EUS in the evaluation of metastatic lesions to the pancreas

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Metastases of the pancreas (MP) are rare and account for approximately 2% of all pancreatic malignancies.[1] They may be a manifestation of widespread malignant disease or isolated local metastatic tumors.[2] Currently, the detection rate of MP seems to be increasing, probably due to the more strict surveillance of patients with a prior definite diagnosis for malignancy. MP is usually detected accidentally through imaging, such as computed tomography, although more diagnostic options for primary and secondary pancreatic lesions include EUS. First reports with regard to EUS diagnoses of MP were in the 1990s and mainly described metastases from renal cell carcinoma (RCC).[1] Simultaneous development of EUS-guided sampling highly improved recognition of secondary lesions.[3] Our actual knowledge is mainly based on case reports. Nevertheless, assessment of MP with EUS remains challenging, as endosonographic features of metastases usually do not clearly distinguish between primary and secondary lesions, especially neuroendocrine tumors as both are usually well localized with well-defined borders. The final diagnosis is made with EUS-guided biopsy, including immunohistochemical assessment, in most cases.

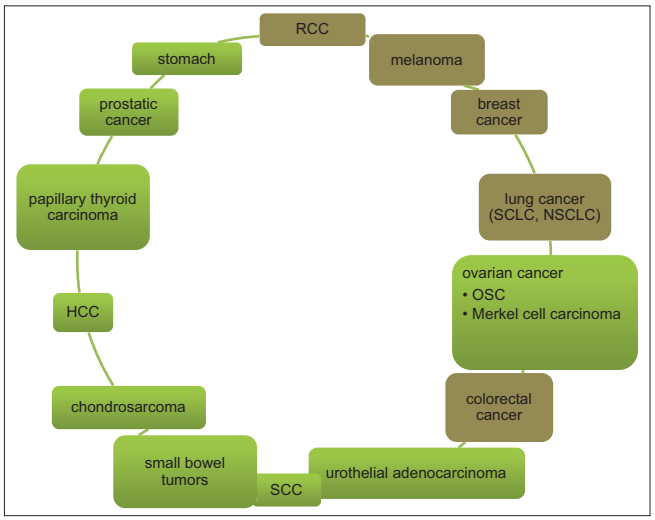

Figure 1. Types of metastases of the pancreas. Among all of metastases of the pancreas, the most common are renal cell carcinoma, melanoma, breast cancer, lung cancer, and colorectal cancer

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MP may occur in the setting of various types of malignancies [Figure 1]. The first descriptions of MP were mainly originating from RCC (54.3%–83.3%).[4] However, El Hajj *et al.*[5] conducted a 12-year retrospective assessment of pancreatic metastases in a group of 49 patients, which included primary neoplasms such as RCC, small-cell lung carcinoma (SCLC) and non-SCLC, hepatocellular carcinoma, melanoma, adenocarcinoma of the breast and colon, urothelial carcinoma, ovarian serous carcinoma, squamous cell carcinoma (SCC) of the stomach SCC, and small-bowel malignant tumors such as carcinoid and leiomyosarcoma. Smith *et al.*[6] additionally described metastasis of mesenchymal chondrosarcoma, prostatic adenocarcinoma, and papillary thyroid carcinoma. In terms of incidence, RCC dominates as primary cancer, while metastases of lung, melanoma, colon, and breast adenocarcinoma are significantly less common.[7] Patients with metastasis of RCC usually have a better prognosis. On the contrary, ovarian, colorectal adenocarcinomas, and sarcoma have a poorer prognosis, resulting from highly advanced disease progression at the time of diagnosis.[1]

The definition of meta- and synchronous MP has not been established and it varies depending on the type of primary cancer. MP may occur at any time after the primary neoplastic lesion diagnosis. MPs are usually metachronous (diagnosed >3–12 months of initial diagnosis of cancer); however, reports of synchronous lesions (metastases diagnosed within ≤3 months of initial diagnosis of cancer) have also been noted.[4] In previous case reports, the median interval between

Table 1. Immunohistochemical differentiation of selected metastases of the pancreas

Type of metastases	Immunohistochemistry	
	Positive	Negative
RCC	Vimentin	
	CD10	
Lung cancer	p63	TTF1
	CK 5/6	TTF1
	(NSCLC): Keratin	
	Chromogranin	
	Synaptophysin	
Brest cancer	ER	ER
	PR	PR
	Her	Her
	NeuR	NeuR
Rectal cancer	CK20	CK7
	CDX2	TTF-1
Colorectal cancer	CK20	CK7
	CX2	
Melanoma	HMB-45	S-100
	Melan A	
	SOX-10	
	B-catenin	
Ovarian cancer	CK7	CK20
	Serous: S-100, pCEA	Serous: ER, PR
Bladder	Cytokeratin 7	TTF1
	CDX2	Uroplakin
	Cytokeratin 20	

