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Metastatic Merkel Cell Carcinoma (MCC) of Pancreas

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Rezumat

Carcinom cu celule Merkel (MCC) prezentând metastază pancreatică

Carcinomul cu celule Merkel (MCC) este o formă neoplazică agresivă, neurocutanată, cu potențial înalt de malignizare. Prezentăm cazul unei paciente în vârstă de 59 de ani, îndrumată către Secția de Chirurgie Generală în urma unor acuze de durere epigastrică. Examenul CT abdominal a decelat prezența unei mase cu diametrul de 3 cm la nivelul capului pancreasului. Particularitatea legată de antecedentele personale patologice ale pacientei constă în faptul că acesteia îi fusese excizat un carcinom cu celule Merkel cu 7 luni înainte, cu dimensiunea de 5 cm, din regiunea gluteală. Pacienta a fost supusă unei operații de pancreaticoduodenectomie prin procedura Whipple, în vederea înlăturării masei tumorale. Având în vedere similitudinea proprietăților morfologice ale tumorii actuale cu neoplasmul primar, aceasta a fost acceptată ca fiind o metastază a MCC. Ulterior operației pacienta a fost supusă chimioterapiei adjuvante, iar la controlul efectuat la 30 de luni postoperator s-a observat că pacienta nu prezintă nici un semn de boală sau de complicații legate de posibila progresie sau recurență a acesteia. Deși MCC este o tumoră agresivă, asociată cu un prognostic slab, rezultate bune pot fi obținute prin intermediul unui diagnostic corect și al unui tratament chirurgical adecvat.

Cuvinte cheie: metastază, carcinom cu celule Merkel, pancreas

Abstract

Merkel cell carcinoma (MCC) is a rare, agressive, neurocutaneous malignancy with a high potential to metastasize. We present a 59 year-old woman referred to general surgery department with a complaint of epigastric pain. The abdominal computed tomography (CT) performed and revealed a mass of 3 cm in the head of the pancreas. The significant debate in the patient's medical history was that she had a MCC in size of 5 cm removed from the left gluteal region 7 months ago. Following preoperative preparation a pancreaticoduodenectomy with Whipple procedure was performed fort he pancreatic head mass. As the tumor showed morphologically similar properties with the patient's primary neoplasm, it was accepted as a metastatic MCC. Following the operation the patient received adjuvant chemotherapy and at a 30 months follow-up it was observed that the patient is disease free and has no complications related to the disease progression or recurrence. Although MCC is an aggresive and poor prognostic tumor, good results can be obtained with correct diagnosis and proper surgical treatment.

Key words: metastatic, Merkel Cell Carcinoma, pancreas

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Background

Merkel cell carcinoma (MCC, Trabecular Carcinoma) was first

described in 1972 by Cyril Toker (1). It is a rare, potentially fatal, neurocutaneous tumor with a poor prognosis. MCC affects predominantly caucasian over the age of 65 and young immunocompromised patients (2, 3). The incidence rate is approximately 0.6/100000 per year and it increases with age, immunodeficiency and exposure to sun (3, 4).

In the United States, the incidence of MCC showed an increase of 3 fold, from 0.15 cases per 100000 in 1986 to 0.44 cases per 100000 in 2001 (5). This rise is more dramatic than the increased incidence of cutaneous melanoma in US. Also similar data have been reported for Australia (6). In this study we aimed to attract attention to this rapidly increasing metastatic malignancy.

Case report

A 59 year-old Turkish woman was referred to General Surgery Department of Hacettepe University School of Medicine with a complaint of epigastric pain. In the physical examination no pathologic findings were found. Laboratory tests including hemogram, urea, creatinine, alanine transaminase (ALT), aspartate aminotransferase (AST), tumor markers; Cancer Antigen (CA) 15-3, CA 19-9, CA 125, Alpha Fetoprotein (AFP) were within normal limits. An abdominal computed tomography was performed. A 3 cm solid, irregular mass was detected in the head of the pancreas (Fig. 1). There was no evidence of vascular involvement of portal vein, superior mesenteric artery and vein, and no distant metastasis were shown radiologically. The tumor considered as resectable and surgical treatment planned.

In the patient's medical history, she had a firm, painless, asymptomatic skin lesion in her left gluteal region. Lesion was surgically excised by a plastic surgeon in an urban hospital 7 months ago. In the pathological examination the tumor diagnosed as primary MCC of the skin. The specimen was 5x4,5x1,5 cm sized, cream-colored, solid, soft tissue sample. The neoplastic cells were immunohistochemically positive for Snaptophysin, Chromogranin, CD56, Melan-A and CK20; and negative for S100, HMB-45, LCA, PanCK and Desmin.

After the completion of medical evaluation, standart Whipple procedure was performed. No intraoperative complications occured during the surgery. The patient was observed in the intensive care unit for the first postperative day. On the postoperative fourth day oral intake started and well tolerated. Patient was discharged on the postoperative 8th day with no surgical complications.

The pathological examination revealed a 1.8 ×1.5 ×1.4 cm sized tumor in the uncinate process of the pancreas. All the surgical margins were tumor free. Grossly, the mass displayed glossy cut surface containing areas of necrosis and hemorrhage, 26 lymph nodes were identified and all of them were negative. The tumor was immunohistochemically pan-cytokeratin focal positive, staining strongly for CD56, chromogranin, synaptophysin and cytokeratin-20. Thyroid transcription factor-1 (TTF-1) was negative and proliferative activity (Ki-67) reached approximately 50%. As the tumor showed morphologically similar properties to the patient's primary neoplasia, it was accepted as metastatic MCC. The patient was referred to the department of medical oncology for adjuvant chemotherapy. She was administered six cycles of cisplatin and etoposide. At 40-months follow-up, it was found that the patient was disease free and had no complications related to the disease progression or local/distant recurrence.

