CASE REPORT

Cutaneous melanoma single metastasis to the pancreas: Results of combined treatment with surgical resection and immunotherapy

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Abstract Metastatic melanoma to the pancreas was first described in 1931. Pancreatic metastasis occurs commonly in patients with diffuse disease with solitary metastasis being quite rare. The role of pancreatic metastasectomy in patients with malignant melanoma is currently not defined because there are very few available reports. The case is reviewed of a 54-year-old male patient with a history of left thigh Stage IIIC malignant nodular melanoma. After 11-month follow-up, a single metastasis to the head of the pancreas was detected. To improve our understanding on these lesions, a case treated with pancreatic resection in our hospital is described. Here, clinical features of presentation, treatment and follow-up are discussed, along with a literature review. Most authors recommend surgery as the treatment of choice for pancreatic metastases that are amenable to resection since it appears to be the only treatment able to prolong survival, although there are no large studies fully demonstrating this assumption. This review suggests that, in a patient with favorable tumor characteristics, surgery should be considered a viable treatment option, but studies have to be conducted with larger numbers of patients. (creativecommons.org/licenses/by-nc-nd/4.0/).

KEY WORDS
Malignant cutaneous melanoma; Pancreatoduodenectomy; Immunotherapy

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CLINICAL CASE

The case is reviewed of a 54-year-old male Caucasian patient who was native of Germany and resident of Mexico since 14 years prior. He was vegetarian and had no history of chronic diseases. He had a 2-year history of a left thigh ulcerated malignant nodular skin melanoma with 6.5 mm Breslow’s depth, Clark level 5 and 3 mitoses per mm, treated with wide resection of the lesion plus inguinal lymphadenectomy, with seven positive lymph nodes. It was classified as Stage IIIC due to pN3. Subsequently, the patient received adjuvant radiotherapy (RT) to the inguinal region at 50 Gy in 20 fractions with a 6 MV photon beam linear accelerator using the volumetric modulated arc therapy technique. A follow-up positron emission tomography-computed tomography (PET-CT) 2 months after the surgical event reported a SUVmax increase of 5.8 in soft tissue heterogeneous zone, in addition to, the right inguinal canal prominence with SUVmax of 4 associated with inflammation (Fig. 1). The patient was considered to be a candidate to adjuvant treatment with interferon alpha 2b at 10 million units (MUs) doses Monday through Friday for 4 weeks, and subsequently, at 10 MU 3 times a week for 12 months. After 11-month asymptomatic follow-up, a control abdominal CT scan documented main pancreatic duct dilatation caused by a small tumor mass; lipase and amylase were higher than 2000 IU, and there was no hyperbilirubinemia (Fig. 2). A new PET-CT documented a solid tumor on the head of the pancreas with SUV of 8. An endoscopic ultrasound demonstrated a 10 mm × 7 mm lesion on the head of the pancreas close to the neck. A fine-needle aspiration biopsy establishes the diagnosis of malignant neuroendocrine tumor (Fig. 3); tumor markers were negative (carcinoembryonic antigen and carbohydrate antigen 19.9), there was no carcinoid syndrome, and chromogranin A and 5-hydroxyindoleacetic acid were negative. Studies for disease extent were negative. A pancreatic scintigram with octreotide reported tumor activity only in the pancreatic head, and the lesion was classified as a second primary tumor. The patient underwent pancreaticoduodenectomy without pyloric preservation with no complications. Transoperatively, a tumor was found in the neck of the pancreas, solid on palpation and of approximately 1.5 cm in size, which caused important dilatation of the duct of Wirsung (Fig. 4); lymph nodes were macroscopically negative. The patient was dis...

Figure 1. Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography 2 months after initial treatment with report of SUVmax increase of 5.8 in soft tissue heterogeneous zone in addition to the right inguinal canal prominence with SUVmax of 4 in association with inflammation, with no additional distant lesions being appreciated.

