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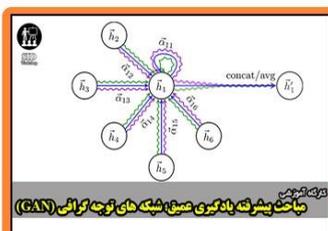


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کارگاه های آموزشی مرکز اطلاعات علمی جهاد دانشگاهی



کارگاه آنلاین آشنایی با پایگاه های اطلاعات علمی بین المللی و ترند های جستجو



مباحث پیشرفته یادگیری عمیق؛ شبکه های توجه گرافی (Graph Attention Networks)



کارگاه آنلاین مقاله نویسی IEEE و ISI ویژه فنی و مهندسی

Review of the Findings of Endosonography and Fine Needle Aspiration in Patients with Cystic Tumors of Pancreas

Bijan Shahbazkhani¹, Amin Shafaroudi², Mohammad Jafar Farahvash¹, Hossein Forootan³, Reza Taslimi⁴, Najmeh Aletaha⁴, Amir Hossein Shahbazkhani⁵, Amir Mirbagheri³

¹ Associate Professor, Department of Gastroenterology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

² Gastroenterologist, Department of Gastroenterology, Guilan University of Medical Sciences, Langroud, Iran

³ Professor, Department of Gastroenterology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

⁴ Assistant Professor, Department of Gastroenterology, Imam Khomeini Hospital, Tehran University of Medical Sciences, Tehran, Iran

⁵ Researcher, Tehran University of Medical Science, Tehran, Iran

ABSTRACT

Background:

Improvements in imaging techniques has led to an increase in the number of diagnosed pancreatic cysts. Although most of the detected cases are benign, a significant percentage of them are malignant or are potentially malignant. Currently, endosonography, and analysis of cyst morphology, fine needle aspiration (FNA) of the cyst contents, and measurement of the amylase and carcinoembryonic antigen (CEA) levels of the aspirated fluid are the common methods used for evaluating such lesions (80% accuracy in the final diagnosis). We have used these same techniques to analyze cystic lesions of the pancreas, in two referring centers in Iran.

Materials and Methods:

This is a descriptive case series study. In addition to demographic information and findings of the cystic morphology, we determined the cytology of the centrifuged sediments of cystic fluid aspirations, and the amylase and CEA levels of the fluid.

Results:

Sixty eight patients were included in the study with an average age of 51 years. 68% of the participants were female (n=46). Analysis of the lesions was performed based on the cytology findings as well as the other results (CEA, amylase, cyst morphology, and history of pancreatitis). The patients who were diagnosed as having pseudocysts were the youngest group, with an average age of 41 years, and those with cystic adenocarcinoma were the oldest group, with an average age of 62 years. The most common types of lesions were pseudocysts (n=18, 26.5%), mucinous cystic neoplasms (n=11, 16%), serous cyst adenomas (n=10, 14.7%), intraductal papillary mucinous neoplasms (n=9, 13.2%), and cystic adenocarcinoma (n=9, 13.2%). The most common location of cysts was the head of pancreas (n=25, 35.2%). Excluding the neuroendocrine tumors, all other types of lesions were more common in women than men. Septation in the cysts was observed in cystic adenocarcinomas, serous cystadenomas, and intraductal papillary mucinous neoplasms (IPMNs). Lesions smaller than 2 cm were found most frequently in IPMNs, endocrine tumors, and simple tumors whilst pseudocysts were all greater than 2 cm in maximum diameter.

Conclusion:

47% of the patients in this study had malignant or premalignant lesions, which despite being asymptomatic, they needed follow-up imaging or surgery. Endosonography played an important role in the diagnosis of the cystic tumors of the pancreas. Diagnosis of premalignant lesions and providing appropriate treatment increase patients' life expectancy. Diagnosis of benign cysts, leads to fewer unnecessary surgeries.

Keywords: Mucinous cystic neoplasm, Serous cystadenoma, Intraductal papillary mucinous neoplasm, Fine needle aspiration

please cite this paper as:

Shahbazkhani B, Shafaroudi A, Farahvash MJ, Forootan H, Taslimi R, Aletaha N, Shahbazkhani AH, Mirbagheri A. Review of the Findings of Endosonography and Fine Needle Aspiration in Patients with Cystic Tumors of Pancreas in Two Hospitals. *Govaresh* 2016;21: 48-54.

