Intrapancreatic Accessory Spleen Issues: Diagnostic and Therapeutic Challenges

Nikolaos Arkadopoulos¹, Panagiotis Athanasopoulos¹, Vaia Stafyla¹, Andreas Karakatsanis¹, Vassilios Koutoulidis³, Theodosios Theodosopoulos¹, Eleni Karvouni², Vassilios Smyrniotis¹

¹Second Department of Surgery, ²Pathology Laboratory, and ³First Department of Radiology, Athens University Medical School, Aretaieion Hospital. Athens, Greece

ABSTRACT
Context Intrapancreatic accessory spleen is an exceptionally rare entity, commonly mistaken for a pancreatic neoplasm. Preoperative diagnosis based on radiologic imaging features is difficult. Aspiration cytology may be misleading due to poor sampling. Case report We report a very rare case of an intrapancreatic accessory spleen which radiologically and cytologically mimicked a neuroendocrine pancreatic tumor. Conclusion Modern imaging techniques will probably lead to an increasing number of intrapancreatic accessory spleens being discovered, posing significant diagnostic and therapeutic challenges.

INTRODUCTION
Ectopic accessory splenic tissue can be found anywhere along the splenic vessels, in the wall of the jejunum, in the mesentery, in the greater omentum, in the pelvis or the left scrotum. Though rarely noticed radiologically, it is relatively common, occurring in approximately 10% of the population according to autopsy studies. Accessory spleens are located at or near the splenic hilum in 80% of the cases. In the remainder of the cases it occurs either in the pancreatic tail or close to it [1, 2]. Accessory spleens usually pose no clinical threat and the radiologic findings of the currently advanced imaging techniques are helpful diagnostic tools for avoiding surgery [3]. The only safe diagnostic method is direct sampling, unless it falsely yields pancreatic islet cells, as in our case. In this report we analyze the case of a surgically treated intrapancreatic accessory spleen (IPAS) which radiologically and cytologically mimicked a neuroendocrine pancreatic tumor.

CASE REPORT
A 60-year-old Caucasian male was referred to our clinic for further evaluation and treatment of an incidental solitary mass, in the body of the pancreas, mimicking an endocrine tumor.

Figure 1. Post contrast CT depicting a small enhancing lesion in the body of the pancreas. Arrows show the lesion.

Received March 12th, 2009 - Accepted April 14th, 2009
Key words Endosonography; Neuroendocrine Tumors; Pancreatectomy
Abbreviations HDRBC: heat-damaged red blood cell; IPAS: intrapancreatic accessory spleen; ITP: idiopathic thrombocytopenic purpura; SPECT: single photon emission computed tomography; SPIO: superparamagnetic iron oxide
Correspondence Vaia Stafyla
88 Winchester Court, W8 4AF, London, United Kingdom
Phone: +44-7.503.462.245; E-mail: vstafyla@hotmail.com
Document URL http://www.joplink.net/prev/200907/03.html
In a routine check-up, the patient had a slight elevation of the carbohydrate antigen (CA) 19-9 to 40 U/mL (reference range: 0-37 U/mL). Contrast spiral computed tomography (CT) showed a round homogeneous lesion, 1.2 cm in diameter, located in the upper part of the pancreatic body (Figure 1). Contrast magnetic resonance imaging (MRI) disclosed a round, well-defined mass, 1 cm in diameter, with low signal intensity on T1-weighted images, heterogeneous lesion enhancement during the arterial phase on gadolinium-enhanced T1-weighted images and hyperintensity on fat-saturated T2-weighted images (Figure 2).

Endoscopic ultrasonography (EUS) showed a well-delineated nodule, about 1.2 cm in size, relatively homogeneous with well-defined and smooth margins, increased blood supply and mixed echogenicity. These attributes were compatible with a neuroendocrine tumor. The mass was located in the body of the pancreas, directly peripherally to the celiac trunk and between the pancreatic duct and the gastric wall. No regional lymph nodes or other pathological findings were noted.

An EUS-guided fine needle aspiration (FNA) biopsy resulted in cell clusters of various size, immunopositive for chromogranin, glucagon, gastrin and somatostatin and with a Ki-67 proliferation index less than 2%; these findings were morphologically and immunohistochemically characteristic of a neuroendocrine neoplasm (Figure 3).

