Digestive and Liver Disease 45 (2013) 957–960

Contents lists available at ScienceDirect

Digestive and Liver Disease

journal homepage: www.elsevier.com/locate/dld

Short Report

Preoperative diagnosis of a solid pseudopapillary tumour of the pancreas by Endoscopic Ultrasound Fine Needle Biopsy: A retrospective case series

Antonella Maimone[a], Carmelo Luigiano[b], Paola Baccarini[c], Adele Fornelli[d], Vincenzo Cennamo[a], Annamaria Polifemo[a], Marta Fiscaletti[e], Dario de Biase[c], Francesca Jaboli[f], Clara Virgilio[b], Liliana Stelitano[b], Nicola Zanini[g], Michele Masetti[g], Elio Jovine[g], Carlo Fabbri[a,*]

[a] Unit of Gastroenterology, AUSL Bologna Bellaria-Maggiore Hospital, Bologna, Italy
[b] Unit of Gastroenterology and Digestive Endoscopy, ARNAS Garibaldi, Catania, Italy
[c] Unit of Anatomic Pathology, AUSL Bologna Bellaria Hospital, Bologna, Italy
[d] Unit of Anatomic Pathology, AUSL Bologna Maggiore Hospital, Bologna, Italy
[e] Unit of Radiology, AUSL Bologna Bellaria Hospital, Bologna, Italy
[f] Centre for Gastroenterology Royal Free Hospital, Pond Street, London, United Kingdom
[g] Unit of General Surgery, AUSL Bologna Maggiore Hospital, Bologna, Italy

ARTICLE INFO

Article history:
Received 24 March 2013
Accepted 18 June 2013
Available online 19 July 2013

Keywords:
Endoscopic ultrasound
Fine-needle biopsy
Pancreatic mass
Solid pseudopapillary tumour

ABSTRACT

Background: A solid pseudopapillary tumour of the pancreas (SPTP) is a rare neoplasm.
Aim: We herein present five cases of SPTP diagnosed using endoscopic ultrasound (EUS) guided fine-needle biopsy (FNB) using a needle with side fenestration (ProCore-needle).
Methods: From January 2011 to June 2012 in five patients with SPTP tissue acquisition was carried out with a 19-gauge (4 patients) or a 22-gauge (one patient) needle.
Results: The mean age of the patients was 30.8 years, the mean lesion size was 49 mm and the most common location was the tail of the pancreas (3 cases). When the samples were evaluated macroscopically, small core fragments were observed in all cases. A preoperative diagnosis of SPTP was made in all patients on the basis of the histocytological and characteristic immunophenotypic patterns and was confirmed at final surgical histology.
Conclusions: In our experience, EUS-FNB is an effective and secure method for a preoperative diagnosis of SPTP.

1. Introduction

Tissue diagnosis is essential for the correct management of patients with pancreatic neoplasms, and endoscopic ultrasound (EUS) with fine-needle aspiration (FNA) is a useful diagnostic tool for these types of patients.

Solid pseudopapillary tumour of the pancreas (SPTP) is a rare neoplasm with a reported frequency of between 1% and 2% of all exocrine pancreatic tumours [1].

Diagnosing SPTP represents a significant challenge, even when a multidisciplinary approach is adopted. The differential diagnosis of a pancreatic mass is connected to a vast spectrum of diseases with varying characteristics, biological behaviour and treatments, as well as autoimmune pancreatitis, focal chronic pancreatitis, secondary lesions, pancreatic endocrine tumours, acinar cell carcinomas and cystic neoplasms [2,3].

An accurate preoperative diagnosis would be highly preferable because local surgical excision is usually curative in patients with SPTP [1].

In this setting, the possibility of obtaining adequate tissue samples would increase the diagnostic yield of a preoperative diagnosis in patients with SPTP.

In recent years, a EUS-guided biopsy needle with side fenestration (ProCore needle) was developed in order to enable fine-needle biopsy (FNB) under EUS guidance.

* Corresponding author at: Unit of Gastroenterology and Digestive Endoscopy, AUSL Bologna, Bellaria Hospital, Via Altura, 40139 Bologna, Italy.
Tel.: +39 0516225162; fax: +39 0516225247.
E-mail address: carlo.fabbri@ausl.bologna.it (C. Fabbri).

