrees, however serous cyst adenomas (SCA) usually have no malignant transformation risk. Histopathological pattern of the lesion has great importance in treatment plan. Diagnosis, follow-up and treatment options and, even surgical procedures (i.e. total or partial pancreatectomy) may differ between centers. Lesions with malignant transformation risk should be followed-up closely or resected after diagnosis.

In this paper, the characteristics of 21 patients with CNP were reviewed under the light of current literature.

Material and Method

Twenty-one patients with histological and/or radiological diagnosis of CNP treated between 2000 and 2008 were evaluated retrospectively. The patients in whom pseudocyst was not delineated were excluded.

Patients' and tumor characteristics such as age, gender, clinical and/or radiological findings, localization and proven histopathologic and cytologic diognosis were recorded. The patients with malignant transformation and/or relapse were also recorded. Tumor types and time to recurrence were also recorded in patients with recurrence. The current status of the patients was obtained either by phone calls or hospital records.

Results

Ten patients were male and 11 were female. Median age was 56 (30-77). Six patients (28.5%) had CNP diagnosis incidentally during abdominal radiological evaluations for other reasons. Fifty seven percent (n=12) of the patients had CNP located in the head, 23.8% (n=5) in the corpus and the rest in the tail of the pancreas. Only one patient had more than one cystic lesions. Cyst size was also measured during radiological imagings, and mean cyst size was 29,5 mm (range, 10-60 mm). It was possible to make a differantial diagnosis between serous and mucinous cysts in 71.4% (n=15) of the patients, but the others could only be described as 'cystic neoplasia of pancreas' radiologically. Nine patients were followed-up without biopsy. Radiologically guided biopsy was performed for twelve patients, including six patients who had not-specified radiological lesion definition. Five patients who had been reported to have radiologically suspicious findings for malignancy such as septation, pancreatic and bile ductus dilatation, calcification and nodularity were also applied percutaneous biopsy, but only one of them had proven to be malignant. Abdominal pain, nausea and loss of appetite were the most common symptoms among symptomatic patients.

Seventeen patients were followed-up radiologically. Two of them, one MCA and one IPMN, were found to have malignant transformation within a period of 21 and 25 months. Both had neither radiological nor cytological malignancy suspicion criteria at initial diagnosis period. The other fifteen patients were not seen to have clinical evidence of malignancy during the follow up period of 15.8 months.

Four patients treated surgically had their lesions located in the head of the pancreas and were resected with pyloris preserving subtotal pancreatectomy. In one of these patients, a nodularity on cyst wall had been reported and fine needle aspiration biopsy (FNAB) had revealed atypical cells. At final pathology report, this patient was reported to have invasive adenocarcinoma on the background of IPMN and intraepithelial neoplasia in another area. One another patient with peripancreatic lymphadenopathy had been diagnosed as MCA with FNAB. This patient was also reported to have carcinoma in situ on the background of MCA. There was no recurrence in these two patients during the follow up period. Although, remaining two symptomatic patients did not have any radiological or cytological malignancy criteria, they were operated for pain and vomiting control and they had no malignancy reported on final pathological evaluation.

Patient characteristics according to their diagnosis are summarized in Table 1.

Discussion

Fifty percent of CNP is MCA, and they often occur in the corpus and tail of the pancreas [5,6]. MCAs are defined as large cysts with thick wall septates which are unrelated with ductal system according to World Health Organization (WHO) classification [7]. Cystic component is musinous and more viscous than others. However, SCAs consist of 30-35% of CNP and half of them occur in the head of pancreas [8,9]. They do not contain musin. They are stained with Periodic acid-Schiff (PAS) while they are not stained with cytokeratins AE1 or AE3 on immunohistochemical staining. Remaining 10-15% of CNP is IPMN, and half of them localize in the head of pancreas. In WHO classification, they are described as large cysts with columnar epithelium, especially in the main pancreatic ductus [10].

Serous cystic tumors are more common in the fifth decade whereas IPMNs are common in the sixth and seventh decades. However, musinous tumors generally occur between 35 and 90 years of age [11]. In our study, most of the patients are in the fifth decade. Tumor growth rate might affect the time to diagnose CNPs. Slower growth rate may delay the clinical diagnosis since CNPs are slow growing tumors, and it may take years to clinically diagnose a CNP. However, tumors can be diagnosed at smaller sizes with the development of beter imaging techniques. The tumors with smaller sizes even in asymptomatic patients may be easily diagnosed radiologically and this may contribute to earlier diagnosis of CNP in younger patients. Actually, mean cyst size in our patients was found to be smaller than the reported in the literaure [12]. The relationship between cyst size and malignant transformation is controversial [7,13-15]. Besides, it was reported that malignancy risk had been higher in the patients older than 70 years [16].

