

Role of endoscopic ultrasound-guided fine-needle aspiration in the diagnosis of space occupying lesions of the pancreas

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Abstract

Introduction: Space occupying lesions (SOLs) of the pancreas are commonly encountered in day to day practice either as an incidental finding or during evaluation of symptomatic patients. The aim of the present study was to compare the final diagnosis at follow-up with diagnosis made at computed tomography (CT)/magnetic resonance imaging (MRI) and endoscopic ultrasound (EUS). **Materials and Methods:** Retrospective analysis of EUS data of 131 patients referred for tissue diagnosis of SOL in pancreas was done. The lesions were classified as malignant, benign, and nonneoplastic by both CT/MRI and endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) in conjunction with clinical presentation, biochemical parameters, and tumor markers. Follow-up cases with a final diagnosis alone were included for the comparative analysis. **Statistical Analysis:** Chi-square test, sensitivity, specificity, positive predictive value (PPV), and negative predictive values (NPV) for CT/MRI and EUS-FNA were computed against the follow-up data. **Results:** Of the 131, there were 78 males (59.5%). The median age of presentation was 48 years (range: 11–82 years). Follow-up information on the final diagnosis was available for 54 patients. Confirmed diagnosis at follow-up was malignant lesion in 18, benign in 13 and 23 with a nonneoplastic lesion. When EUS-FNA outcome was compared with the definitive diagnosis of the 54 patients, it had a higher sensitivity for malignant (66.7% vs. 61.1%) and nonneoplastic lesions (78.3% vs. 73.9%) and was similar to CT/MRI for benign lesions (76.9% for both). EUS-FNA had a higher specificity (87.8% vs. 80.5%) with a good PPV for benign lesions (66.7% vs. 55.6%). CT/MRI was less accurate than EUS-FNA in predicting benign (79.6% vs. 85.2%) and nonneoplastic lesions (79.6% vs. 81.5%) compared to malignant lesions wherein it was similar at 81.5%. The high NPV with a lower PPV for both EUS/FNA and CT/MRI suggests that follow-up definitive diagnosis was superior to both –. **Conclusions:** Endoscopic ultrasound-guided fine-needle aspiration had a higher specificity, but low sensitivity for the both neoplastic and nonneoplastic lesion of the pancreas compared to the world literature. The overall EUS-FNA yield was low when compared to the follow-up definitive diagnosis.

Key words

Endoscopic ultrasound, fine-needle aspiration, pancreatic lesion

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Introduction

Space occupying lesions (SOLs) of pancreas, both cystic or solid are detected during ultrasound screening in either a symptomatic patient with obstructive jaundice, recurrent pancreatitis, or unprecedented loss of weight and appetite or as an incidental finding in an asymptomatic individual. Computed tomography (CT) and magnetic resonance

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imaging (MRI) confirm and stage the lesion and also provide morphological interpretation. CT-guided aspiration cytology is not recommended for fear of needle track seeding.

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is a safe and complimentary investigation to CT/MRI imaging. The major advantage is the feasibility of tissue diagnosis. Fine-needle aspiration (FNA) cytology and fluid analysis together with morphological characteristics helps differentiate malignant/premalignant pancreatic lesions from those that are benign.^[1] The reported sensitivity and specificity of EUS-FNA for various SOLs in pancreas are as high as 97%.^[2]

Few case reports from India have highlighted the role of EUS-FNA in diagnosis of pancreatic tuberculosis^[3-7] and other SOLs of pancreas.^[8-10] However, there are no large series reporting the validity and accuracy of EUS-FNA for various SOLs of pancreas from major tertiary centers in India, possibly due to lack of follow-up data.

The aim of the present study was to compare the outcome of the final diagnosis at follow-up with diagnosis made at CT/MRI and EUS-FNA.