1590-8658/$36.00 © 2013 Published by Elsevier Ltd on behalf of Editrice Gastroenterologica Italiana S.r.l.
http://dx.doi.org/10.1016/j.dld.2013.06.005

We herein present five cases of SPTP diagnosed by means of a EUS-FNB using this needle.

2. Materials and methods

From January 2011 to June 2012, as part of routine clinical care at our institution, all EUS guided tissue sampling for pancreatic lesions was performed using ProCore needles (Cook Endoscopy Inc., Limerick, Ireland). The choice of needle size was based on the location, size and characteristics of the pancreatic lesions. The data of all patients were retrospectively analysed and five patients with a diagnosis of solid pseudopapillary tumours were identified. Clinical data for these patients were obtained by reviewing all available medical records regarding hospitalisation and outpatient visits at the Endoscopy, the Surgery and the Oncology Departments as well as from consultation of the laboratory, instrumental and pathological archives of our Institution.

The demographic and clinical data of the 5 patients and the characteristics of the pancreatic masses studied are presented in Table 1.

The EUS-FNBs were performed using a linear echoendoscope (Fujinon, Inc., Saitama, Japan) by experienced echoendoscopists with a current case volume of 700 cases per year (200 FNAs).

Tissue acquisition was carried out using a 19 or a 22-gauge ProCore needle (Cook Endoscopy Inc.) with a pathologist on site.

Tissue acquisition was carried out according to a standardised protocol. After the target lesion was endosonographically visualised and the region was scanned for interposing vessels using colour pulsed Doppler, FNB was performed as follows: (1) the FNB needle was advanced into the target lesion under EUS guidance; (2) once inside the lesion, the stylet was removed and negative suction pressure was applied using a 10-mL syringe for 30 s; (3) three to-and-fro movements within the lesion were made; (4) suction was then released by closing the lock of the syringe and (5) the needle was finally removed.

The aspirated material was placed in a tube containing 4% formaldehyde solution for cell block preparation; the remaining material was smeared on microscope slides for on site examination or immediately fixed in 95% ethanol for Papanicolaou staining. Immunohistochemical analysis was carried out on cell block tissue. The *KRAS* exon 2 and exon 3 mutational analysis was carried out using allele-specific locked nucleic acid qPCR (ASLNAqPCR) and Next Generation Sequencing (454-GS Junior Roche) [4].

The final surgical histological results were compared with the results of the fine-needle biopsy.

3. Results

The mean (±SD) age of the patients (1 man and 4 women) was 30.8 ± 13.3 years (range 17–47). The pancreatic mass was initially studied by computed tomography (CT) (Fig. 1a) or by magnetic resonance imaging (MRI) (Fig. 1b) during investigation for abdominal pain in one patient, for acute pancreatitis in one patient, and the remaining 3 lesions were discovered incidentally.

The mean (±SD) lesion size was 49 ± 19 mm (range 20–70) and the most common location was the tail of the pancreas (3 cases).

All pancreatic tumours were morphologically well-defined on EUS, as an hypoechogenic mass in 4 patients (Fig. 1c) and as a cystic lesion with peripheral calcification in one patient.

Fine-needle biopsy was performed with a 19-gauge needle in 4 patients (using the transgastric approach) and with a 22-gauge needle in one patient (using the transduodenal approach).

The mean (±SD) number of FNB passes was 2.4 ± 0.9 (range, 1–3).

When the samples were evaluated macroscopically after the needle content was flushed into a tube containing a liquid-based preparation, small core fragments were observed in all cases.

A preoperative diagnosis of SPTP was made in all patients on the basis of histocytological and characteristic immunophenotypic patterns.

In all cases, the slides showed monotonous, poorly cohesive cells, intermingled with branching papillary fronds. The nuclei were round to oval with dispersed or somewhat granular chromatin and indistinct nucleoli. Nuclear grooves (or clefted nuclei) were frequently noted. In one case (#2, see Table 1), abundant necrotic debris was seen (Fig. 2).

The results of the immunohistochemical analysis are summarised in Table 1. No mutations in the *KRAS* gene were observed.

None of the 5 patients developed any procedure- or sedation-related immediate or delayed complications related to the EUS-FNB.

Surgical resection (Fig. 3a) was performed in all cases. Laparoscopic resection was planned preoperatively and was successfully completed in four patients. The preoperative cytohistological diagnosis of SPTP was confirmed in all patients at final surgical histology (Fig. 3b).