Corresponding author:

Amin Shafaroudi, MD
Rasoul Akram Hospital, Rasht, Iran
Tel: + 98 1342527779
E-mail: shafaroudiamin@yahoo.com
Received: 07 Jan. 2016
Edited: 16 Mar. 2016
Accepted: 17 Mar. 2016

INTRODUCTION

Cystic lesions are important group of pancreatic tumors. The prevalence of these lesions has increased from 1% of all pancreatic tumors in early studies, to 29% of tumors in more recent studies (1,2). This increase is mainly due to advances in diagnostic devices. As these lesions are increasingly diagnosed, more attention has

been paid to the assessment and treatment of them.

The WHO classification, based on histology, has divided cystic lesions of the pancreas into two main groups: mucinous and non-mucinous(3). Mucinous cystic neoplasms (MCNs) and intraductal papillary mucinous neoplasms (IPMNs) are parts of the mucinous tumor group and serous cystadenoma (SCA) is a non-mucinous tumor. Based on the degree of epithelial dysplasia, mucinous cysts are further divided into benign, borderline, and malignant lesions. Other pancreatic cystic tumors include those that are non-neoplastic (pseudocysts, and congenital simple cysts), as well as those that are caused by solid tumor degeneration (pseudopapillary tumor, cystic neuroendocrine tumors, and cystic ductal adenocarcinoma).

Although most of these cysts are asymptomatic, and are found by chance in imaging studies unrelated to the pancreas, a significant number of them are malignant, or premalignant - with the high potential to become malignant and require surgery or other types of treatment. The conventional approach to non-neoplastic cystic lesions (pseudocysts, and congenital simple cysts) and non-mucinous tumors is routine follow-ups, especially when the patient is asymptomatic. However, in cases of mucinous lesions, because of their high malignancy potential, the clinical approach is based on the balance between the chances of malignancy and surgical risk (3).

Currently, endosonography is a precise diagnostic tool used to evaluate pancreatic lesions detected on routine scanning. By providing a detailed image of the tumor, this technique provides the clinician with a description of the type of lesion, as well as its relationship to the pancreatic ducts. Using the fine needle aspiration (FNA) technique, a biopsy can be taken from any part of the lesion that is more accessible, and the cyst contents can also be aspirated in order to analyze the tumor markers and the aspirated cells. The pancreas is located in the retroperitoneal space, and a computed tomography (CT)-guide biopsy or a surgical biopsy is difficult and may cause the spread of the malignant cells. The accuracy of endosonographic reports in differentiation of benign, borderline, and malignant cystic lesions in reported series varies between 40-93% (4,5). The sensitivity of FNA in combination with endosonography in the

evaluation of cystic pancreatic tumors is 22-95% (6-9). The diagnosis and classification of these lesions are performed by using the cyst fluid analysis (7,9-13).

Definitive diagnosis of cystic lesions, without surgical resection and pathological analysis, is not possible. Cytology is often non-diagnostic, due to the low cellularity of the aspirated fluid (14). CEA with a cut-off greater than 192 ng/mL has 79% accuracy in differentiating mucinous from non-mucinous lesions (73% sensitivity, 84% specificity) (14,15). CEA level in cyst fluid is more accurate than lesion's morphology obtained by endosonography or cytology in differentiating between mucinous and non-mucinous lesions. Different combinations of morphological studies, cytological studies, and CEA evaluation do not enhance diagnostic accuracy compared with CEA evaluation alone (14). By using a combination of morphology, cytology and CEA evaluations, a sensitivity of 91% has been reported, however it does not have a high specificity (14). In one study, CEA levels higher than 30 ng/mL had a positive predictive value (PPV) of 84% in determining mucinous cysts(15). A CEA less than 30 ng/mL with an amylase level greater than 8500 U/L can identify up to 91% of pseudocysts, while amylase levels less than 350 U/L correlate with SCA up to 85% (15). CEA levels less than 4 ng/mL have 100% sensitivity and 93% specificity for SCA (15). To differentiate various mucinous lesions, a high amylase level is more likely indicating IPMN in comparison with MCN. In other studies, in addition to the parameters discussed, the viscosity of the aspirated fluid, along with other tumor markers such as CA19-9, and DNA analyzing is used to differentiate lesions. Analyzing DNA and loss of heterozygosity, especially K-ras mutations, have been very helpful in the diagnosis of malignant cystic lesions (3).

