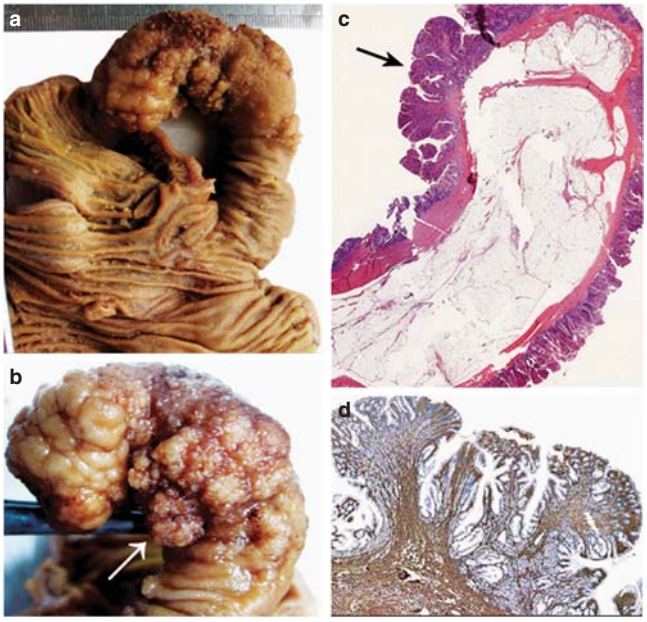

Figure 2. Gross and histologic features of the inverted Meckel's diverticulum and associated Peutz-Jeghers type hamartomatous polyp (PJP). (**a**) The opened, resected surgical specimen shows an inverted Meckel diverticulum on the luminal side of the ileum. (**b**) Closer inspection reveals a sessile lesion with coarse lobulated surface at the middle portion of the inverted Meckel's diverticulum (white arrow). (**c**) Whole mount section of the inverted Meckel's diverticulum. The PJP is at the left-upper portion (black arrow). (**d**) Immunohistochemical stain of α-smooth muscle action highlights the irregularly organized smooth muscle bundles of the PJP, which extend from the muscularis mucosa to the mucosal surface.

sporadic. However, some studies showed that sporadic PJPs were not always associated with a low risk of cancer (8,9), and the risk of developing carcinomas in gastrointestinal tract or other organs could not be ignored.

The commonest symptom of inverted Meckel's diverticulum is intussusception, followed by bleeding, anemia, and abdominal pain (1,10). Patient who does not have an acute abdomen, as in our patient, may undergo a series of examinations to investigate the cause of obscure bleeding or anemia. Inverted Meckel's diverticulum may appear as a pedunculated polyp endoscopically and polypectomy on such lesion can be a rare cause of iatrogenic gut perforation (11). Therefore, inverted Meckel's diverticulum should be considered and treated carefully in patient with an elongated pedunculated polyp in the distal ileum, even if a diagnosis of benign hamartomatous polyp has been made histologically by biopsy.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Usefulness of Circulating Tumor Cell Detection in Pancreatic Adenocarcinoma Diagnosis

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To the Editor: Pancreatic cytology by endoscopic ultrasound-guided fine needle aspiration (EUS-FNA) is considered to be the first diagnostic procedure in patients with unresectable pancreatic mass or when preoperative treatment is planned. Detecting circulating tumor cells (CTCs) in blood is equivalent to a "liquid biopsy". A new diagnostic method based on CTC detection was prospectively evaluated in 40 patients. CTCs were detected in 15 out of 27 patients with pancreatic adenocarcinoma with a