Materials and Methods

The study was a retrospective analysis of EUS-FNA data of 131 patients referred for tissue diagnosis of SOL in pancreas. EUS-FNA was done by a single operator using GF UCT 140 linear scope. FNA cytology was done for all the lesions using 22 G/25 G Wilson Cook needle, except for those that were highly vascular. Fluid analysis included analysis for amylase content, carcinoembryonic antigen (CEA) levels, triglyceride levels (when milky) and culture (turbid fluid and suspected infection). Immunohistochemistry was done when deemed necessary.

The CT/MRI diagnosis for SOLs of pancreas was made in conjunction with clinical presentation, biochemical parameters (normal serum amylase: Up to 85 U/L; normal serum lipase: Up to 300 U/L), and tumor markers (serum CEA [normal: Up to 3.0 ng/mL (smokers <6.2 ng/mL and nonsmokers <3.5 ng/mL; serum CA-19-9 [Normal: Up to 37 U/mL]))).

The SOLs detected at CT/MRI and EUS-FNA were classified as:

- Nonneoplastic when patients had coexisting clinical features, biochemical parameters, and CT/MRI suggestive of acute or chronic pancreatitis and were negative for tumor markers. It also included an infected pseudocyst and suspected tuberculous lesions
- Neoplastic lesions were defined as benign and malignant based on morphological characteristics and FNA cytology.

A SOL at EUS was considered as malignant if biopsy or FNAC was positive for adenocarcinoma, malignant gastrointestinal stromal tumor (GIST), sarcoma, Hodgkin's disease, etc.,. A lesion was considered as benign if EUS characteristics were typical of a benign and confirmed at FNA. Well-differentiated neuroendocrine tumor, solid pseudopapillary neoplasm and nonmalignant GIST were classified as benign after confirmation by immune-histochemistry. Patients positive for tuberculosis (granulomas or acid-fast *Bacillus* positive), pseudocysts (infective or noninfective), inflammatory lesions or those that disappeared during follow-up were classified as nonneoplastic.

For analysis, CT/MRI and EUS-FNA diagnosis were compared with the final outcome diagnosis obtained either from follow-up of cases, hospital records and/or telephonic interview. FNA or histological diagnosis at surgery or posttherapeutic endoscopy procedure (post EUS) was taken as the gold standard for final diagnosis.

The final diagnosis was correlated with the CT/MRI and EUS-FNA diagnosis.

Ethics Committee of the Institution approved the study.

Statistical analysis

Validation was done using the Chi-square test and Fisher's exact test. Sensitivity, specificity, positive predictive value (PPV), negative predictive values (NPV), and accuracy of CT/MRI and EUS-FNA were computed against the follow-up data.

Results

Of the 131 patients who had EUS and FNA, there were 78 males (59.5%). The median age of presentation was 48 years (range: 11–82 years). Table 1 summarizes the baseline characteristics of the patients. The median size of benign and malignant lesion were 3.5 cm (range: 0.4–12 cm) and 2.9 cm (range: 1.6–7 cm), respectively.

Ninety-four patients could be contacted. A definite diagnosis was available for only 54 patients (57.4%). The rest were not aware of their diagnosis. When EUS-FNA outcome was compared with the definitive diagnosis of the 54 patients [Table 2], it had a higher sensitivity for malignant (66.67% vs. 61.1%) and nonneoplastic lesions (78.3% vs. 73.9%) and was similar to CT/MRI for benign lesions (76.9% for both). EUS-FNA had a higher specificity (87.8% vs. 80.5%) with a good PPV (66.7% vs. 55.6%) for benign lesions. CT/MRI was less accurate than EUS-FNA in predicting benign (79.6% vs. 85.2) and nonneoplastic lesions (81.5 vs. 79.6) compared to malignant lesions wherein it was similar (81.5 for both). The NPV was high for both EUS-FNA and CT/MRI suggesting the yield by definitive diagnosis was superior to both investigative

modalities. However, comparing the 2 modalities against the gold standard of the final outcome, there was no statistical difference between the 2 for all three SOL types.

Except for one patient who developed ischemic heart disease after the procedure and recovered with supportive treatment there were no EUS-FNA procedure-related complications.