Collection of the results of the evaluations of the cystic lesions of the pancreas in Iran is a novel step. By evaluating the type of lesion, the age and sex distribution, the presence or absence of malignancy, measurements of the amylase and CEA levels of the cyst fluid, as well as the other morphological characters of tumors, we provide beneficial information for practitioners.

Table 1: Patients' demographics and amylase/CEA levels based on the type of pancreatic cysts

Type of Tumor	Number of Cases		Average age of the participants (years)	Sex		Average size of tumors (mm)	Standard deviation	CEA (ng/mL)	Amylase (units/L)
	N	%		Female	Male				
SCA	10	14.7	56	6	4	34.2	20.42	8.6	38.7
IPMN	9	13.2	51	5	4	28.6	16.90	214	15386
MCN	11	16.2	55	8	3	38	11.04	946	8.1
Pseudo cyst	18	26.5	41	12	6	63	33.93	1.8	35952
Cystic adenocarcinoma	9	13.2	67	6	3	32.7	9.79	1982	133.4
Cystic endocrine tumor	3	4.4	39	1	2	42	30.11	9.7	160.3
Simple cysts	8	11.8	53	8	0	35	17.94	31.3	53

MATERIALS AND METHODS

This is a descriptive case series study. Data from all patients with cystic lesions of the pancreas referring to the endoscopy center of the Imam Khomeini Hospital during 2010-11 and Pars Hospital of Tehran during 2009-11 for endosonography and FNA, by two expert gastroenterologists, were analyzed. The patients' cystic lesions had been detected using sonography or CT, all of which were greater than 10 mm. Endosonography was performed using a linear Olympus UC 24OP-AL5, and FNA was performed using a number 22 (13mm) Wilson-Cook needle.

Prior to the endosonography, coagulation studies had been performed for all the patients. While they were monitored on a pulse oximeter, 5 mg intravenous midazolam was administered as a sedative. The patients were monitored for two hours after the procedure and were then released if no complications occurred. Anyone with an INR (international normalized ratio) >1.5, a platelet count <50000 per microliter acute pancreatitis, pertinent anatomical stricture/obstruction, or anyone with comorbidities that served as a barrier/contraindication to endosonography were excluded from the study. FNA was performed for all the patients while receiving antibiotics. Antibiotic use was continued for an additional 48 hours after FNA. Morphological features such as the location and size of the cyst, as well as the presence of septation in the cyst, communication with the main pancreatic duct, and calcification on the cyst wall or in central parts of cyst were all noted on the endosonography.

The patients' demographic and clinical information, in addition to the endosonography and FNA results

were all analyzed using SPSS software version 18. Quantitative variables were expressed in domains as the mean value \pm standard deviation, and qualitative variables were expressed as frequencies (percentages). Exact Fisher test, and chi square t-Tests were used to evaluate statistical differences among the variables and a p value <0.05 was considered as statistically significant.

Histological data were only available for a few of our patients who had undergone surgical resection. Therefore, except for cases whose cytology results of the aspirated fluid was diagnostic (cystic adenocarcinoma, cystic endocrine tumor, and simple cysts), other diagnoses are not definite and are based on the history of pancreatitis, cyst morphology, and the results of the amylase and CEA levels in the aspirated fluid. Diagnostic criteria for the pseudocysts were a history of pancreatitis, radiological evidence of inflammatory changes in the pancreas, as well as high amylase (>8500 U/L) and low CEA (<30 ng/mL) levels in the cyst fluid. Most patients with mucinous tumors (IPMN and MCN), had CEA >192 ng/mL and a proportional endoscopic image. Three IPMN cases had CEA levels of 132, 80, and 40 ng/mL. But high amylase levels and their grape-like multilocular shape and location in the pancreatic head in two cases were indicative of IPMN. There were two cases of MCN with CEA levels of 180, and 32 ng/mL that had also cyst morphology consistent with MCN (one with wall thickness, the other with peripheral calcification). All cases of SCA had an amylase level <350 U/L and CEA levels <6.5 ng/mL. In these lesions, a multi-microcystic image was observed (Table 1).