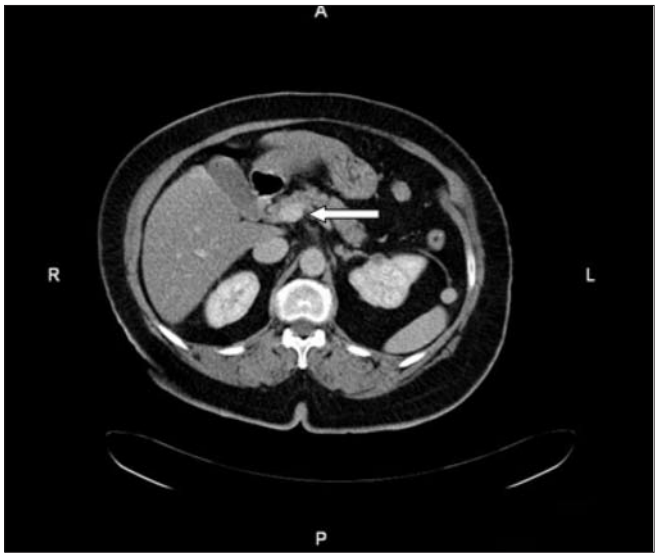

Figure 1. *Metastatic MCC in the head of the pancreas*

Discussion

In 1972, Cyril toker described "trabecular cell carcinoma" in five patients as an aggressive skin cancer associated with immunosupression, senility and exposure to sun. Toker named the neoplasm as trabecular carcinoma because of the perceived pattern of growth of the tumor cells (1, 7).

MCC is derived from Merkel cell residing in the basal layer of epidermis which are assumed to be neuroendocrine cells (8). MCC most often presents a painless, firm, elastic raised skin lesion in sun-exposed areas. Lesions are usually less that 2 cm but some have been reprorted as 12 to 15 cm in siz. In 50% of cases, MCC appears on the head and neck. The next most common site is the extremity (40%) followed by trunk and genitals (< 10%) (9, 10).

The nonspecific appearance of MCC may cause a delay in diagnosis. Immunochemistry and electron microscopy are mandatory for confirmation of the diagnosis. Histologically it is difficult to distinguish MCC from other poorly differenciated small-cell tumors, lymphoma and malignant melanoma. The diagnosis can be confirmed by positive multinuclear labelling of tumor cells with low molecular weight cytokeratins, marked cytoplasm reactivity for neuron specific enolase and negative staining for S-100 protein and leukocyte common antigen. *Table 1* shows immunohistochemical stains which are used for differentiating small cell carcinoma of lung, Merkel cell carcinoma, B-cell lymphoma and malignant melanoma (2, 10).

Table 1. *Immunohistachemical stains for small cell carcinoma of the lung, malignant melanoma, B-cell lymphoma and Merkel cell carcinoma (2)*

Immunohistochemistry	Small Cell Carcinoma	Melanoma	B-cell Lymphoma	Merkel Cell Carcinoma
TTF-1	+	-	-	-
CK 20	-	-	-	+
Chromogranin	-	-	-	+ / -
S-100	-	+	-	-
LCA	-	-	+	-
NSE	+ / -	-	-	+

TTF-1: Thyroid transcription factor-1, LCA: Leukocyte common antigen, NSE: Neuron-specific enolase

Distant metastasis of MCC have been reported in various organs, including oral cavity, stomach, pancreas, liver, lung, cerebellum and genitourinary tract (3, 10- 12). Most patients have localized disease at initial diagnosis (70-80%) (3, 13). The majority of the patients develop matastatic disease either synchronously or metachronously with a frequency varying from 20% to 75%. Patients with lymph node metastasis demonstrate a two to three fold higher mortality rate when compared with those without nodal involvement (2, 14).

Pancreatic metastases, although uncommon, are an increasing clinical entity. Surgical resection is often advocated when the lesion is single and for patients fit to perform a pancreatectomy. The usefulness of pancreatic resection is mainly linked to the biology of the primary tumor metastasizing to the pancreas. The benefit of metastasectomy in terms of patient survival has been observed for metastases from RCC, while for other tumors the role of surgery is mainly palliative (15)

There is no information available about the exact incidence of pancreatic metastasis of MCC. We found only ten metastatic cases affecting pancreas in medical literature (3, 13-22). With the addition of our patients, this number increased to 11. All of these 11 patients were over 50 years old when they diagnosed as metastatic MCC of pancreas. The 4 of the patients were male while 7 of them were female.

The tumor was localized at sun-ecposed areas in eight of these 11 patients while 3 of the patients' tumor were in none UV exposed areas. Six of 11 patients had a poor prognosis whose tumors were inoperable so they were only treated with supplementary medication. All of these 6 patients died from cancer related diseases. This information matches with the data about the poor prognosis of metastatic MCC. The remaining five patients were treated surgically. Except our patients' follow up, we could not reach any data about the prognosis of other surgically treated patients.

Conclusions

MCC is currently accepted as a rare malignant tumor with an exponentially rising incidence. Although MCC is an aggresive and poor prognostic tumor, as seen in our patient, good results can be obtained with correct diagnosis and proper surgical treatment. It is unlikely that in the foreseeable future, MCC and its matastasis will be a strenuous problem for both the patients and medical employees.

Competing interest

The author(s) declare that they have no competing interests.

Author's contributions

KK carried out the molecular genetic studies, participated in the sequence alignment and drafted the manuscript

EH, conceived of the study, and participated in its design and coordination and helped to draft the manuscript. All authors read and approved the final manuscript.

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