

# Pancreatic Ganglioneuroma Presenting in an Octogenarian

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## ABSTRACT

Pancreatic ganglioneuromas occur mostly in children and rarely in young adults, with no cases reported in adults older than 60 years. An 86-year-old woman, with active advanced multiple myeloma, presented with epigastric pain for 2 days. Abdominal and pelvic computed tomography demonstrated a distended gallbladder, mildly dilated biliary tree, and a 13 × 8-mm hypodense mass in pancreatic body, without extrapancreatic invasion at endoscopic ultrasound. Fine-needle endoscopic ultrasound-guided core biopsy revealed characteristic histopathology of ganglioneuroma, as confirmed by immunohistochemical positivity for S100, SOX-10, and synaptophysin. This demonstrates novel finding of pancreatic ganglioneuroma occurring in the elderly. Lesion inclusion in the differential diagnosis may mandate tissue for pathologic diagnosis and complete lesion resection.

## INTRODUCTION

Pancreatic ganglioneuroma is a rare, usually benign, well-differentiated variant of neuroblastic tumors that arise in pancreas.<sup>1-3</sup> The tumor typically presents in childhood, extremely rarely presents in young adulthood, with only 5 cases reported in adults, mostly in their twenties, and has never been reported in adults older than 60 years.<sup>3</sup> A case is reported of this rare pancreatic tumor and its novel presentation in an octogenarian. This report extends the age spectrum of presentation, which is clinically important because this tumor (i) requires tissue for definitive diagnosis because imaging findings are generally nonspecific; (ii) requires screening for neuroendocrine tumors regardless of symptomatology; and (iii) generally requires complete resection because of rare, late, metastases.

## CASE REPORT

An 86-year-old woman, with active advanced multiple myeloma, and multiple compression fractures secondary to severe osteoporosis treated by kyphoplasty, presented with right upper quadrant and epigastric pain and nausea for 2 days. Physical examination revealed normal vital signs, dry mucous membranes, a soft, nondistended abdomen, with mild right upper quadrant and epigastric tenderness, normoactive bowel sounds, and no hepatosplenomegaly. Laboratory tests revealed hemoglobin of 8.7 g/dL, leukocyte count of 5.6 bil/L, platelet count of 170 bil/L, creatinine of 0.8 mg/dL, blood urea nitrogen of 24 mg/dL, calcium of 10.7 mg/dL, and albumin of 2.75 g/dL. Alkaline phosphatase, aspartate aminotransferase, alanine aminotransferase, total bilirubin, and lipase were normal.

Urinalysis revealed 100 mg/dL of proteinuria. Quantitative serum immunoglobulins revealed immunoglobulin A of 2,360 mg/dL, IgG of 320 mg/dL, and IgM of 10 mg/dL. Free light chains had free kappa of 0.87 mg/dL, and free lambda of 10.16 mg/dL, for a free K/L ratio of 0.09. Serum protein electrophoresis revealed IgA lambda monoclonal gammopathy of 1.8 mg/dL. Urine protein electrophoresis revealed free lambda chains and a small amount of comigrating IgA lambda monoclonal protein (<50-mg/24-hour protein).



**Figure 1.** Abdominal computed tomography (A) axial section showing 13 × 8-mm hypodense pancreatic mass (horizontal arrow), and dilated CBD at 13 mm wide (vertical arrow) and (B) coronal section showing hypodense pancreatic mass (arrow), and dilate gallbladder (star).

Abdominal ultrasound showed heterogeneous hepatic echotexture,  $\geq 5$  hepatic cysts, dilated biliary tree, and 12-mm-wide common bile duct. Abdominal and pelvic computerized tomography (CT) with intravenous and oral contrast, and abdominal and pelvic CT, per pancreatic protocol, with intravenous contrast but not oral contrast, demonstrated a 13 × 8-mm hypodense mass in pancreatic body, distended gallbladder, dilated biliary tree, 13-mm-wide common bile duct, 4-mm-wide proximal pancreatic duct, and  $\geq 5$  hypodense hepatic cysts (Figure 1). Magnetic resonance cholangiopancreatography could not be performed because of patient's claustrophobia. Therapeutic endoscopic retrograde pancreatography was offered to the patient because of her moderately dilated biliary tree and distended gallbladder, but the patient refused because her liver function tests were all normal and her right upper quadrant pain had remitted.

