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## Nonfunctional paraganglioma of the head of the pancreas: A rare case report



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## ABSTRACT

**BACKGROUND:** Paragangliomas are rare neoplasms that originate from the neural crest. They are malignant in approximately 10% of cases, with a 50% survival rate at 5 years from diagnosis. In most cases, manifestations of malignancy (such as metastasis) are lacking, and paragangliomas are considered benign lesions. Pancreatic paragangliomas are extremely rare, with only 31 cases described in the scientific literature to date.

**CASE SUMMARY:** Here we describe a case of a 55-year-old Caucasian male patient referred to our institution in September 2013 for lumbar pain lasting five months. The ultrasound and the CT scan revealed a 2.5 cm solid nodule located in the uncinat process of the pancreas. On the basis of this evidence, the preoperative diagnosis was a pancreatic neuroendocrine tumor (NET), which was further confirmed by a subsequent In-Pentetreotide Scan examination. A pylorus-preserving duodenocephalopancreatectomy was performed. Pancreatic paraganglioma was the final pathological diagnosis. Rare localizations of paraganglioma are often discovered casually, during imaging examinations for other clinical reasons, as happened in the case of our patient. It appears evident that the preoperative diagnosis of pancreatic paragangliomas is extremely challenging. Surgery represents the cornerstone of the clinical management of these neoplasms, primarily for the need of a definitive diagnosis, which is difficult to assess preoperatively in most cases.

**CONCLUSIONS:** Our strategy is the same as that adopted for the management of pancreatic NETs; the dimensional limit for a conservative resection is 2 cm, while major resections (Whipple's approach or distal pancreatectomy) should be employed in larger tumors, which are generally associated with a worse prognosis.

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### 1. Introduction

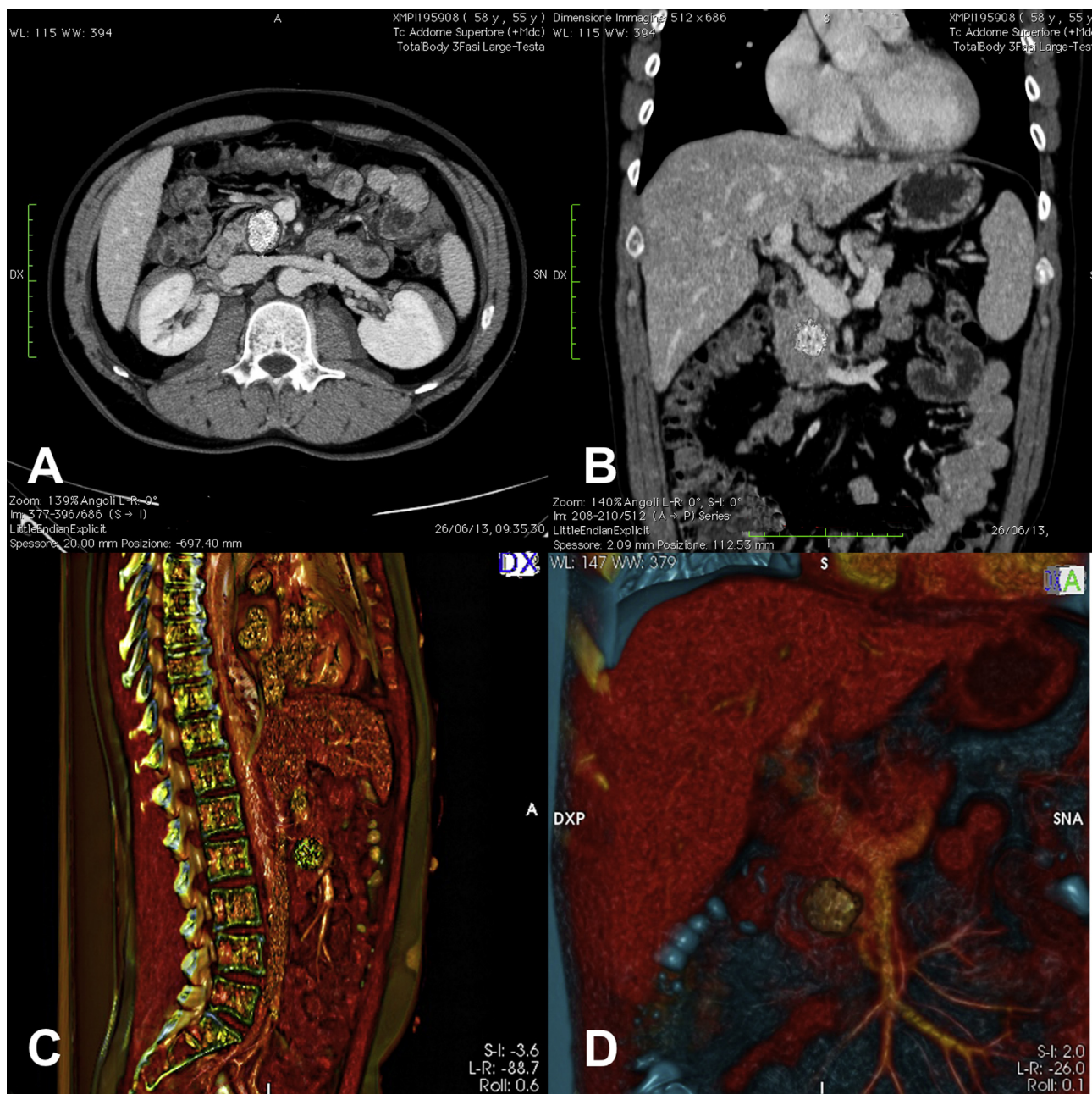
Paragangliomas are rare neoplasms that originate from the neural crest and involve both the sympathetic and parasympathetic ganglia [1]. They are malignant in approximately 10% of cases, with a 50% survival rate at 5 years from diagnosis. In most cases, manifestations of malignancy (such as metastasis) are lacking, and paragangliomas are considered benign lesions. Pancreatic paragangliomas are extremely rare, with only 31 cases described in the scientific literature to date.

