# An unusual neoplasm of the pancreas : Pancreatic metastasis of a Merkel cell carcinoma. Case report and review of the literature

Emmanuel De Cock[1], Marcus Remery[2], Manuel De Vuyst[3], Katrien Lecluyse[2]

(1) Medical student, Ghent University, Belgium ; (2) Department of internal medicine, General Hospital Oudenaarde, Belgium ; (3) Department of anatomical pathology, General Municipal Hospital Aalst, Belgium.

## Abstract

**Isolated pancreatic metastases are rare. The differential diagnosis of pancreatic neoplasms can be difficult, especially it can be troublesome to obtain tissue diagnosis. However, pancreatic lesions in patients with a history of a malignancy must be considered to be metastases.**

**We present a case of a patient with a history of a Merkel cell carcinoma (MCC) in the neck. Twelve months after this diagnosis a follow-up CT shows a large isolated tumor in the head of the pancreas. Histological and immunohistochemical studies of specimen obtained through ultrasound-guided transabdominal biopsy, show similar characteristics as the primary MCC.**

**To our knowledge twelve cases of a pancreatic metastasis of a MCC have been reported in English literature. A review of the literature was performed.** (Acta gastroenterol. belg., **2015**, 78, **340-343**).

**Key words** : Merkel cell carcinoma, pancreatic metastasis, pancreatic neoplasm.

## Introduction

The majority of pancreatic tumors are primary pancreatic neoplasms, only 2-3.9% are secondary neoplasms (1). 90% of primary pancreatic neoplasms are pancreatic ductal adenocarcinomas (2). Secondary neoplasms in the pancreas most commonly originate from the lungs, the gastrointestinal tract, lymphomas and the kidneys (2). Tumors of the pancreas may pose a diagnostic challenge. Radiological distinction between a primary and a secondary pancreatic neoplasm is limited and it is often difficult to obtain a specimen of a pancreatic neoplasm.

Endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA) is regarded as a safe and accurate procedure to obtain tissue diagnosis of a pancreatic lesion, especially if CT or US guided biopsy is not possible. EUS-FNA has a sensitivity of 75-95% and a specificity of 88-100% for the diagnosis of a pancreatic lesion (3). EUS can detect small lesions (< 3 cm) and vascular structures can be avoided during FNA by using color Doppler (3). Furthermore EUS-FNA has a low complication rate. However, EUS-FNA has a steep learning curve (3). EUS-FNA traditionally provides a smear specimen for cytological examination, but more recently cell block specimens can be obtained for histological examination (3). The precise role of cell block specimens obtained by EUS-FNA in the diagnosis of pancreatic lesions still needs to be determined.

The following case report describes a patient with a history of a MCC on the neck who presents with an asymptomatic pancreatic neoplasm during follow-up 12 months after the presentation of the MCC.

## Case report

We present a case of a 81-year-old Caucasian woman without any significant medical history besides a Merkel cell carcinoma (MCC) on her neck. On a follow-up CT of the abdomen 12 months after the initial presentation of the MCC, a heterogeneous tumoral enlargement of the head of the pancreas was visible, with a diameter of 3.3 cm (Fig. 1). There were multiple pathological lymph nodes para-aortic and aortocaval. A CT of the neck and thorax showed no abnormalities. The patient had no symptoms and blood analysis showed a CA 19.9 of 8 kU/L (reference < 39 kU/L). An endoscopic ultrasound study showed a lesion in the head of the pancreas (diameter 2.9 × 3.0 cm) with presumed invasion of nearby blood vessels and one pathological lymph node next to the lesion. Fine needle aspiration cytology of the lesion was inconclusive. Magnetic resonance of the abdomen did not provide any additional information about the nature of the tumor or lymph nodes. Due to the unclear nature of the tumor in the pancreas (at this point most likely pancreatic ductal adenocarcinoma or metastatic MCC), the presumed bad prognosis either way with limited therapeutic options, the age of the patient and her being asymptomatic, it was advised merely to do a follow up of the tumor.