Whole body $^{111}$indium-octreotide scintigraphy was negative for somatostatin receptors. During the patient’s preoperative management, laboratory tests did not reveal any abnormal findings nor were there any tumor markers such as carcinoembryonic antigen (CEA), alpha-fetoprotein (AFP) and CA 19-9 (15 U/mL). Serum levels of glucagon, gastrin and somatostatin were reported as 77.2 pg/mL (reference range: 30-210 pg/mL), 20 pg/mL (reference range: 0-110 pg/mL) and 19.3 pg/mL (reference range: 5-27 pg/mL) respectively.

To rule out multiple endocrine neoplasia type 1 syndrome (MEN-1), the following serum hormone levels were measured: parathormone (PTH) intact (82.4 pg/mL; reference range: 15-65 pg/mL), triiodothyronine (T3: 0.9 ng/mL; reference range: 0.7-1.5 ng/mL), thyroxine (T4: 7.4 μg/dL; reference range: 4.5-12 μg/dL), thyroid stimulating hormone (TSH: 1.8 μIU/mL; reference range: 0.4-4.5 μIU/mL), free thyroxine index, (FTI: 9.7μg/dL; reference range: 6.3-12.4μg/dL). Pituitary MRI was unremarkable.

On the basis of the above results, a nonfunctioning endocrine tumor was suspected and a distal pancreatectomy with splenectomy was performed. The surgical specimen contained a round, well-demarcated, smooth, dark-red nodule, 1 cm in diameter, surrounded by pancreatic tissue. No other
lesions were identified grossly, following meticulous sectioning. Microscopically, the nodule had the structure of a spleen. Thus, the mass was diagnosed as an IPAS (Figures 4 and 5). Eight lymph nodes, identified at the splenic hilum, were benign.

**DISCUSSION**

Ectopic splenic tissue can be classified in two categories: splenosis due to autotransplantation of splenic tissue (usually after splenectomy) and accessory spleens which constitute congenital foci of healthy splenic tissue separated from the main body of the spleen [3]. Embryologically, the spleen is derived from mesenchymal tissue which lies between the layers of the dorsal mesogastrium. During the 6th through the 8th weeks of life, the spleen is in close proximity to the most cephalad extension of the mesonephros [4]. After splenorenal fusion, an accessory spleen may be found pararenally and retroperitoneally or it may descend into the pelvis or scrotum [5]. On gross examination, an IPAS is usually surrounded by a fibrotic capsule which separates it from the adjacent pancreatic parenchyma. Its histology is similar to the orthotopic spleen [6]. Lesions or processes regarding the spleen, such as hemosiderosis, leukemia, lymphoma and hypersplenism can affect accessory splenic tissue. Thus, a careful search for accessory spleens should be considered in the differential diagnosis of nodular densities demonstrated by radiologic study of the pancreas [7].

The existence of an IPAS should be considered when a pancreatic mass has the CT densities and/or MRI signal intensities similar to those of the spleen, on the precontrast and contrast-enhanced images of all imaging modalities. In particular, inhomogeneous enhancement of an IPAS in its early phases may be a diagnostic clue. Angiographic demonstration of a splenic blood supply could be helpful in excluding a pancreatic or an adrenal tumor [3, 8].

Differential diagnosis for intra- and peri-pancreatic accessory spleens might include pancreatic neuroendocrine tumors, lymphoepithelial cysts, lymphomas, hypervascular metastases, solid pseudopapillary tumors and pancreatic adeno-
carcinomas [9]. Currently, there are no clinical or radiographic criteria for the diagnosis or differentiation of an IPAS from a malignancy [10].

The Radiological findings and preoperative diagnosis of the referred, surgically resected and pathologically confirmed IPAS are summarized in Table 1. Most cases were initially considered to be nonfunctioning endocrine tumors or islet cell tumors and only one in twelve cases was conclusively diagnosed preoperatively as an IPAS after unsuccessful repetitive surgical treatment for idiopathic thrombocytopenic purpura (ITP). The size ranged from 1.0 to 2.5 cm, with a mean value of 1.55 cm [11]. Non-functioning endocrine tumors account for 15-41% of endocrine pancreatic tumors and the rate of their malignant transformation is 62-92%, depending on the type of tumor [12, 13]. Total tumor resection is the ultimate predictor of long-term survival, independently of size, location, histological differentiation, lymph node involvement and other parameters [14].

Since no cut-off size has been established to differentiate between malignant and benign non-functioning neuroendocrine tumors of the pancreas, it has been suggested that all such tumors greater than 1 cm should be excised if the patient is a good candidate for surgery [15].