### 2. Case report

A 55-year-old Caucasian male patient was referred to our institution in September 2013 for lumbar pain lasting five months. Inflammatory, degenerative and rheumatic alterations were excluded by clinical examination, while the clinical examination of the abdomen did not evidence any manifestation of disease. The subsequent ultrasonographic (US) examination revealed a 2.5 cm solid nodule, located in the uncinat process of the pancreas. The lesion was further studied by contrast enhancement ultrasound (CEUS) and computed tomography (CT) scan (Fig. 1A and B). Arterial phase hypervascularity and slow wash-out were observed (Fig. 1C and D), leading to the hypothesis of a neuroendocrine pancreatic tumor (NET), which was further confirmed by a subsequent In-Pentetreotide Scan examination. The patient had no personal or family history of neoplastic diseases. All the biochemical tests returned results within normal ranges, including

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**Fig. 1.** A–B Computed tomography (CT) scan “arterial phase” showed a hypervascularity and slow wash-out. B–C Computed tomography (CT) scan showed a 2.5 cm solid nodule located in the uncinate process of the pancreas.

chromogranin, blood catecholamines, and urinary metanephrines, as well as serum tumor markers (Ca19-9, CEA, Ca15-3). On the basis of this evidence, the preoperative diagnosis was a pancreatic NET. A pylorus-preserving duodenocephalopancreasectomy was performed in September 2013.

On gross pathological examination the pancreatic lesion measured 1.3 cm, was brownish in color, solid consistency, and well-circumscribed. Microscopically, the lesion was organized in nests of variable dimensions, with numerous blood vessels and hemorrhagic areas (Fig. 2a). The neoplastic cells showed high variability in size and shape. The nuclei were pleomorphic, sometimes very large, and the cytoplasm abundant, finely granular and eosinophilic (Fig. 2b). Strong immunohistochemical positivity for chromogranin A and synaptophysin was observed (Fig. 2c), as well