Two months later, the patient presented with epigastric pain and weight loss. A transabdominal ultrasound at this point showed that it could be possible to perform a US guided transabdominal biopsy of the tumor (maximal diameter 3.0 cm). This biopsy indicated the neoplasm was a metastasis of the MCC (Fig. 2). Histologically, the specimen showed a small cell neoplasm with minimal

Correspondence to : Lecluyse K., M.D., Department of internal medicine, General hospital Oudenaarde, Minderbroedersstraat 3, 9700 Oudenaarde, Belgium. E-mail : katrien.lecluyse@azoudenaarde.be

Submission date : 01/02/2015
Acceptance date : 25/02/2015

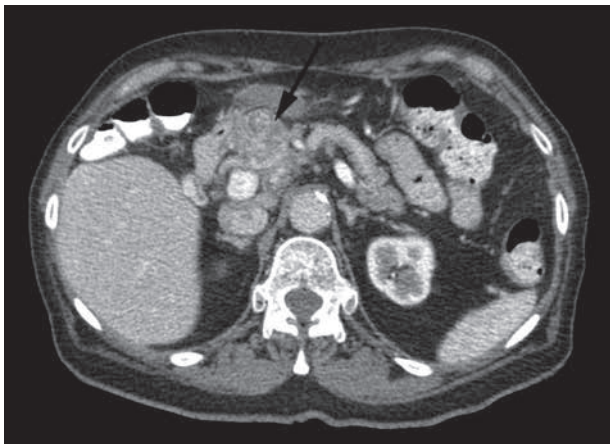

Fig. 1. — This computed tomography of the abdomen during follow-up of a Merkel cell carcinoma, shows a tumoral enlargement of the head of the pancreas (arrow).

cytoplasm and finely granular chromatin. Immunohistochemistry showed similar characteristics as the primary skin nodule : positive for cytokeratin 20 (CK20) with a paranuclear dot-like pattern, positive for CD56 and only a focal weak staining pattern for thyroid transcription factor-1 (TTF1). Serum neuron-specific enolase (NSE) at this point was 41.3 $\mu$g/L (reference < 12.5).

Twelve months before the presentation of the pancreatic neoplasm, the patient presented with a skin nodule (maximal diameter 1.1 cm) on the left side of her neck with the appearance of a basal cell carcinoma. The lesion was resected with a small margin. However, it showed to be a moderately differentiated Merkel cell carcinoma (MCC) with invasion of the cut edge. The tumor was positive for CK20 with a paranuclear dot-like pattern, positive for CD56 and negative for TTF1 in the immunohistochemical studies. A computed tomography (CT) of the neck, thorax and abdomen showed no signs of distant metastasis but showed two hyperemic lymph nodes with contrast captation in the neck. A sentinel node procedure was performed. The sentinel node and three other lymph nodes were resected and the margin of the initial resection was extended by 2 cm. Three of the four resected lymph nodes were invaded with extracapsular extension of one lymph node. A PET-CT showed no signs of distant metastasis. Next, adjuvant radiotherapy was given. Three months after completion of radiotherapy, a CT of the neck showed no additional lymph nodes.