Over a mean (±SD) follow-up period of 15 ± 6 months (range 6–21), the survival rate was 100% and there has been no evidence of recurrence.

4. Discussion

To the best of our knowledge, these are the first five cases of EUS-FNB in which a ProCore needle was used for the preoperative diagnosis of SPTP.

Despite the increased awareness of the characteristics of this tumour, which include a distinct female preponderance and low malignant potential, the rate of preoperative misdiagnosis is rather high [5–7].

Radiological preoperative diagnosis of SPTP is still difficult because the characteristics overlap with other pancreatic focal diseases [7].

Yu et al. [7] reviewed and analysed 553 cases of SPTP reported in the Chinese literature between January 1996 and January 2009; of these 553 cases, only 23.7% had preoperative suspicion of SPTP based on imaging characteristics while, in the remaining cases, the misdiagnosis rates for pancreatic adenocarcinoma, cystadenoma, cystadenocarcinoma, islet cell tumour, pancreatic cyst, neuroendocrine tumour, teratoma, and others were 24.6%, 10.7%, 3%, 13.2%, 7.3%, 8.6%, 1.9%, and 7%, respectively.

Given the pleomorphic appearance, only tissue analysis can provide a reliable diagnosis.

Fine needle aspiration is usually the method of obtaining the specimen needed for a correct preoperative assessment of SPTP [1].

However, a review in an article showed that only 7% were diagnosed by radiological FNA, and puncture-related complications and seeding of the needle tract by neoplastic cells have been reported [1].

Endoscopic ultrasound permits a better evaluation of SPTP, but the findings are not specific. A small SPTP, an often non-cystic tumour most frequent in males, might have the EUS appearance of a solid endocrine neoplasm, and it might be difficult to differentiate between the two [8].

The percutaneous approach has been replaced by EUS-guided FNA, because it correlates with a higher yield preoperative diagnosis having fewer complications and a decreased possibility of neoplastic seeding [1–3].

Table 1
The demographic and clinical data of the patients, the characteristics of the pancreatic masses studied and the results of the immunostaining.

	Case 1	Case 2	Case 3	Case 4	Case 5
Sex	Female	Male	Female	Female	Female
Age (years)	17	17	47	36	37
Clinical history	Negative	Abdominal trauma	Dyspepsia	Gallstone	Negative
Clinical presentation	Asymptomatic	Acute abdominal pain	Asymptomatic	Pancreatitis	Asymptomatic
Blood test	Normal	Normal	Normal	Cholestasis Leukocytosis Hyperamylasemia	Normal
Tumour size (mm)	40	60	70	20	55
Tumour location	Head	Tail	Tail	Tail	Body
Endoscopic ultrasound characteristics	Hypoechogenic mass, round with local ectasia of the main pancreatic duct.	Hypoechogenic mass with anechogenic internal gaps. The cleavage plane with the spleen and the stomach is defined.	Cyst with calcified capsule	Hypoechogenic mass with echogenic spots	Hypoechogenic mass with internal calcifications and peripheral vascularisation. The cleavage plane with the adjacent structures is defined
Size of needle	22-Gauge	19-Gauge	19-Gauge	19-Gauge	19-Gauge
Endoscopic ultrasound approach	Transduodenal	Transgastric	Transgastric	Transgastric	Transgastric
Number of needle passes	3	2	3	1	3
Tissue Diagnosis	Yes	Yes	Yes	Yes	Yes
Results of immunostaining					
Vimentin	+	+	+	+	+
CD 10	+	+	+	+	+
Progesterone receptor	+	+	+	–	+
Cytokeratin	+	–	–	–	–
Chromogranin	–	–	–	–	–
Synaptophysin	+	–	–	–	–
Beta-catenin	+	+	+	+	+
p53	–	–	–	–	–
Ki67	+	+	+	+	+
Neuron specific enolase	+	+	+	+	+
Surgery	Pancreaticoduodenectomy	Distal pancresectomy and splenectomy	Distal pancresectomy and splenectomy	Distal pancresectomy and splenectomy	Distal pancresectomy and splenectomy
Postoperative complications	None	None	Pancreatic abscess which underwent endoscopic ultrasound-guided drainage	None	None
Follow-up (months)	21	19	17	12	6

Endoscopic ultrasound-guided tissue acquisition has an important role in diagnosing SPTP and could provide an accurate preoperative diagnosis.