Table 2: Cyst location and other morphological characteristics of the different types of pancreatic cysts

Type of Tumor	Location of cysts				Septum presence		Size		Cyst wall thickness (>5mm)		Classification		Communication with main pancreatic duct	
	Head	Neck	Body	Tail	n	%	<2cm	>2cm	n	%	Central	Periphera	n	%
SCA	2	2	4	3	7	70	2	8	0	0	2	0	1	10
IPMN	4	1	2	2	6	67	3	6	1	11	0	0	2	22
MCN	6	0	2	3	5	45	1	10	5	45	0	1	1	9
Pseudo cyst	2	1	7	8	3	17	0	18	0	0	0	0	0	0
Cystic adenocarcinoma	6	1	4	0	7	78	1	8	2	22	0	1	1	11
Cystic endocrine tumor	1	0	2	0	0	0	1	2	1	33	0	0	0	0
Simple cysts	4	2	2	0	0	0	2	6	1	12	0	0	0	0

RESULT

Data from 68 patients were included and analyzed in this study. The average age was 51 years, and 68% of the patients (n=46) were women. A patient with SCA developed infection secondary to FNA, which was subsequently resolved by using antibiotics.

The patients with pseudocysts were the youngest group of the study population with an average age of 41 years, whilst those with cystic adenocarcinoma were the oldest, with an average age of 62 years. The youngest patient was a 13 years old girl with a simple cyst, and the oldest patient was an 82 years old man with cystic adenocarcinoma. Excluding the neuroendocrine tumors, all other types of lesions were more common in women than men. All the simple cysts were also observed in the female participants.

The most common types of lesions were pseudocysts (n=18, 26.5%), MCN (n=11, 16.2%), SCA (n=10, 14.7%), IPMN (n=9, 13.2%), cystic adenocarcinoma (n=9, 13.2%), simple cysts (n=8, 11.8%), and cystic endocrine tumors (n=3, 4.4%). The most common location of cysts was in the head (n=25, 35.2%), and in the body (n=23, 32.4%) of the pancreas. In IPMN, MCN, cystic adenocarcinomas, and simple cysts, the lesions were commonly seen in the pancreatic head, while pseudocysts were most commonly seen in the body or tail of the pancreas. Although SCA was observed in all the three locations, most cases were in the pancreatic body (Table 2).

Twenty eight cysts (41.2%), had internal septations, most of which were seen in the cystic adenocarcinomas, SCAs, and IPMNs. Simple cysts

and endocrine tumors had no septum. Four cysts (5.9%) had calcification (50% central and 50% peripheral). In five cysts (7.5%), communication with pancreatic duct was seen, most of which were IPMNs. Fifty eight (85%) cysts were larger than 2 cm. The largest average sizes were 63 mm, 42 mm, and 38 mm, which were seen in the pseudocyst, endocrine tumor, and MCN groups respectively. The smallest average size (28.5 mm) belonged to the IPMN group. Lesions smaller than 2 cm were primarily seen in IPMNs, endocrine tumors, and simple cysts, while pseudocysts were all greater than 2 cm.

Cyst wall thickness was most common in MCNs and cystic adenocarcinomas (>5mm thickness). None of the pseudocysts had wall thickness. Amylase levels in IPMNs and pseudocysts, as well as CEA levels in IPMNs, MCNs, and cystic adenocarcinomas were very high, which were significant indicators used for the diagnosis.

DISCUSSION

To our knowledge, this is the first study analyzing the endosonography and FNA results of patients with cystic pancreatic lesions in Iran. Forty seven percent of lesions were malignant, or potentially malignant, while 53% were benign and with no malignant potential (pseudocysts, SCAs, and simple cysts). If the pseudocysts were excluded, 64% of the lesions would be malignant or potentially malignant (IPMNs, MCNs, cystic adenocarcinomas, and cystic endocrine tumors).

In a study conducted in the US, analysis of 41 patients with cystic pancreatic masses who had

undergone surgical resection revealed that two thirds of the cases were benign and only one third were borderline or malignant (16).