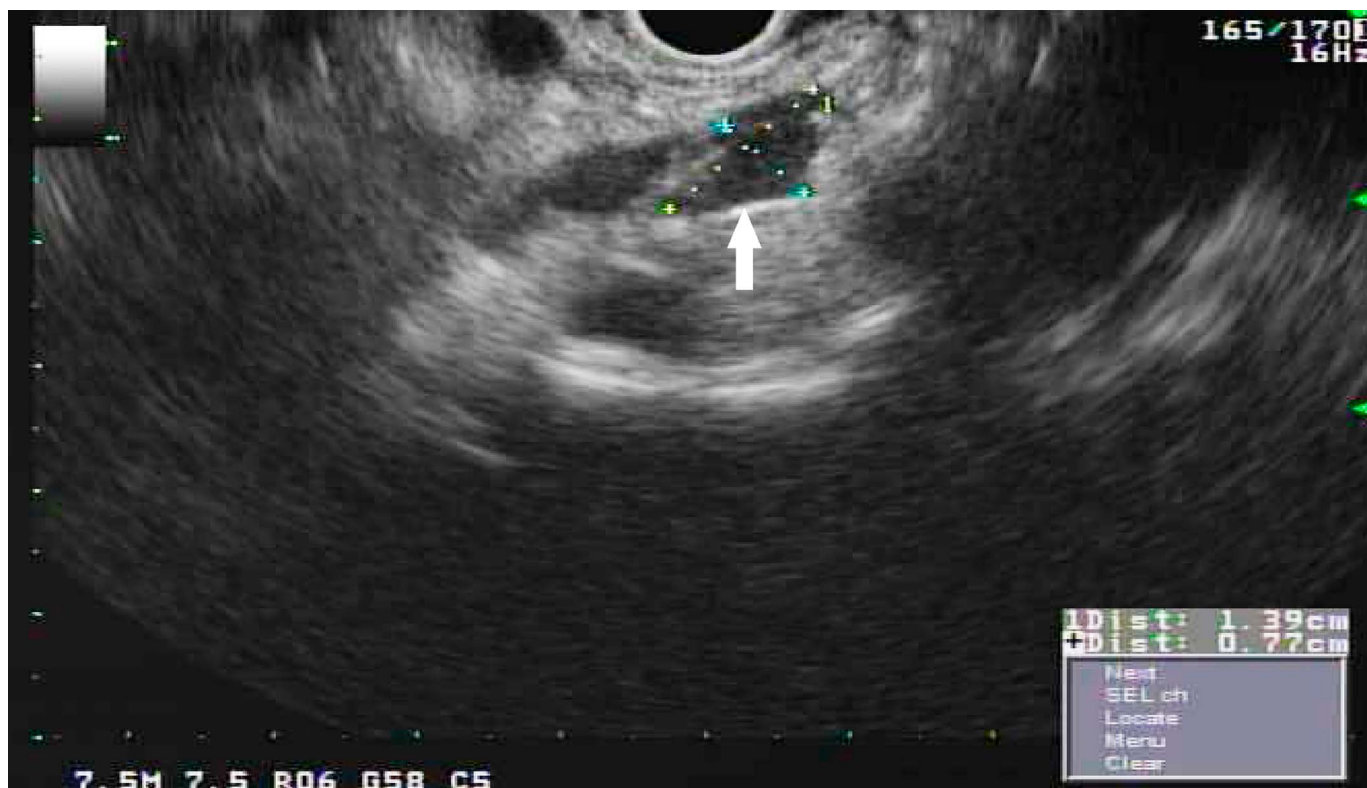
Endoscopic ultrasound (EUS) showed a 14 × 9-mm irregular hypoechoic mass in pancreatic body with well-defined borders, without extrapancreatic invasion (Figure 2). Histopathology using hematoxylin and eosin stain of a fine-needle EUS-guided core biopsy revealed characteristic findings of ganglioneuroma, as confirmed by immunohistochemistry showing positivity for S100, synaptophysin, and SOX-10 (Figure 3). The patient had no symptoms of catecholamine excess, sometimes associated with this tumor. The tumor was

not excised because of her poor prognosis from advanced multiple myeloma. Patient was discharged to inpatient rehabilitation, and went home 2 weeks later, after symptomatically improving, for management of multiple myeloma and ganglioneuroma. Patient expired 4 months later from severe metastatic disease.