However, in the largest multicentre retrospective series of 28 cases undergoing EUS-FNA for the diagnosis of SPTP, the preoperative diagnostic accuracy was only 75% [3].

Solid pseudopapillary tumours of the pancreas represent a significant diagnostic challenge even for experienced cytopathologists, especially in unsuspected cases and when immunohistochemical analysis is not available. This neoplasm has few specific cytologic characteristics (other than papillae) which can also be seen in intraductal papillary tumours with low grade dysplasia. However, one could search for a nuclear groove in order to support a cytological diagnosis of SPTP. Moreover, papillary architecture is not present throughout the tumour and, if the sampling is obtained from solid areas, papillae would not be seen by the pathologist. The immunostaining analysis is of pivotal importance for diagnosing the histotype [9].

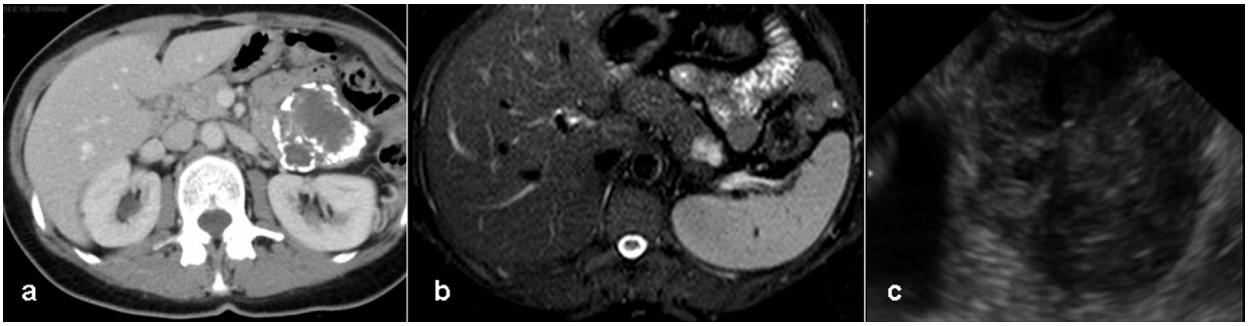

Fig. 1. (a) Enhanced computed tomography scan showing a low density mass of the tail of the pancreas with ringed calcification and slightly enhanced solid peripheral areas; (b) axial fat-saturated T2-weighted magnetic resonance image showing a small well-demarcated mass in the tail of the pancreas appearing hyperintensely heterogeneous; (c) endoscopic ultrasound images of a solid pseudopapillary tumour of the pancreas appearing as a round hypoechogenic mass measuring 40 mm in diameter.

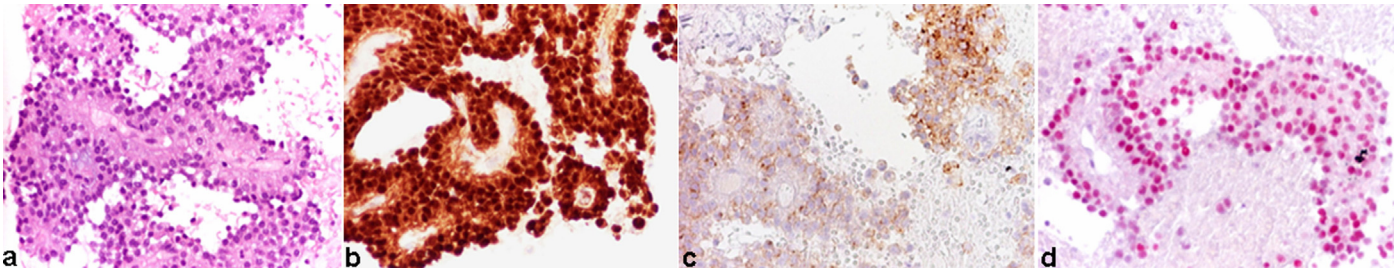

Fig. 2. Solid pseudopapillary tumour of the pancreas cytological preparation, 200× magnification: (a) haematoxylin/eosin (H/E) routine stain; (b) beta-catenin diffuse nuclear stain; (c) CD10 membranous labelling of neoplastic cells; (d) progesterone receptor immunohistochemical positivity in most of the nuclei.