Table 1. Patient and tumor characteristics

Gender	Age (years)	CTC	EUS-FNA	Size (mm, EUS)	Lymph node invasion (EUS)	Tumor status (CT scan and EUS)	Diagnosis
M	54	Positive	Positive	23	No	Resectable	Adenocarcinoma
F	57	Positive	Positive	30	Yes	Resectable	Adenocarcinoma
F	56	Positive	Positive	30	No	Resectable	Adenocarcinoma
M	70	Positive	Positive	30	No	Resectable	Adenocarcinoma
M	61	Positive	Positive	30	No	Locally advanced	Adenocarcinoma
M	71	Positive	Positive	35	No	Locally advanced	Adenocarcinoma
F	82	Positive	Positive	36	Yes	Locally advanced	Adenocarcinoma
M	65	Positive	Positive	35	No	Locally advanced	Adenocarcinoma
M	65	Positive	Positive	50	Yes	Locally advanced	Adenocarcinoma
F	74	Positive	Positive	27	Yes	Locally advanced	Adenocarcinoma
M	64	Positive	Positive	40	Yes	Metastatic	Adenocarcinoma
F	84	Positive	Positive	40	Yes	Metastatic	Adenocarcinoma
F	80	Positive	Positive	25	Yes	Metastatic	Adenocarcinoma
F	74	Positive	Positive	30	No	Metastatic	Adenocarcinoma
M	51	Positive	Negative	30	No	Metastatic	Adenocarcinoma
M	62	Negative	Positive	33	No	Resectable	Adenocarcinoma
F	69	Failure	Positive	29	No	Resectable	Adenocarcinoma
F	72	Negative	Positive	30	No	Resectable	Adenocarcinoma
F	73	Negative	Positive	67	Yes	Locally advanced	Adenocarcinoma
F	77	Negative	Positive	40	No	Metastatic	Adenocarcinoma
M	82	Failure	Positive	41	No	Metastatic	Adenocarcinoma
M	63	Negative	Positive	50	Yes	Metastatic	Adenocarcinoma
F	50	Negative	Negative	18	No	Resectable	Adenocarcinoma
M	44	Negative	Negative	26	Yes	Resectable	Adenocarcinoma
M	74	Negative	Negative	26	No	Locally advanced	Adenocarcinoma
M	56	Negative	Negative	30	Yes	Locally advanced	Adenocarcinoma
F	70	Negative	Negative	50	No	Metastatic	Adenocarcinoma
M	65	Negative	Negative	15	NA	NA	Lymphoma
F	18	Failure	Negative	70	NA	NA	Mucinous lesion
M	66	Negative	Negative	35	NA	NA	Chronic pancreatitis
M	71	Negative	Negative	20	NA	NA	Benign lesion
M	57	Negative	Negative	18	NA	NA	Cystic lesion
M	70	Negative	Negative	27	NA	NA	Chronic pancreatitis
F	82	Negative	Negative	20	NA	NA	Undetermined
F	30	Negative	Negative	20	NA	NA	Endocrine tumor
M	47	Negative	Negative	20	NA	NA	Endocrine tumor
M	51	Negative	Negative	25	NA	NA	Chronic pancreatitis
M	88	Negative	Negative	25	NA	NA	Undetermined
M	55	Negative	Failure	20	NA	NA	Chronic pancreatitis
F	48	Negative	Failure	No mass found	NA	NA	Undetermined

CTC, circulating tumor cell; CT scan, computed tomography scan; EUS-FNA, endoscopic ultrasound-guided fine needle aspiration; F, female; M, male; NA, not applicable.

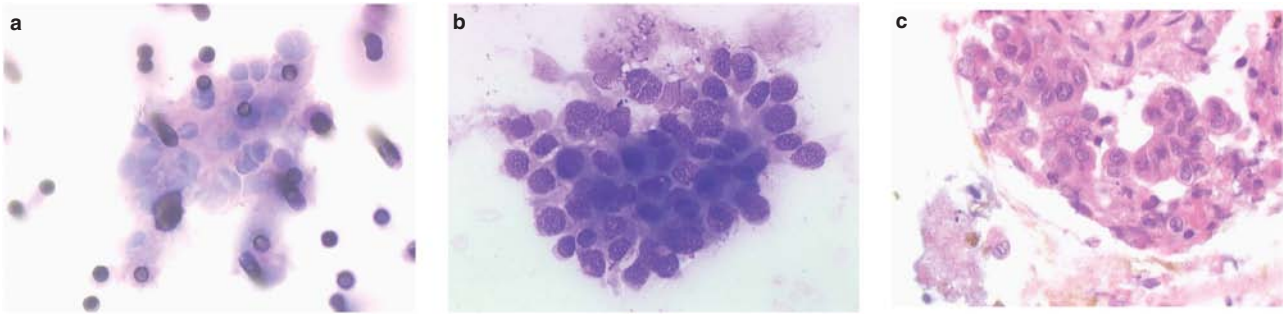

Figure 1. Morphological analysis of tumoral cells obtained from one patient. (**a**) Circulating tumor cells after ScreenCellCyto filtration: cluster of very atypical cells (May–Grunwald–Giemsa (MGG) staining). (**b**) Cytological proof of malignancy (endoscopic ultrasound-guided fine needle aspiration): cluster of abnormal cells with tumoral aspects (MGG staining). (**c**) Histological proof of pancreatic adenocarcinoma performed on cytoblock analysis (hematoxylin and eosin staining).

diagnostic accuracy of 70%. This blood test using CTC detection appears to be clinically relevant and may avoid EUS-FNA procedure in one-half of patients presenting with a pancreatic mass.