On gray-scale baseline ultrasound, an IPAS is usually seen as a round or oval mass with a mildly echogenic and homogeneous texture, surrounded by a high-amplitude interface and showing enhancement behind the lesion. On color or power Doppler ultrasound, a characteristic blood supply (representing the vascular hilum entering the mass), has been reported to offer a 90% sensitivity in the diagnosis of an IPAS [16]. In contrast-enhanced ultrasonography (CEUS) using Levovist® (Schering, Berlin, Germany), an IPAS shows inhomogeneous enhancement in the early vascular phase, enhancement similar to that of spleen during the postvascular phase and prolonged enhancement in the hepatosplenic parenchymal phase [17].

Findings at EUS include a round-to-oval lesion with sharp regular margins and homogenous echo texture, ranging from hypo- to hyper-echoic [18]. EUS-guided FNA cytology reveals a population of predominantly

---

**Figure 4.** Intrapancreatic spleen (H&E, x100). Arrow shows the wall of the lesion.

**Figure 5.** Spleen, white and red pulp (H&E, x100).
small lymphocytes and a mixed inflammatory infiltrate representing white pulp. A conspicuous vascular component comprised of thin-walled blood vessels representing the splenic sinuses is also observed. These sinuses are well-visualized on cell block sections. Interestingly, the plump splenic sinus endothelial cells characteristically immunostain for CD8, which is more commonly recognized as a T-cell marker. Staining appears to be specific, because systemic endothelial cells and hemangiomas are negative for CD8 [19, 20, 21]. In cases where FNA of the accessory spleen yields only lymphocytes, without other splenic elements, flow cytometry and immunohistochemistry can be employed to exclude a lymphoproliferative disorder, including Hodgkin’s lymphoma, even if a definitive diagnosis of accessory spleen cannot be confirmed [22, 23]. Schreiner et al. reported three cases of IPAS being diagnosed by EUS-guided FNA biopsy [24]. In our case, probably due to sampling of islet cell clusters from the adjacent pancreatic parenchyma, the same procedure was indicative of a neuroendocrine tumor, leading to surgical overtreatment.

A similar false positive EUS-FNA, in which a pancreatic splenic nodule was mistaken for an islet cell tumor has also been reported by Ardengh et al. [25]. In general, EUS-FNA has a high (80-90%) sensitivity and specificity for pancreatic neuroendocrine tumors although its accuracy for such tumors is considered to be lower than that for pancreatic adenocarcinoma [26]. In order to minimize diagnostic errors, EUS-FNA of small neuroendocrine tumors should be performed by experienced endoscopist and cytopathologic assessment should be combined with immunohistochemistry [25]. 

99mTc-Technetium heat-damaged red blood cells (99mTc-HDRBC) scintigraphy, combined with single photon emission computed tomography (SPECT), is a highly sensitive and specific method for detection of splenic tissue, since up to 90% of the injected HDRBCs are trapped by this tissue [27]. Although scintigraphy allows selective splenic visualization with an excellent spleen-to-liver ratio, splenic visualization is still difficult in conditions in which minimally functioning splenic tissue is present, as in cases of accessory spleens [8]. Furthermore, scintigraphy, even with

