ANNALI ITALIANI DI CHIRURGIA

Digital Edition
e-publish on-line
ISSN 2239-253X
Direttore Nicola Picardi

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Ann Ital Chir, 2023; 12 - Nov. 13
pii: S2239253X23039737
Online Epub

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Management of incidental pancreatic neuroendocrine tumor: a case report with literature review

BACKGROUND: *Pancreatic neuroendocrine tumors (PNETs) are rare and accounting for less than 5% of all pancreatic neoplasms. Their management depends on dimension of the lesion, main pancreatic duct (MPD) caliber, tumor malignancy features and evolutive potential.*
CASE REPORT: *Incidental finding of a lesion 1.2 cm wide of the pancreatic body, after contrast enhanced total body CT, in a 71 years old obese Caucasian male (BMI>25), during follow-up for cutaneous melanoma. The lesion was confirmed by MRI and 68-Ga pancreatic scintigraphy. EUS showed a second hypoecogenic and hypovascularized lesion compatible with pancreatic tail PNET. After FNB, Ki-67 was below 3%.*
DISCUSSION: *68-Gallium PET-CT was the preferred technique for the staging of the neuroendocrine neoplasm, for treatment planning, for the localization of the pancreatic lesion, excluding the presence of unknown extra-pancreatic lesions. EUS-FNB is indicated in patient with suspicion of PNET, although further investigation is needed to include it as a routine diagnostic examination.*
CONCLUSION: *Surgery is mandatory in case of PNETs larger than 2 cm, with MPD dilation, Ki-67>20% and compression symptoms.*

KEY WORDS: Case report, Management, Neuro Endocrine Tumor, NET, Pancreatic Neuro Endocrine Tumor, PNET

Introduction

Pancreatic neuro-endocrine tumors (PNETs) are uncommon neoplasms, accounting for less than 5% of pancreatic tumors, with an incidence of 1-1.5 cases/100.000 [1].

These tumors are classified as functional or non-functional depending on whether they release peptide hormones that produce specific hormone-related symptoms [2].

In more than half cases PNETs are non-functional, leading to a late diagnosis, mostly based on a secondary mass effect or on metastasis suggestive findings [3,4]. The spontaneous rupture of PNETs is an extremely rare event cause of acute abdomen [5].

In some cases diagnosis is incidental during instrumental exams for other diseases, leading to an increase in the incidence of PNETs in recent years [6]. Diagnosis of a PNET is based on serologic (hormonal) tests, instrumental and histological examinations [7].

Pervenuto in Redazione Maggio 2023. Accettato per la pubblicazione Giugno 2023
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Contrast enhanced CT and MRI are mandatory for the diagnosis; an instrumental finding of a dilated main pancreatic duct (MPD) is considered a feature of increased aggressiveness [8].
Typically, PNETs express Somatostatin receptors on their cell membrane providing a target for instrumental diagnosis, stadiation, for Somatostatin analogues based therapy and for clinical response evaluation [9,10].
[68] Ga-DOTATATE PET TC is the most sensitive imaging exam for PNETs identification [11].
In all cases with a suspicion of PNET, fine needle aspiration (FNA) or fine needle biopsy (FNB) during endoscopic ultrasonographic evaluation is necessary, as it allows further investigation for genetical mutations and histological features of increased aggressiveness (Ki-67>20%) [12].
In clinical practice EUS-FNB is preferred as it provides a higher amount of information [13].
For some Authors the role of plasmatic Chromogranin A (CgA) titration is of high usefulness in diagnosis and response to treatment evaluation while other Authors, on the contrary, find it as a marker of low significance [14,15] .
PNETs larger than 3 cm in diameter show a tendency to metastasize, showing an heterogeneous post-contrastographic enhancement during imaging exams.
For some Authors, surgery is the treatment of choice in functioning PNETs larger than 2 cm, and in non-functioning tumors with symptoms of compression [16].
More recently, guidelines suggest watchful waiting for asymptomatic PNETs up to 2 cm in diameter [17-19].
Palliative treatment is indicated in cases of disseminated disease or unresectable liver metastases [4] . Poorly-differentiated PNETs have a poor prognosis and are treated by chemotherapy, while patients with higher differentiated neoplasms (G1-G2) show better response to medical treatment [3,10] .