Figure 2. Double-contrast helical tomography of the abdomen 11 months after initial treatment, where main pancreatic duct dilatation is observed, caused by a small tumor mass; a second primary lesion is suspected.
charged 9 days after the surgical event due to improvement. The pathology report determined metastatic melanoma of 1.2 cm × 0.9 cm × 0.9 cm in size, located at the pancreatic neck, with negative margins, tumor necrosis, and presence of lymphatic, vascular and perineural invasion (Fig. 5); all lymph nodes were negative for metastatic disease. The diagnosis was corroborated by immunochemistry studies: S-100 protein, HMB-45, MART-1, and tyrosinase were positive.

The patient evolved satisfactorily with 2-month follow-up free of symptoms and no evidence of relapse in other sites. Since BRAF V600 tested negative, starting management with ipilimumab was decided. 12 months after treatment completion, the patient is on surveillance, asymptomatic and with no evidence of disease progression.

DISCUSSION

Isolated metastasis to the pancreas from another primary tumor is quite rare (<2%) and portends a poor prognosis,
with 5-year survival lower than 10% and median survival of 6-9 months. Nevertheless, several retrospective studies have suggested a survival increase after pancreatic metastasis complete resection, which generates great interest on this approach. However, there is very little literature on pancreatic resection for metastatic melanoma. Pancreatic metastases occur only in 2% of resectable metastatic disease cases. Primary tumors that most commonly metastasize to the pancreas are breast, lung, kidney, and colon tumors and less frequently, melanoma and sarcoma. Metastatic melanoma to the pancreas was first described in 1931. Pancreatic metastases commonly occur in patients with diffuse disease. Single metastasis is quite rare, and it has been described mostly in primary ocular melanoma. On the other hand, metastatic melanoma has an unfavorable prognosis: 5-year survival for patients with a single metastasis is 12% (median survival of 11 months), whereas 5-year survival with multiple metastases is 0% (median survival of 4 months). After single metastasis complete resection, 5-year survival shows a significant increase to 18%, with a median survival of 15 months. Survival is dependent on the site of distant metastasis; patients with visceral involvement have less favorable results than those with soft tissue involvement or distant lymph node relapse. In a retrospective study of 49 cases at the Johns Hopkins Hospital in patients with metastasis to the pancreas, the three patients with metastatic melanoma had worse prognosis. The role of pancreatic metastasectomy in patients with malignant melanoma is currently not defined because there are very few available studies. Traditionally, metastasectomy was deemed useless owing to a bad prognosis associated with highly extended disease. However, some patients with limited metastatic disease are able to survive for a reasonable period after surgery, and there are even reports of cure. This, together with an improvement in operative risk associated with the procedure demonstrated by many groups, has led to a renewed interest on surgical treatment of metastatic melanoma. Most authors recommend surgery as the treatment of choice for pancreatic metastases that are amenable to resection since it appears to be the only treatment able to prolong survival. In addition, pancreatic metastases seem to have a higher resectability index in comparison with pancreatic adenocarcinoma, owing to the fact that metastatic lesions borders tend to be better defined. For patients with unresectable lesions, surgery still offers good palliation with the quality of life improvement and very low associated morbidity. However, the role of surgery for melanoma metastases to the pancreas is less clear, since there is very scarce literature available demonstrating a survival advantage. In one series, 5-year survival of patients with multiple metastases was improved from 23% to 37.5% with surgical treatment in selected patients. Median disease-free interval (DFI) in these patients was 24 months. In another series involving four patients, two had died at 25-month follow-up, and two were still alive at 30 and 76 months. The patients who survived were observed to have a DFI of 4 and 14 years, respectively. However, other studies fail to show a significant survival improvement after surgery. Patient survival appears to depend on two main factors: The capability to completely resect the metastases, which makes for the patient to remain disease-free and a prolonged DFI. A DFI increase is thought to be the result of more favorable tumor biology, where tumor cells are less aggressive, slower to divide, and less likely to metastasize. Unfortunately, currently, there is no effective non-surgical treatment, and the role of adjuvant chemotherapy and immunotherapy is under study.

CONCLUSION

Studies suggest that, in a patient with favorable tumor characteristics, discernible by DFI length and complete resection of a solitary metastatic lesion, surgery should be considered as a viable treatment option, but these results have to be corroborated with larger studies.

DECLARATION OF INTEREST

The authors declare not having any conflicts of interests.

REFERENCES