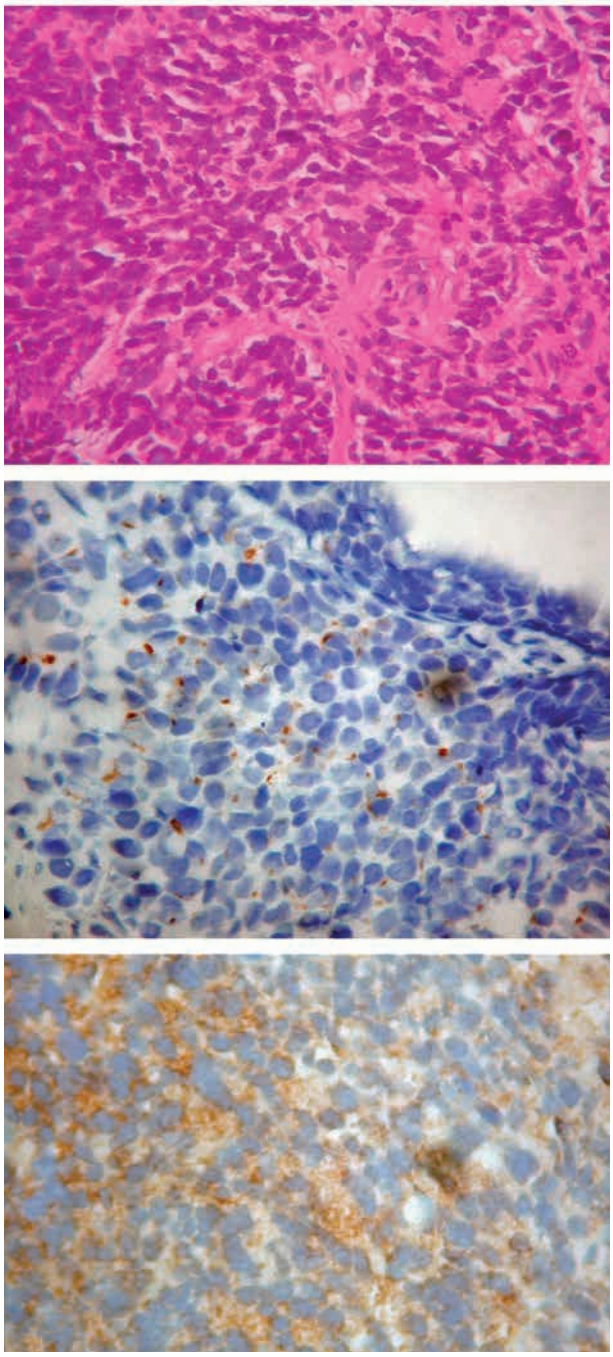

Fig. 2. — Cytomorphological and immunohistochemical features of a specimen from a Merkel cell carcinoma metastasis in the pancreas, obtained through transabdominal biopsy. (A) Hematoxylin and eosin staining shows a small cell neoplasm with little cytoplasm and hyperchromatic nuclei ; (B) Paranuclear dot-like pattern Cytokeratin 20 staining (brown) ; (C) Cytoplasmic CD56 staining (brown).

## Discussion

MCC is an aggressive neuroendocrine carcinoma of the skin with a high tendency for local recurrence, lymph node metastasis and distant metastasis (4,5). MCC is a rare neoplasm, but its incidence has been rising from 0.15 to 0.44 cases per 100.000 from 1986 to 2001 (4,6). Currently, its incidence is approximately 0.60 per 100.000 (7,8). The rising incidence is partly due to improved diagnostic techniques and improved awareness (7). There seems to be an association between MCC and immunosuppression caused by chronic lymphocytic leukaemia, human immunodeficiency virus (HIV) infection and in organ transplant recipients (4,7,9). More recently an association was discovered between MCC and

Table 1. — **Summary of case reports presenting a Merkel cell carcinoma metastasis to the pancreas, in order of publication date**

| Case | Age [year] / sex | Time of diagnosis after primary tumor [Months] | Clinical presentation of pancreatic metastasis | Diagnosis | Location in the pancreas |
|---|---|---|---|---|---|
| Safadi *et al*. (14) | 69/F | 24 | Jaundice | Post mortem | Head |
| Bachmeyer *et al*. (10) | 57/M | 6 | Jaundice, abdominal pain | Post resection | Body |
| Ouelette *et al*. (2) | 64/M | 48 | Jaundice | Post resection | Head |
| Adsay *et al*. (12) | N/A | N/A | N/A | Post resection | Tail |
| Bachmann *et al*. (4) | 82/F | 24 | Abdominal mass, weight loss | Post resection | Tail |
| Patel *et al*. (15) | 65/M | 10 | Jaundice, abdominal pain, vomiting | Radiological | A : Body<br>B : Head |
| Dim *et al*. (13) | 79/F | 15 | Abdominal pain | EUS-FNA | Tail |
| Krejci *et al*. (7) | 62/M | 4 | Asymptomatic | Radiological | Head |
| Bernstein *et al*. (8) | 56/M | 5 | Asymptomatic | EUS-FNA | Tail |
| Vernadikis *et al*. (6) | 67/F | 30 | Abdominal mass and discomfort, weight loss | Post resection | Tail |
| Manatsathit *et al*. (9) | 65/M | 24 | Epigastric pain, nausea and vomiting | EUS-FNA | Head |
| Bhardwaj *et al*. (3) | 62/F | 108 | Epigastric pain, bloating, annorexia | Biopsy | Body |
| Current case | 81/F | 12 | Asymptomatic | Biopsy | Head |

N/A, not available.
EUS-FNA, endoscopic ultrasound-guided fine-needle aspiration.