For pancreatic tumor, guidelines recommend pancreatic cytology examination by EUS-FNA as the first diagnostic procedure in unresectable patients or when preoperative treatment is planned (1). Material obtained by needle biopsy may be noninformative with a sensitivity for pancreatic adenocarcinoma ranging from 68 to 92%. Detecting CTCs in blood could have the role of a "liquid biopsy", which would avoid the need for tumor biopsies (2). The usefulness of CTC detection in the clinical management of patients presenting with a pancreatic tumor has not been established yet (3,4). Here, we aimed to prospectively evaluate the accuracy of a diagnostic method based on CTC detection performed before EUS-FNA. All patients referred from January 2011 to March 2012 for EUS-FNA procedure in a context of pancreatic solid tumor diagnosis were prospectively enrolled after their consent. All patients underwent a thoracic and abdominal computed tomography scan for initial tumor staging. Before EUS-FNA procedure a sample of 10 ml peripheral blood was collected (using EDTA tube). CTCs were analyzed using the ScreenCell method (see Supplementary Data online). Cells visualized on the filter under light microscopy were considered as tumoral, if they met the following morphological criteria: nuclear diameter >14 µm, anisocytosis, anisocaryosis, nuclear membrane irregularities, the presence of large nucleolus, clots of tumoral cells with platelets and fibrin. The results were expressed qualitatively: positive with at least one CTC detected or negative (5). All analysis was performed by an experienced pathologist blinded to the EUS-FNA results. EUS-FNA procedure was performed with curvilinear echoendoscope (Olympus UCT-180). Olympus 22-G needle (Olympus, Japan) was inserted into the working channel of the EUS. Once in the target lesion, the stylet was removed and aspiration was performed by moving the needle back and forth within the lesion at least three times. Samples were immersed in Hank's solution and analyzed by two pathologists. Size of pancreatic mass and the presence of regional suspect node or metastatis in the left hepatic lobe were recorded. If the first EUS-FNA was negative, a second procedure was planned. The diagnosis of pancreatic adenocarcinoma was defined either by pathological evidence based on FNA (using cytological or histological formalin-fixed paraffin-embedded cytoblock preparations) or surgical specimen, or by clinical outcome with metastatic evolution and CA19.9 serum level rather than 10-fold normal value.

A total of 40 patients were included and their characteristics are described in **Table 1**. A pancreatic adenocarcinoma was confirmed in 27 out of 40 patients (68.3%). In 21 of the 27 patients, pathological proof of adenocarcinoma was obtained by EUS-FNA. For the diagnosis of adenocarcinoma, sensitivity and specificity of EUS-FNA were 77.8% (CI 95% [65.4%; 90%]) and 100% (CI 95% [75%; 100%]), respectively. The diagnostic accuracy of FNA was 85%. In six patients, adenocarcinoma was confirmed with surgical specimen ($n=2$), third EUS-FNA ($n=2$), or metastatic evolution with CA 19–9 serum level rather than 10-fold upper normal value ($n=2$). CTC detection was positive in 15 patients (**Figure 1a** and **b**). Sensitivity and specificity were 55.5% (CI 95% [40.1%; 70.9%]) and 100% (CI 95% [75%; 100%]), respectively. The diagnostic accuracy of CTC was 70%. In three cases, CTC detection was not informative because of blood coagulation ($n=2$) and platelet aggregation ($n=1$). Metastatic status, lymph node involvement, vascular invasion, size of tumor, and CA19.9 serum level were not statistically associated with CTC detection, $P=1$, 0.69, 0.70, 0.67, and 0.70, respectively. We suggest that CTC detection be applied as first-line procedure before EUS-FNA in the strategy of pancreatic tumor diagnosis. With the implementation of this blood test on a routine basis, approximately one-half of these patients could avoid invasive EUS-FNA procedure.

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CONFLICT OF INTEREST

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drafting of the manuscript: Paul Basile; acquisition of data, technical support: Emmanuel Toure; acquisition of data: Michel Antonietti, Stephane Lecleire, Aude Di Fiore, Alice Oden-gangloff, France Blanchard, and Francoise Lemoine; study concept and design, drafting of the manuscript: Frederic Di Fiore; critical revision of the manuscript for important intellectual content: Jean Christophe Sabourin; study concept and design, drafting of the manuscript, study supervision: Pierre Michel.

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