Most of the patients with SCA are asymptomatic, but some of them might have mild symptoms such as pain due to large mass [3,14]. The patients with MCA may have also non-specific symptoms such as abdominal pain, loss of weight, jaundice or palpable mass. The patients with IPMNs seem to be more prone to have symptoms. In spite of being non-patognomonic, it was pointed out that those with jaundice, weight loss and loss of appetite might have higher rates of malignancy [17-18]. The patients may also be asymptomatic even in the presence of malignancy. Fernandez et al. reported that 18% of asymptomatic patients had early stage cancer whereas 42% had malignancy potential and 40% had benign lesions [2]. In our series, five of six asymptomatic patients were diagnosed to have SCA. Abdominal pain and weight loss were leading symptoms in four patients with malignancy.

The differential diagnosis can be made with radiological (i.e. computurized tomography, magnetic resonance imaging) imaging or cytological (i.e. FNAB) examination. Combination of radiological tecniques may increase the rate of accurate diagnosis in expense of increased cost. FNAB can be applied to the patients in whom the lesions were difficult to differentiate or had malignancy criteria on radiological imaging. In our study, only one of five patients with radiological malignancy criteria had cytologically proven malignant disease. In our series, the sensitivity and specificity of FNAB was 70% and 80%, respectively. This sensitivity rate was similar to the rates reported in literature, but specifity rate was lower [2]. The accuracy rates of endosonography guided biopsy were also reported to be quite higher [8].

Follow-up with conservative treatment is usually recommended for asymptomatic SCAs since malignant transformation is extremely rare. But, symptomatic patients should have resections[8]. Resection is generally not suggested for asymptomatic, patients who have MCA and IPMN, but the treatment is quite controversial. Malignant transformation rate is 6-60% in resected mucinous cystic tumors while it is 13-20% in the lesions smaller than 3 cm [16,19-21]. Five year survival rate is 80-100% in resected benign mucinous cystic tumors and 27-100% in resected invasive mucinous cystic tumors [4,22]. Partial pancreatic resections seems to be an appropriate option in pancreatic mucinous cystic tumors according to tumor localization size. Close follow-up of asymptomatic patients without any radiological malignancy criteria in tumors less than 3 cm is generally preferred [23]. However, quite higher rates of surgical mortality (3-4%) and morbidity (58%) rates even in experienced centers and over-treatment risk for a benign lesion may justify the disagreement of other authors [19,22,24]. Additionally, adenocarcinomas may arise anywhere in the pancreas independent of the localization of these lesions [25]. Nevertheless, relapse rate was reported to be 7-22% in patients who had resections for invasive IPMN [19]. Tada et al. reported 7 invasive cancers in 197 patients (mean age 72.1) who were followed-up for 42 months with tumor markers and clinically indicated additional imaging [25]. They suggested to follow-up of these patients.

In conclusion, treatment of pancreatic cystic neoplasms is quite controversial in the literature. Treatment should be individualized with clinical and radiological malignancy criteria and surgical risks should be taken into account. The combination of diagnostic procedures should be used in whom radiological imaging is unclear and surgical risk is high. Total pancreatectomy seems to be appropriate surgical option for those who were decided to be operated.

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Table.1 Patients' characteristics

	Sex (Male/ female)	Mean Age	Mean tumor size	Localization	Symptomatic	RMC	FNAB	Surgery	Malign Transformation
SCA (n:9)	4/5	51	17.8 mm	Head: 4 Corpus:4 Tail:1	Yes: 4	Yes:1	Yes:3	Yes:1	Yes:0
					No: 5	No:8	No:6	No:8	No:9
MCA (n:7)	4/3	59.5	30.4 mm	Head:5 Corpus:1 Tail:1	Yes: 6	Yes:4	Yes:5	Yes:1	Yes:1
					No:1	No:3	No:2	No:6	No:6
IPMN (n:5)	2/3	58.4	36.3 mm	Head:4 Corpus:0 Tail:1	Yes:5	Yes:3	Yes:4	Yes:2	Yes:1
					No:0	No:2	No:1	No:3	No:4

SCA: serous cystic adenoma,

MCA: mucinous cystic adenoma

IPMN: ıntraductal papillary mucinous neoplasia

RMC: radiologic malignancy criteria

FNAB: fine needle aspiration biopsy