Case report

A 71 years old obese (BMI>25) Caucasian male, with recent history of cutaneous melanoma of the left lumbar region (pT1b), with negative ipsilateral axillary sentinel lymph-node, was submitted to contrast-enhanced total body CT scan during melanoma follow-up.
Incidentally, it showed a hypervascularized lesion 1.2 cm wide located at the pancreatic body-tail passage (Fig. 1).
The lesion was confirmed by CE-MRI without dilation of the MPD (Fig. 2).
68 Ga-DOTATATE PET-CT showed pathological hyperfixation in correspondence of the aforementioned lesion (Fig. 3).
During EUS, a double hypoecogenic lesion was found, the larger one 12 mm wide located in the tail, the smaller about 3.8 mm wide at the isthmus. Both lesions showed contrast enhancement (Sonovue) (Fig. 4).

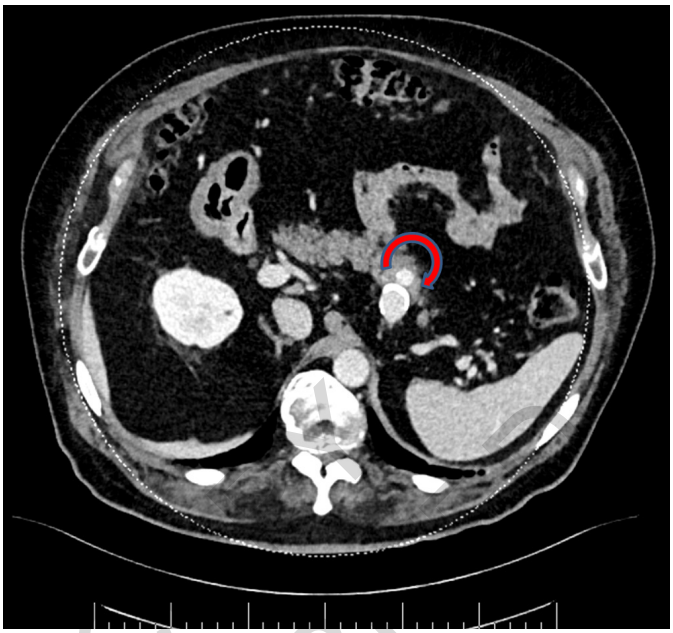

Fig. 1: Abdominal contrast-enhanced CT scan. Axial image: A well-defined nodular aspect of the area (arrow).

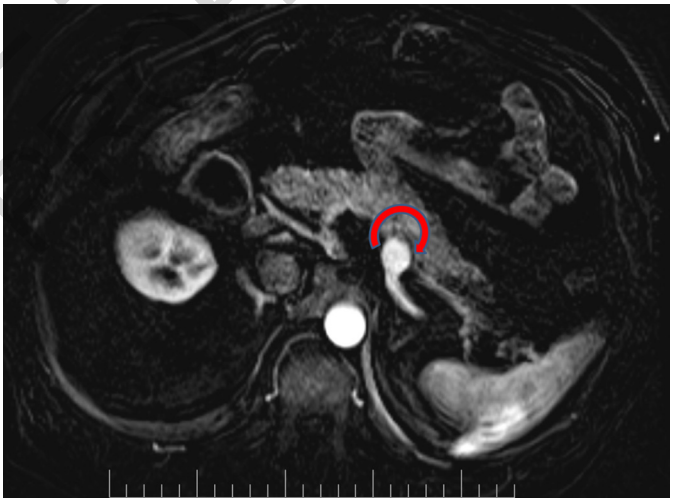

Fig. 2: T1-MRI sequence after contrast administration: The pancreas shows a 12-mm-nodular area in the body (arrow).

FNB with 22 Gauge needle was performed for histological and immunohistochemical evaluation, with cellular clusters showing molecular pattern (panCK+, Cromogranin A+, Sinaptofisin+, CK7-, EMA-) suggestive for PNET. Ki-67 was below 3%.
The procedure was complicated by an intragastric bleeding leading to hematoma formation, and acute pancreatitis.
Plasmatic biomarkers showed negativity for neural crest and epithelial tumors: Cg A: 8.1 ug/l (v.n.<100), NSE: 8.3 ng/ml (v.n. 17.0),CEA : 0.86 ng/ml (v.n. 0.60-6.90),CA 19-9 : 2.0 U/ml (v.n. 0-37.0).