a specific type of polyomavirus, called Merkel cell polyomavirus (4,9). This polyomavirus is thought to have an important role in the pathogenesis of most cases of MCC (4,7). It can be detected in as many as 80-90% of MCCs (8). Ultraviolet (UV) radiation also plays an important causative role in the etiopathogenesis of MCCs (4). MCCs are much more common in sun-exposed skin (4,5). 50 % of MCCs appear on the head and neck area, 40% appear on the extremities and less than 10% appear on the trunk and genitals (4,5,8). Furthermore MCCs are much more common in Caucasian patients over the age of 65 years (4,5). The mean age of patients at diagnosis of a MCC is 76.2 years for women and 73.6 for men (7).

A MCC usually presents as a rapidly growing painless indurated dome-shaped nodule or plaque (4,5). It may be skin coloured, purple or red (4,5). Histologically, MCCs present as a small round blue cell neoplasm with minimal cytoplasm and finely granular chromatin (3). MCCs can be distinguished from other small round cell tumors (for example small cell lung cancer) by means of immunohistochemical studies (4). The epithelial marker CK20 is a very sensitive and specific marker of MCC (3,4,10). A paranuclear "dot-like" pattern of staining with cytokeratin stains is specific for MCC (3). Chromogranin, synaptophysin and CD56 (neural cell adhesion molecule) are neuroendocrine markers which may also be positive but are less specific for MCC (3,4). TTF1 and CK7 are positive in small cell lung cancer but are usually negative in MCCs (3,4).

66-80% of patients with MCC present with localised disease at the time of diagnosis (4,5,7,8). 27-30% already have regional lymph node metastasis and 4-7% have metastatic disease at this point (3-5,7). Local recurrence after excision of a MCC occurs in 25-50% of cases (6,11). Regional lymph node metastasis develops in about 50-75% of patients and distant metastasis eventually develops in 34-60% of patients (5,6,10,11). The most common sites for distant metastases of a MCC are the liver, brain, bone, skin, lung and non-regional lymph nodes (5,11). Patients with local disease at presentation have a 5 year relative survival rate of 64%, compared to 39% in patients with positive regional lymph nodes and 18% in patients with metastatic disease (7).

Robust evidence is lacking about the best management of MCC because of the infrequent nature of the tumor (4,11). The initial treatment of MCCs is usually based on aggressive surgery and in a lot of cases adjuvant radiotherapy (4,7,9,11). Chemotherapy is usually being reserved for patients with distant metastatic disease or patients at high risk for development of distant metastatic disease (4,5,11). Even in distant metastatic disease, there is no evidence of improvement in overall survival in response to chemotherapy (4). Many combinations of chemotherapeutic agents have been used in systemic disease with poor results (10). Usually the same chemotherapy regimens are being used for MCC as for small cell lung cancer.

To our knowledge, twelve other cases of pancreatic metastasis of MCC have been reported in English literature (Table 1) (1-3,5,6,8-10,12-15). Similarly to the current patient, all but one patient presented with a single metastatic tumor in the pancreas. The mean age of the described patients is 67.4 years with an equal sex ratio (6 female and 6 male). The mean interval between the presentation of the primary MCC and the discovery of

the pancreatic metastasis is 25.8 months, ranging from 4 to 108 months. In the majority of cases (75%) the interval was less than two years. The head, body and tail of the pancreas were involved in respectively 46.1%, 23.1% and 38.5%. The most common clinical presentation was abdominal pain/discomfort (50% of cases). One third of patients presented with obstructive jaundice and one fourth of patients was asymptomatic. Tissue material for the diagnosis of the metastasis was obtained through EUS-FNA in three cases and through transabdominal biopsy in two cases. Only five publications reported follow-up information. The mean survival after discovery of the pancreatic neoplasm was 7.2 months, ranging from 2 to 19 months.

## Conclusion

In most cases, an isolated pancreatic neoplasm turns out to be a primary pancreatic ductal adenocarcinoma. Nonetheless the diagnosis of an isolated metastasis must be considered in patients with a history of a malignancy, even in the case of a malignancy that rarely spreads to the pancreas such as a Merkel cell carcinoma. Therefore it is important to obtain tissue diagnosis of a pancreatic lesion.

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