### Table 1. Surgically resected intrapancreatic accessory spleen (IPAS).

<table>
<thead>
<tr>
<th>Case</th>
<th>Author</th>
<th>Year</th>
<th>Sex/Age</th>
<th>Size (cm)</th>
<th>Preoperative diagnosis</th>
<th>CT findings</th>
<th>MRI findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>Takayama et al. [29]</td>
<td>1994</td>
<td>F/62</td>
<td>1.2</td>
<td>Asymptomatic endocrine tumor</td>
<td>Enhanced CT and angiography: well-defined hypervascular mass</td>
<td>-</td>
</tr>
<tr>
<td>#2</td>
<td>Harris et al. [30]</td>
<td>1994</td>
<td>F/50</td>
<td>1.5</td>
<td>Islet cell tumor</td>
<td>-</td>
<td>MRI: low signal on T1, increased signal on contrast-enhanced T1, bright signal on T2</td>
</tr>
<tr>
<td>#3</td>
<td>Chatei et al. [8]</td>
<td>1998</td>
<td>M/38</td>
<td>2.0</td>
<td>Islet cell tumor or non-functioning adenoma</td>
<td>Enhanced CT: homogeneously enhanced mass</td>
<td>MRI: low signal on T1, homogeneous enhancement on enhanced T1, high signal on T2</td>
</tr>
<tr>
<td>#4</td>
<td>Lauffer et al. [31]</td>
<td>1999</td>
<td>M/71</td>
<td>1.5</td>
<td>Pancreatic neoplasm</td>
<td>Enhanced CT: hypervascular, homogeneous enhancement</td>
<td>-</td>
</tr>
<tr>
<td>#5</td>
<td>Sica and Reed [32]</td>
<td>2000</td>
<td>F/40</td>
<td>2.5</td>
<td>Solid enhancing mass</td>
<td>CT: focal, mass-like enlargement on plain CT</td>
<td>MRI: iso- to mildly hyperintense on T2, low on T1, moderate homogeneous enhancement on enhanced T1</td>
</tr>
<tr>
<td>#6</td>
<td>Brasca et al. [33]</td>
<td>2004</td>
<td>F/52</td>
<td>1.0</td>
<td>Non-functional neuroendocrine tumor</td>
<td>-</td>
<td>MRI: mildly hyperintense on T2, hypointense on T1, conspicuous enhancement on enhanced T1</td>
</tr>
<tr>
<td>#7</td>
<td>Hamada et al. [34]</td>
<td>2004</td>
<td>M/61</td>
<td>1.5</td>
<td>Nonfunctioning endocrine tumor</td>
<td>CT: well-defined isodense mass on plain CT, homogeneously enhanced mass on enhanced CT.</td>
<td>-</td>
</tr>
<tr>
<td>#8</td>
<td>Davidoff et al. [35]</td>
<td>2006</td>
<td>M/66</td>
<td>1.6</td>
<td>Non-functioning neuroendocrine tumor</td>
<td>Enhanced CT: hypervascular tumor.</td>
<td>-</td>
</tr>
<tr>
<td>#9</td>
<td>Kim et al. [28]</td>
<td>2006</td>
<td>M/45</td>
<td>1.2</td>
<td>Islet cell tumor</td>
<td>CT: slightly higher attenuation, than the spleen, on the portal venous phase</td>
<td>MRI: slightly higher intensity on T2</td>
</tr>
<tr>
<td>#10</td>
<td>Kim et al. [28]</td>
<td>2006</td>
<td>F/30</td>
<td>2.5</td>
<td>ITP because of IPAS</td>
<td>CT: lobulated and high attenuating nodule in the pancreatic tail and two accessory spleens</td>
<td>MRI: low intensity on T1, high intensity on T2</td>
</tr>
<tr>
<td>#11</td>
<td>Uchiyama et al. [11]</td>
<td>2007</td>
<td>F/81</td>
<td>1.1</td>
<td>Non-functioning endocrine tumor</td>
<td>CT: isodensity on plain CT Homogeneously enhanced tumor</td>
<td>MRI: isointensity on T1, iso- to high intensity on T2</td>
</tr>
<tr>
<td>#12</td>
<td>Present case</td>
<td>2009</td>
<td>M/60</td>
<td>1.0</td>
<td>Non-functioning endocrine tumor</td>
<td>Contrast spiral CT: round homogeneous lesion in the pancreatic body</td>
<td>MRI: round, well-defined mass with low intensity on T1, heterogeneous enhancement during the arterial phase on contrast-enhanced T1, hyperintensity on fat-saturated T2</td>
</tr>
</tbody>
</table>

ITP: idiopathic thrombocytopenic purpura
SPECT, offers inferior spatial resolution compared to other cross-sectional imaging modalities such as CT or MRI. Therefore, scintigraphy is frequently used in conjunction with other cross-sectional imaging techniques. Moreover, superparamagnetic iron oxide (SPIO)-enhanced MRI is reported as an excellent alternative to 99mTc-HDRBC scintigraphy, when an IPAS has a signal drop similar to that of the spleen. In addition to the referred signal drop, another difference between IPASs and hypervascular pancreatic neoplasms is the heterogeneous enhancement on arterial phase CT scan [28].

Accessory spleens may need surgical treatment when they mimic lymphadenopathies or tumors, or when they become symptomatic due to torsion, spontaneous rupture, hemorrhage or cyst formation. All functional splenic tissue should also be removed for the treatment of hematologic disorders such as ITP.

In conclusion, modern imaging techniques will probably lead to an increasing number of intra-pancreatic accessory spleens being discovered in the future, posing significant diagnostic and therapeutic challenges. In such cases all non-invasive diagnostic means should be used in order to obviate unnecessary surgical procedures and decrease overall patient morbidity [3].

Conflict of interest The authors have no potential conflicts of interest

References