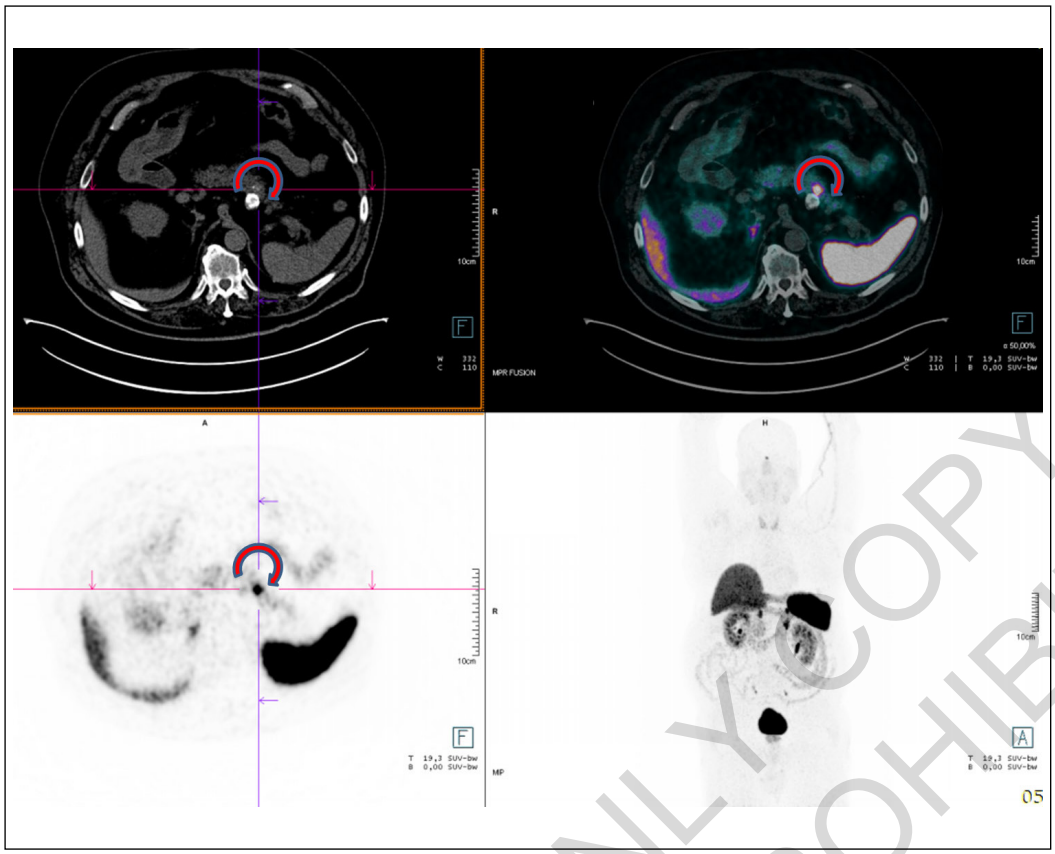

Fig. 3: 68 Ga-DOTATATE PET-CT: Pathological hypercaptation of the lesion (arrows).

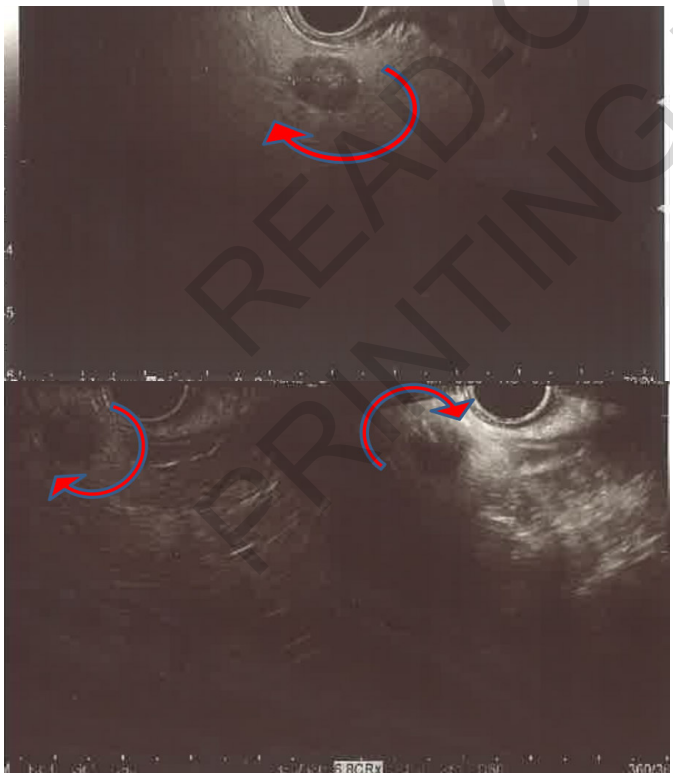

Fig. 4: EUS: In the pancreatic body two nodular lesions (diameter 8.5 mm and 13.3 mm) with finely irregular margins are present (arrows).

Discussion

NETS are rare tumors originating in the GI tract, lungs and pancreas; their incidence has been significantly increased during the last 20 years; the prognosis is related to the dimension of the tumor with a cut-off value of 2 cm [20].