It is known that a significant number of cysts, albeit being asymptomatic, have the potential to be malignant and therefore require surgery or other treatments. Recognition of the potentially malignant lesions, which are well treatable with surgery, makes the use of endosonography and FNA even more important in their early detection.

Some experts performed surgery on all masses that were resectable, and aspiration was only believed to be necessary in advanced tumors in which surgical resection was not possible, so that the aspiration results could guide recommending chemotherapy(17,18).

Based on the results of our study, 26.5% of the observed pancreatic cysts were pseudocysts (32.1% of non-malignant cysts). Previous studies reported their prevalence to be 15-30% among cystic pancreatic masses and in some cases, 75% prevalence has been reported among non-malignant cysts (19-20). In some studies pseudocyst was reported in 30-34% of pancreatic cysts that were removed with surgery (1, 2,20).

MCNs are considered very important because of their natural malignancy potential. These lesions are a common type of cystic neoplasms, involving 10-45% of the pancreatic cystic neoplasm cases, which are primarily seen in female patients (21). In keeping with other studies, our study revealed a 16.2% prevalence of MCNs in our patients, of whom 75% were female. This was the second most common type of lesions observed, after pseudocysts. Of the MCN cases, 54.5% occurred in the head of the pancreas. Many other studies have also described the head of the pancreas as the most common site of such lesions, while in some other report the tail of the pancreas was the most common site (22- 24).

The incidence of IPMNs has been reported as 1-33% of pancreatic lesions (21). In recent studies, IPMNs and MCNs have been reported as the most common types of pancreatic cysts, both of which are often asymptomatic (3). In this study 13.2% of the lesions were IPMN.

SCA are neoplastic lesions of the pancreas, which present in different sizes (up to 25 cm). Published series report SCA in 10-39% of all cystic lesions (21-22). In this study, 14.7% of individuals had SCA.

These patients were primarily women, with a mean age of 56 years, and 80% of the lesions were larger than 2 cm. In the largest published study of serous cystic neoplasms, Galanis and colleagues reported 75% of their patients to be women, with an average age of 62.1 years (25). Our study confirms these results.

Pseudopapillary cystic tumors are often less than 10% of all pancreatic cystic lesions and make up 1-3% of pancreatic neoplasms in reported series (1,19,26,27). This tumor is usually seen in younger women (aged 25-28 years) (1,20). There were no cases of this tumor in our study.

Neuroendocrine tumors of the pancreas compose 1-2% of all tumors, and cystic appearance is seen in 10% of them (28). Most of these lesions are without symptoms. In this study, three cases (4.4%) of this tumor were seen, two of which were in the pancreatic body. All the three cases were men aged less than 50 years.

Among solid pancreatic tumors, adenocarcinomas rarely show cystic appearance (28). In the present study nine patients (13.2%) had adenocarcinoma based on the cytology results of the cyst fluid. It is not clear which lesions originated from solid adenocarcinomas with cystic changes, or from MCN or IPMN with malignant changes. However, the fact that amylase levels were high in two cases suggests that IPMN may be the origin in them.

Despite the potential benefits of endosonography, it is not always performed in the evaluation of pancreatic lesions. Endosonography and FNA have changed the way pancreatic lesions are treated in about 60% of cases, and can prevent unnecessary surgery in individuals whose lesions are not resectable (28). The potential reasons may include a lack of knowledge regarding endosonography among physicians and limited availability of endosonography at health institutions.

CONCLUSION

47% of patients in this study had malignant or premalignant lesions. Although the lesions were asymptomatic, they require serious attention and treatment. Endosonography plays an important role in the diagnosis and treatment of pancreatic cystic tumors. Diagnosis of premalignant lesions and

providing appropriate treatment increase patients' life expectancy, and in the case of benign cysts, prevent unnecessary surgeries. Therefore, spreading the word on the benefits and indications of endosonography is recommended.

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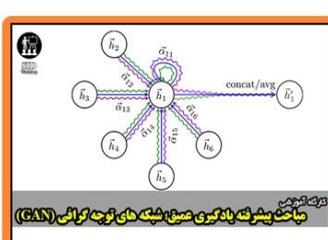


فیلم های آموزشی

کارگاه های آموزشی مرکز اطلاعات علمی جهاد دانشگاهی



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