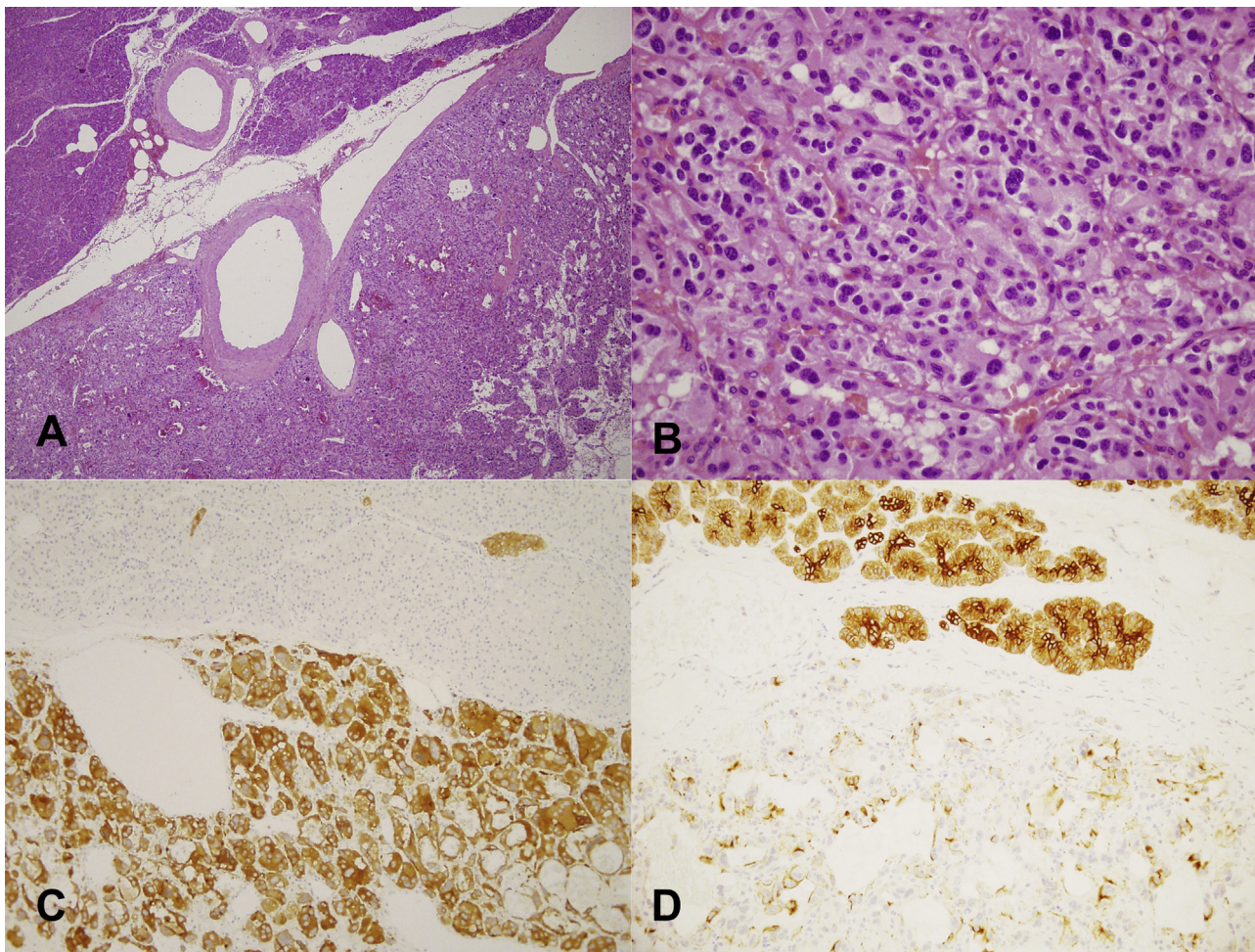
as focal positivity for S100 and somatostatin, while cytokeratins (CAM 5.2) (Fig. 2d) and AE1/AE3 were negative. The final pathological diagnosis was pancreatic paraganglioma.

The patient was discharged on the 15th postoperative day. He underwent a CT scan of the lungs at periods of six months, one year and two years postoperatively, with no evidence of progression of the lung nodule discovered. He is currently alive and disease free. Informed consent for the publication of the present report was obtained; the CARE guidelines were employed for reporting [2].