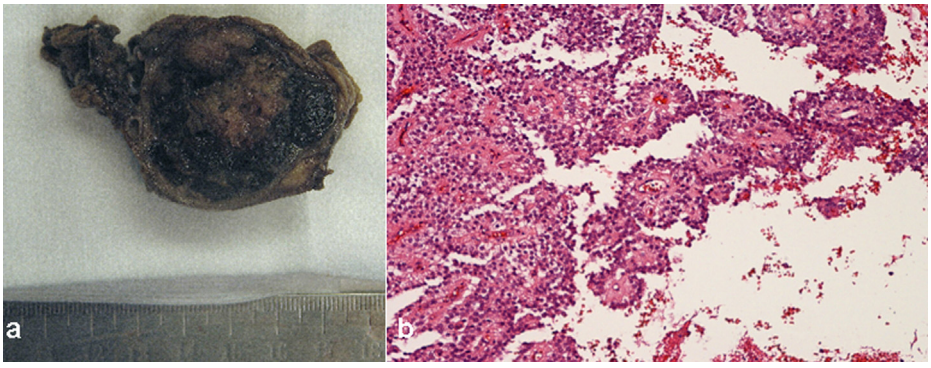

Fig. 3. (a) Gross pathology of a solid pseudopapillary tumour of the pancreas showing a well-demarcated lesion with extensive haemorrhagic and microcystic peripherical spaces and (b) the histology of the lesion showing a solid pseudopapillary pattern of growth, which is mostly artefactual due to the poor cohesiveness of the cells, abundant vascularisation and intratumoural haemorrhage (H&E, 100×).

Endoscopic ultrasound-guided FNB can differentiate SPTP from other pancreatic neoplasms of similar radiological and cytological appearance using a less invasive approach.

In comparison with a standard needle, the ProCore needle gives the possibility of obtaining samples of higher quality and quantity which would increase the diagnostic yield of a preoperative diagnosis in patients with SPTP.

This advantage was evident in our series showing that, in all cases, it was possible to obtain adequate tissue samples for cyto-histological and immunohistochemical evaluation with the use of an EUS histology needle, leading to a conclusive preoperative diagnosis, even in cases which are "atypical" for localisation (head) and gender (male). These approaches should be able to guide the choice of less invasive surgery and improve the management of patients with SPTP. However, additional prospective studies will be necessary in the future to validate our findings.

Conflict of interest

There are no financial arrangements or commercial associations (e.g., equity ownership or interest, consultancy, patent and licensing agreement, or institutional and corporate associations) which might be a conflict of interest in relation to the manuscript submitted.

References

[1] Papavramidis T, Papavramidis S. Solid pseudopapillary tumors of the pancreas: review of 718 patients reported in English literature. Journal of the American College of Surgeons 2005;200:965–72.
[2] Nadler EP, Novikov A, Landzberg BR, et al. The use of endoscopic ultrasound in the diagnosis of solid pseudopapillary tumors of the pancreas in children. Journal of Pediatric Surgery 2002;37:1370–3.
[3] Jani N, Dewitt J, Eloubeidi M, et al. Endoscopic ultrasound-guided fine-needle aspiration for diagnosis of solid pseudopapillary tumors of the pancreas: a multicenter experience. Endoscopy 2008;40:200–3.
[4] Morandi L, de Biase D, Visani M, et al. Allele specific locked nucleic acid quantitative PCR (ASLNAqPCR): an accurate and cost-effective assay to diagnose and quantify KRAS and BRAF mutation. PLoS ONE 2012;7:e36084.
[5] Cheng DF, Peng CH, Zhou GW, et al. Clinical misdiagnosis of solid pseudopapillary tumour of pancreas. Chinese Medical Journal 2005;118:922–6.
[6] Martin RC, Klimstra DS, Brennan MF, Conlon KC. Solid-pseudopapillary tumor of the pancreas: a surgical enigma. Annals of Surgical Oncology 2002;9:35–40.
[7] Yu PF, Hu ZH, Wang XB, et al. Solid pseudopapillary tumours of the pancreas: a review of 553 cases in Chinese literature. World Journal of Gastroenterology 2010;16:1209–14.
[8] Uchimi K, Fujita N, Noda Y, et al. Solid cystic tumor of the pancreas: report of six cases and a review of the Japanese literature. Journal of Gastroenterology 2002;37:972–80.
[9] Mima K, Hirota M, Abe S, et al. Small solid pseudopapilary tumor of the pancreas in a 32-year-old man: report of a case. Surgery Today 2010;40:772–6.