Discussion

Endoscopic ultrasound-FNA is an excellent rescue armamentarium for confirming the diagnosis^[1] of SOLs of pancreas with low complication rates. It is now possible with EUS-FNA, to obtain high-quality imaging of the pancreas and includes morphological characteristics, locoregional anatomy in relation to blood vessels, biliary and pancreatic duct, and nodal involvement. Though morphological features are typical, an ultimate diagnosis of SOL is possible only after FNA, cytology and at times immune-histochemistry of the lesion. Fluid analysis of the cyst for amylase, CEA and/or cytology/biopsy enhances the diagnostic yield by almost 80%.^[11-14] In our series, except in five patients where FNA was contraindicated due to extensive collaterals, EUS-FNA was informative in the remaining.

Our study for the first time has evaluated the diagnostic capability of EUS-FNA among Indian patients being referred to a tertiary care center. The study compared

the outcome of CT/MRI and EUS-FNA with the final diagnosis. The results of the present study have shown a low sensitivity and NPV of EUS-FNA. Several studies have reported EUS-FNA accuracy to range from as low as 54% to as high as 97%.^[2,11-16] For malignant cystic neoplasm, specificity has varied from 83% to almost 100% and sensitivity from 25% to 88%.^[11-13,17-19] Between EUS-FNA and CT/MRI, EUS-FNA was marginally superior in predicting the diagnosis especially for benign and nonneoplastic lesions.

The reason for the low sensitivity of EUS-FNA in our series compared to the western data is not clear. One possibility may be the large dropout rate despite proactive attempts at tracing the cases. Most referrals are from far off centers and these patients at times do not even report to the primary care physician. In the present study while 94 patients (71.8%) could be contacted, a definitive diagnosis was known in only 54 of patients (57.4%), resulting in a low overall rate of follow-up (41.2%).

One other reason could be that the overall sensitivity of EUS-FNA of SOLs of pancreas in India itself may be low. These results need validation from high volume centers.

Conclusion

Though data on final/ultimate diagnosis were not available for all our patients, the present study has highlighted the role of EUS-FNA in SOLs of pancreas. It is complementary and a mandatory investigation in a select group of patients where CT/MRI is inconclusive. A better and close follow-up of patients may enhance the yield of EUS-FNA, which was the major limitation in our study. Today, there is a paramount need to obtain similar validation information from other large volume centers in India.

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Table 1: Baseline characteristics of patients with SOLs of pancreas

Baseline characteristics	Outcome (%)
Age	Median 48 years (range 11-82 years)
Gender	
Males: females	78:53
Diabetes mellitus	40 (30.5)
Raised serum amylase (N: up to 85 U/L)/ serum lipase (N: up to 300 U/L)	23 out of 61 (37.7)
Raised serum CA 19-9 (N: Up to 37 U/mL)	24 (18.3)
Raised serum carcinoembryonic antigen (N: Up to 3.0 ng/mL; smokers: <6.2; nonsmokers<3.5 ng/mL)	14 (10.7)
Raised serum carcinoembryonic antigen or serum CA 19-9	31 (23.6)

SOLs=Space occupying lesions

Table 2: The comparative outcome of CT/MRI and EUS-FNA (in percentage) with the final outcome of 54 patients

Final diagnosis	Sensitivity		Specificity		PPV		NPV		CT/MRI versus EUS-FNA P*
	CT/MRI	EUS-FNA	CT/MRI	EUS-FNA	CT/MRI	EUS-FNA	CT/MRI	EUS-FNA	
Malignant (18)	61.1	66.7	91.7	88.9	78.6	75	82.9	84.2	Not significant
Benign (13)	76.9	76.9	80.5	87.8	55.6	66.7	91.7	92.3	Not significant
Nonneoplastic lesions (23)	73.9	78.3	83.9	83.9	77.3	78.3	81.3	83.9	Not significant

*Two-tailed Fisher's exact test. CT=Computed tomography, MRI=Magnetic resonance imaging, EUS-FNA=Endoscopic ultrasound-guided fine-needle aspiration, NPV=Negative predictive value, PPV=Positive predictive value

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