### 3. Discussion

Paragangliomas are neoplasms originating from the ganglia of the autonomous nervous system, which usually involve both the





**Fig. 2.** A (H&E, 4 $\times$ ) – Hematoxylin and eosin staining showing well circumscribed tumor with numerous blood vessels. B (H&E, 40 $\times$ ) – The tumor cells are arranged in nests (“Zellballen”) bound by sustentacular cell and fibrovascular stroma. Nuclear atypia is common and is not an expression of malignancy. C (synaptophysin, 10 $\times$ ) – Immunohistochemistry of the “Zellballen” neoplastic cells demonstrates positivity for synaptophysin; the normal pancreas is negative. D (CAM 5.2, 20 $\times$ ) – Immunohistochemistry showed negative staining in neoplastic cells for cytokeratin (CAM5.2) and positive staining in non-neoplastic pancreatic cells.

sympathetic and parasympathetic ganglia equally [1]. The former, in their extra-adrenal manifestation, affects mainly the sympathetic chain, while the latter affects generally the head and the neck, especially the ganglia of the vagus and glossopharyngeal nerves. Other localizations, such the one described in our case, are extremely rare [3]. Globally, paragangliomas are rare tumors, with a prevalence of 0.8 cases per 100,000 inhabitants, and approximately 500–1600 new cases per year estimated in the United States.

The gross appearance of paragangliomas is that of a richly vascularized mass, growing typically near to large blood vessels or nerves. Nevertheless, from a histological point of view, differential diagnoses with meningiomas, schwannomas, hemangiopericytomas, melanomas, and various metastatic carcinomas may be challenging [4]. Fortunately, immunohistochemical positivity for neurospecific enolase (NSE), synaptophysin, chromogranin, and no staining for cytokeratins, is diagnostic of paragangliomas [5]. The only certain element of malignancy is, usually, the presence of metastasis [6]. It is evident that the diagnosis of a paraganglioma is often obtained thanks to its clinical manifestations, such as the anatomical localization of the lesion and the presence of hyperadrenalism; clinical diagnosis is difficult in cases of a rare localization, like the case we describe herein, which involve the pancreatic or peripancreatic chromaffin cells.

Paragangliomas of the pancreas are often discovered incidentally, during imaging examinations for other clinical reasons, as

happened in our case. When symptomatic, the clinical manifestations of paragangliomas are due to the compression of neighboring anatomical structures; abdominal pain, dyspepsia, weight loss, and asthenia are the commonest ones. Only 31 similar cases have been described in the scientific literature, this makes the real pancreatic lesions rarer, and the scientific data on their management poorer. The natural history of the disease appears relatively benign. Only in a few cases have loco-regional lymph node involvement or distant metastasis been reported; the liver and the right adrenal gland were the organs affected by distant metastasis in the cases described in literature. Furthermore, no correlations between the dimensions of the lesions and their clinical course were evidenced. Surgery represents the cornerstone of the clinical management of pancreatic paragangliomas, primarily for the need of a definitive diagnosis, which is difficult to assess preoperatively in most cases.

In conclusion, the rarity of these neoplasms makes their clinical management and follow-up really challenging. The choice between a conservative approach, which leads to diagnosis but may require re-intervention to achieve the oncological clearance, or an a priori radical approach, is still a matter of debate. Our strategy is the same as that adopted for the management of pancreatic NETs, described in recent consensus guidelines; the dimensional limit for a conservative resection is 2 cm, while major resections (Whipple's approach or distal pancreatectomy) should be employed in larger tumors, which are generally associated with a worse prognosis.

### Conflict of interest

All authors have no substantial direct or indirect commercial financial incentive associated with publishing the manuscript.

### Authors contribution

Michele Barmina: Writing paper Giorgio.  
C. Ginesu: Writing paper.  
Panagiotis Paliogiannis: Writing paper.  
Maria L. Cossu: Data analysis.  
Claudio F. Feo: Text edit.  
Francesca Addis: Data collection.  
Trombetta Matilde: Data analysis.  
Alberto Porcu: Text edit.

### Ethical approval

Informed consent was obtained from the patient; all authors ensure that all text and images alterations to protect anonymity do not distort scientific mean of the manuscript.

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The study sponsors had no such involvement.

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