## DISCUSSION

Ganglioneuromas are rare, benign, tumors derived from neural crest cells, that are histologically composed of mature Schwann and ganglion cells within fibrous stroma.<sup>3,4</sup> Ganglioneuromas are a member of a group of neurogenic tumors that includes ganglioblastomas and neuroblastomas, but differ in generally being benign.<sup>5</sup> Common tumor locations include posterior mediastinum—41.5%, retroperitoneum—37.5%, adrenal glands—21%, and neck—8%.<sup>6</sup>

Ganglioneuromas often pose diagnostic challenges because they are frequently asymptomatic and have nonspecific imaging characteristics, but occasionally cause symptoms by compressing adjacent organs.<sup>1-3</sup> Pancreatic ganglioneuromas appear as homogenous masses on abdominal ultrasound with nonspecific features.<sup>3</sup> High-dose contrast-enhanced CT occasionally reveals speckled tumor calcifications.<sup>3</sup> The disease is, however, definitively diagnosed by pathologic examination of



**Figure 2.** Endoscopic ultrasound showing irregular, hypoechoic mass in the pancreatic body with well-defined borders (arrow). The mass measures 14 mm × 9 mm as indicated by measuring dots.

resected specimens. EUS with fine-needle aspiration for cytologic and immunohistochemical testing can demonstrate that the mass is neurogenic, but cannot specify tumor subtype, but EUS with fine-needle core biopsy is usually diagnostic.<sup>7</sup> This tumor was diagnosed as a ganglioneuroma by characteristic histopathologic findings with hematoxylin and eosin staining, supplemented by characteristic staining patterns with S100, SOX-10, and synaptophysin.<sup>8</sup> Tumor resection is recommended to prevent rare metastasis if not excised.<sup>1,3,9</sup> Even if tumor excision is problematic, incomplete resection is sufficient as the likelihood of progression is low for tumors <2 cm.<sup>1</sup> Tumors >2 cm may progress after incomplete resection.<sup>1</sup> Comprehensive literature review revealed no cases of minimally invasive therapy for ganglioneuromas, such as endoscopic ultrasound–guided radiofrequency ablation. This may be related to the rarity of this tumor.

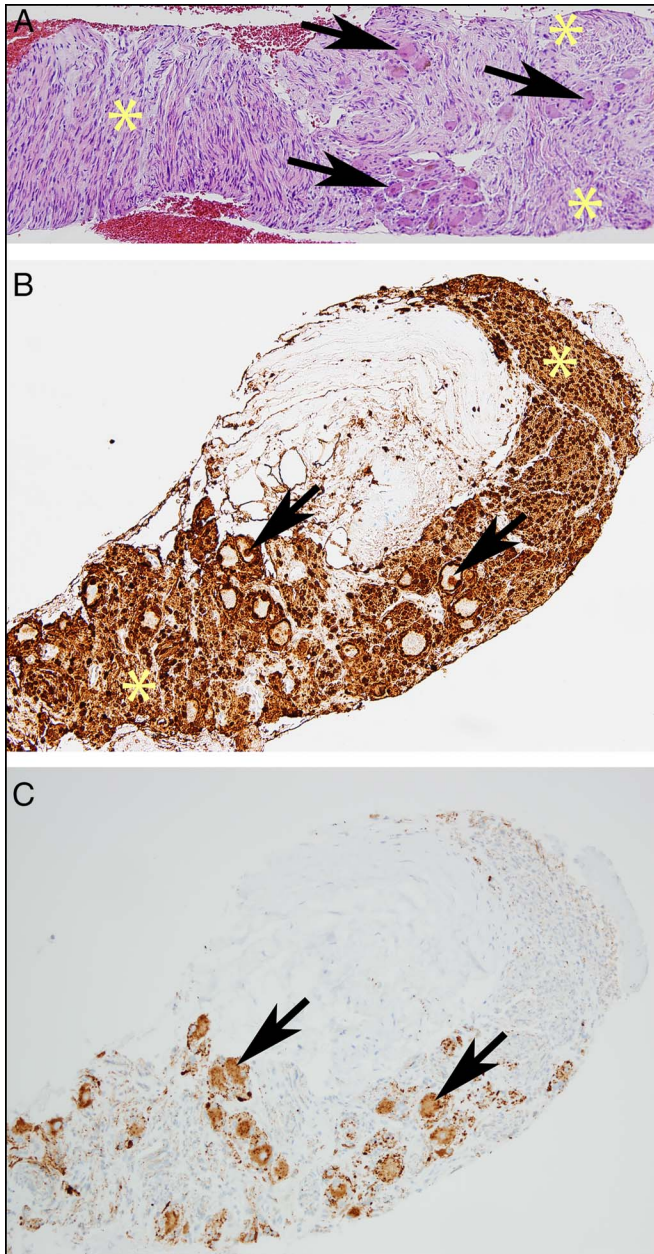
Ganglioneuromas rarely produce secretory vasoactive polypeptide, androgenic hormones, and catecholamines, especially vanillylmandelic acid and homovanillic acid.<sup>10</sup> Patients can develop symptoms, including headaches, diaphoresis, palpitations, and diarrhea, from hormonal secretions. A limitation of this case report is that catecholamine levels should have been determined, although she had no symptoms of catecholamine excess and had a poor prognosis from her advanced multiple myeloma. Patients with pancreatic ganglioneuromas should be tested for hormonal secretions, regardless of