Lesions under 2 cm, in absence of lymph node or distant metastases and local invasion, generally are not associated with disease progression [20-23] .

Nonetheless, all PNETs should be considered potentially malignant until a determination of their Ki-67 value is obtained [15]. In the reported case of an incidental and asymptomatic lesion, CT, MRI and PET-CT played a fundamental role in the differential diagnosis with pancreatic adenocarcinoma, which is more frequent in clinical practice especially. Compared to CE-CT and CE-MRI, for its high accuracy Gallium-68 PET-CT was the preferred technique for the staging of the neuroendocrine neoplasm, for treatment planning, for the localization of the pancreatic lesion, excluding the presence of unknown extra-pancreatic lesions not detected by other instrumental exams [11,14].

In the reported case EUS allowed the identification of a second pancreatic lesion, which was not detected by CT and MRI.

We suggest that the diagnostic algorithm of PNETs should include EUS in all cases to avoid missing of

undetected lesions and FNB for Ki-67 evaluation [13].
In our case Ki-67 was <3%, showing low aggressiveness of the nodular lesion of the pancreatic body-tail.
Our patient was scheduled for a clinical and instrumental follow-up, considered as a valid option [21] .
EUS-FNB post-procedural complications were treated conservatively with success. In the reported case, CgA plasmatic level provided low diagnostic usefulness for its low accuracy and specificity [15] .

Conclusions

Watchful and waiting approach is the preferred option for isolated, asymptomatic PNETs under 2 cm with low proliferation rate. We suggest the use of EUS-FNB for pancreatic neuroendocrine tumors, although further investigation is necessary to include such technique in the diagnostic routine of PNETs. Surgery is mandatory in cases of PNETs with MPD dilation and with histological features of high aggressiveness (Ki-67>20%) [24].

Riassunto

I Tumori Neuro Endocrini Pancreatici (PNETs) rappresentano <5% di tutte le neoplasie pancreatiche e in più della metà dei casi funzionalmente inattivi. In tal caso la diagnosi dipende dal raggiungimento di grandi dimensioni della lesione, con effetto massa secondario, oppure per la presenza di metastasi. In alcuni casi la diagnosi è casuale in corso di accertamenti eseguiti per altre patologie.
Tipicamente i PNETs esprimono i recettori della Somatostatina sulla superficie delle cellule, che rappresenta il target per la diagnosi strumentale, la stadiazione, la terapia con gli analoghi della Somatostatina e la valutazione della risposta clinica.
La chirurgia è il trattamento di scelta nei PNETs funzionanti, non-funzionanti con sintomi da compressione, con caratteristiche istologiche di aggressività (Ki-67 >20%). Le Linee Guida suggeriscono la sorveglianza attiva per I PNETs asintomatici di 2 cm o di dimensioni minori. Qui riportiamo il caso di un maschio caucasico di 71 anni in follow-up per melanoma, con reperto incidentale alla TAC total-body con mdc di formazione ipervascolare del diametro di 1.2 cm a livello del corpo del pancreas, confermata alla RM ed alla 68 Ga-DOTATOC PET-TC, in assenza di dilatazione del dotto di Wirsung. All'UES-FNB, si evidenziava una duplice lesione solida ipoecogena, di 1.2 cm a livello della coda del pancreas e di 3.8 mm a livello dell'istmo, suggestive di PNET. L'indice di proliferazione Ki-67 era <3% ed esprimeva la bassa aggressività della lesione.
La lesione era asintomatica e di scoperta casuale, e la PET con Gallio- 68 è stata la metodica diagnostica efficace per la localizzazione della lesione pancreatica, l'esclusione di lesioni occulte extra-pancreatiche non identificate con le altre metodiche radiologiche, la stadiazione della neoplasia neuroendocrina e di conseguenza la pianificazione della terapia.
Per le piccole dimensioni delle lesioni (1.2 cm e 3.8mm), la mancata dilatazione del dotto di Wirsung, il basso potenziale maligno ed evolutivo (Ki-67 <3%), il paziente è stato avviato a follow-up clinico-strumentale.
Suggeriamo che l'algoritmo diagnostico nei pazienti con sospetto tumore neuroendocrino del pancreas dovrebbe includere l'EUS con FNA o FNB, per evitare la perdita di lesioni non rilevate dalle altre metodiche e per la valutazione della presenza dei fattori istologici espressione di maggiore aggressività della neoplasia (Ki-67>20%) e di mutazioni genetiche.
La chirurgia è mandatoria nei casi di PNETs di diametro >2 cm, in presenza di sintomi da compressione, dilatazione del dotto di Wirsung e caratteristiche istologiche di aggressività con Ki- 67>20%.

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