RCC: Renal cell carcinoma; NSCLC: Non-small-cell lung carcinoma; ER: Estrogen receptor; PR: Progesterone receptor

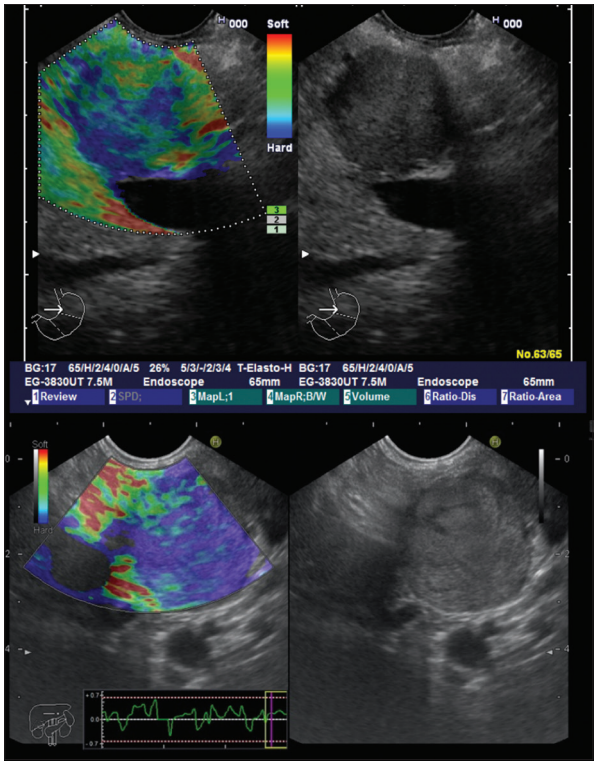

Figure 2. Solitary metachronous metastasis in two different patients, 6 and 9 years after surgical excision of renal cell carcinoma. High-stiffness in elastography is a common feature

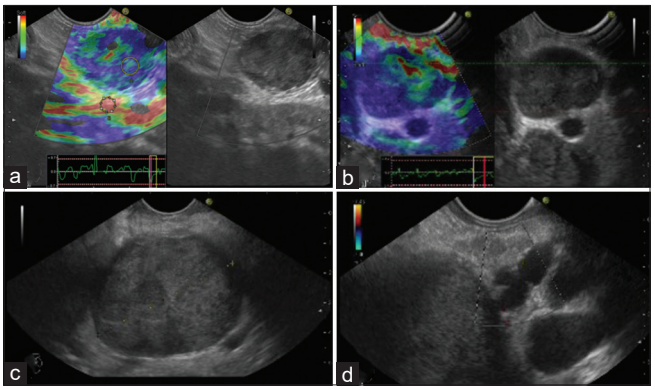

Figure 3. Metastases of the pancreas. (a) Metastases of endometrial sarcoma localized in the body and tail of the pancreas, regular solitary lesion with mixed tissue elasticity. (b) Metastases of non-small-cell lung carcinoma with high stiffness in elastography. Hypoechogenic, regular, well-defined. (c and d) Well-localized hypoechogenic solitary metastasis from melanoma with metastatic lymph nodes

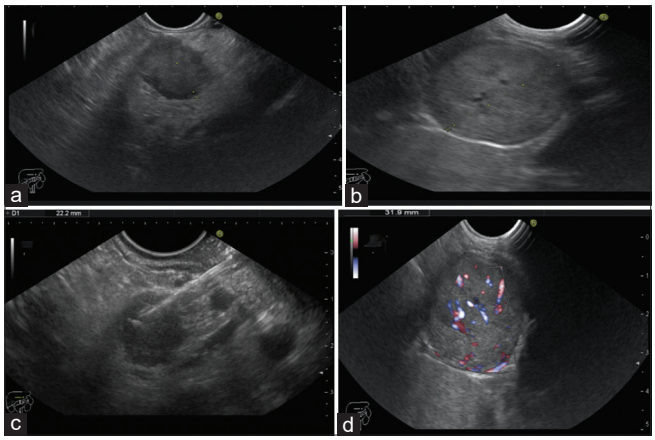

Figure 4. Different appearance of solitary renal cell carcinoma metastases to pancreas. (a) Hypoechogenic, regular with anechoic "halo." (b) Isoechogenic/mixed, well-defined. (c) Hypoechogenic, regular, during FNA biopsy. (d) Vascularized metastases from renal cell carcinoma

resection of primary cancer and development of MP was estimated at 32.5–157 months.[8] Metastases occurring after more than 10 years were referred to as late metastasis.[9] RCC metastases were reported at 6 and even 23 years after nephrectomy.[4] Similarly, MP of ovarian cancer 8 years after primary treatment was observed.[10] Due to the broad diversity of the primary tumor, MPs also have significant clinical and morphological variability. El Hajj *et al.*[5] noted that the vast majority of patients (88%) did not present with any symptoms of metastatic disease, which can explain the poor clinical course of MP due to the mainly asymptomatic course of the secondary tumor.[1] Symptoms that may appear in MP are usually due to a widespread involvement or mass effect.