symptomatology.<sup>10</sup> The tumor was not excised because of her high surgical risks from her advanced multiple myeloma.

The patient presented with poor nutritional status as indicated by hypoalbuminemia. This abnormality was largely attributable to her advanced multiple myeloma, but the pancreatic ganglioneuroma could have contributed somewhat to this abnormality. The patient did not undergo any imaging outside of the abdomen and pelvis to exclude metastases from the pancreatic ganglioneuroma because the patient's prognosis was extremely poor from the known, advanced multiple myeloma.

Pancreatic ganglioneuromas have been previously reported only in patients younger than 60 years, including mostly patients younger than 20 years.<sup>3,5,6</sup> Despite the above limitation, this case report demonstrates the novel finding that pancreatic ganglioneuroma can occur in patients older than 60 years. This is clinically significant. When this tumor is in the differential diagnosis of pancreatic lesions in elderly patients, workup generally requires (i) tissue for definitive pathologic diagnosis because of generally nonspecific imaging findings; (ii) screening for neuroendocrine hormones regardless of symptomatology; and (iii) complete resection to prevent rare, late, metastases. Occurrence of pancreatic ganglioneuromas in elderly patients has not been previously reported. It is typically clinically silent and discovered incidentally by radiologic imaging. Definitive diagnosis and treatment involve complete surgical extirpation,





**Figure 3.** Histopathology of ganglioneuroma tumor (A) medium power photomicrograph of hematoxylin and eosin–stained section of tumor shows an admixture of small-sized, prominent, spindle-shaped Schwann cells (\*), mostly present on the left, and clusters of large ganglion cells (arrows), mostly present on the right. (B) S-100 immunohistochemical positivity (brown color) present in nuclei and cytoplasm of Schwann cell component (\*), as well as in nuclei of the larger ganglion cells (arrows). (C) SOX-10 immunohistochemical positivity (brown color) present in nuclei and cytoplasm of Schwann cell component (\*). The ganglion cell component of the tumor lacks immunohistochemical positivity for SOX-10.

despite the benign nature of the tumor, because of potential late metastases. This work reports occurrence of pancreatic neuroganglioma in an octogenarian. In cases of an incidentally detected pancreatic mass, lacking distinctive radiologic

features, ganglioneuromas should be considered in the differential even in an octogenarian, and further abdominal imaging and biopsy is warranted.

## DISCLOSURES

Author contributions: AA Shaheen, I. Gill, AI Edhi, and MS Cappell wrote the manuscript. M. Amin performed and interpreted the pathology. AA Shaheen and MS Cappell are primary authors and contributed equally to this manuscript.

Financial disclosure: M. Cappell, as a consultant of the U.S. Food and Drug Administration (FDA) Advisory Committee for Gastrointestinal Drugs, 2014–2019, affirms that this article does not discuss any proprietary, confidential, pharmaceutical data submitted to the FDA. He was a member of the speaker's bureau for AstraZeneca and Daiichi Sankyo, comarketers of Movantik until >2 years ago. M. Cappell received 1-time honoraria from Shire and Mallinckrodt >2 years ago. This work does not discuss any drug manufactured or marketed by AstraZeneca, Daiichi Sankyo, Shire, or Mallinckrodt.

Informed consent was obtained for this case report.

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