Morphologically, as evidenced from prior observations, MPs are located mainly in the head of the pancreas with usually regular borders, although occasionally irregular.[1,3] A retrospective analysis of Palazzo *et al.*[3] showed that MPs are single (16/22) than multiple. In terms of echogenicity, hypoechogenic tumors predominate. However, hyperechoic metastases from bladder cancer or anechoic metastases from melanoma have been also observed. The mixed nature of MP is not uncommon, as is the case with RCC, where the echogenicity may be diverse. Similarly, the consistency of MP may vary, from solid to cystic and heterogeneous (mixed) [Figures 2-5].

As noted, the endosonographic features of MP may not be pathognomonic; therefore, it is essential to obtain a reliable history of prior primary malignancy before

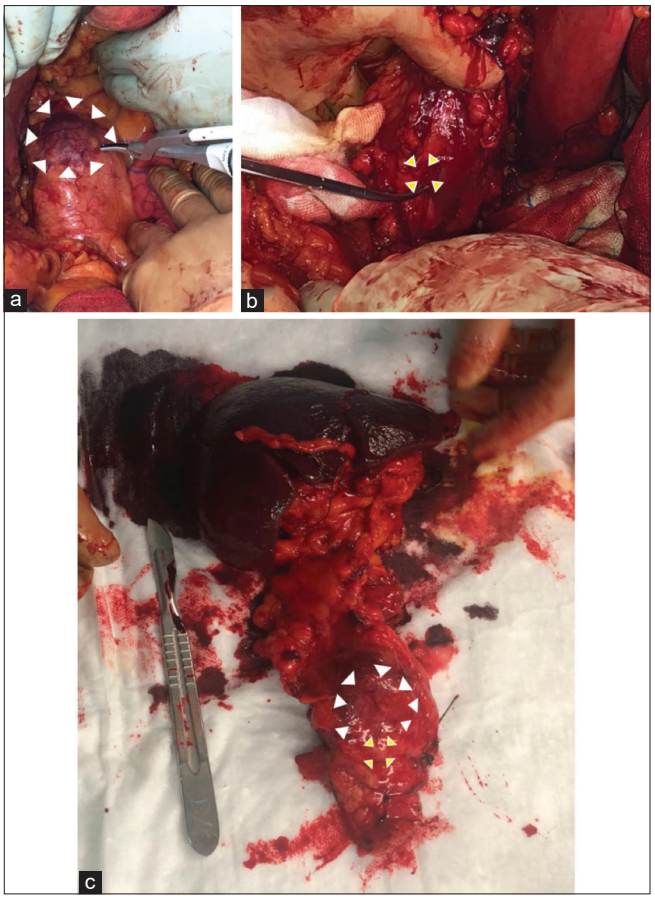

Figure 5. Intra- and postoperative evaluation of two metachronous renal cell carcinoma metastases to pancreas in the same patient. A large one in the pancreatic body ([a and c]; white arrows) and a small one in the pancreatic neck ([b and c]; yellow arrows)

the performance of EUS. Apart from the assessment of the morphology of MP in the EUS, the final diagnosis is based on EUS-guided biopsy followed by the cytological and immunohistochemical staining (IHC). Limited available reports show that EUS-fine-needle aspiration (FNA) sampling adequacy is similar in MP compared to primary tumors of the pancreas.[11] However, the addition of immunocytochemical staining is indispensable for confirming the diagnosis of metastasis[2] [Table 1]. Cytological samples obtained by EUS-FNA provide relatively high diagnostic accuracy. However, cytological evaluation alone is not sufficient to diagnose MP. Recently, fine-needle biopsy (FNB) needles have been introduced to improve the quality of tissue sampling[12] and are generally thought to be better in obtaining tissue cores compared to FNA needles.[13] Tissue cores collected by FNB can provide a sample with preserved architecture and enables conducting IHC, which is crucial for the diagnosis of MP. Furthermore, core material enables the introduction of novel diagnostic techniques and research purposes

such as next-generation sequencing, molecular analysis, and organoid generation.[14] More data are needed on the benefits of different needle types, and prospective randomized studies could shed more light on this specific group of pancreatic lesions.

Conflicts of interest

There are no conflicts of interest.

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