

Isolated Malignant Melanoma Metastasis to the Pancreas

Anne K. Larsen, MD*
 Christen Krag, PhD*
 Poul Geertsen, PhD†
 Linda P. Jakobsen, PhD*

Summary: Malignant melanomas rarely develop isolated pancreatic metastases. We describe a unique patient who is still alive 22 years following an isolated pancreatic melanoma metastasis, and we review the sparse literature in the field. (*Plast Reconstr Surg Glob Open* 2013;1:e74; doi: 10.1097/GOX.000000000000018; Published online 25 November 2013.)

Malignant melanoma rarely metastasizes to the pancreas with isolated metastases. The literature on isolated metastatic melanoma to the pancreas is limited. There is no consensus on the management of isolated pancreatic melanoma metastasis.¹⁻³

Metastatic tumors to the pancreas represent about 2% of all pancreatic malignancies. It is common that renal, breast, lung, and colon cancers metastasize to the pancreas, but less common is malignant melanoma. The malignant melanoma pancreatic metastases occur as either one manifestation in widespread disease or even more rare as an isolated metastasis.^{1,3,4}

Commonly the appearance of distant metastases in melanoma patients is associated with a poor prognosis. Nikfarjam et al reports a study showing that 6 patients with isolated metastases to pancreas achieved a median survival of 24 months and 5-year survival of 50% after complete surgical resection.⁵

We report a unique case of isolated pancreatic metastatic malignant melanoma in a patient with history of cutaneous malignant melanoma. The isolated

metastasis was surgically resected, and the patient is still alive with no sign of recurrence 22 years later.

CASE REPORT

A 32-year-old female was treated for a nodular cutaneous malignant melanoma (Clark level III, Breslow thickness 1.57 mm) on her upper back in 1988. The melanoma was excised in total 5.5 cm margin and in depth to the muscle fascia according to guidelines at that time. The skin defect was reconstructed with a split skin graft (Fig. 1).

In 1991, the patient developed upper abdominal pain, itching, and jaundice. An abdominal computed tomography (CT) scan and a transabdominal ultrasonography-assisted biopsy from the pancreas revealed a large malignant melanoma metastasis (5 cm in greatest dimension) localized in the head of the pancreas (Fig. 2). The patient received 3 cycles of systemic treatment with interleukin-2 and interferon- α over a period of 3 months. A CT scan after the first period of systemic treatment 1 month later showed regression of the tumor (Fig. 3). The systemic treatment was followed by 40 Gy radiotherapy (8 fractions of 5 Gy) resulting in complete remission 4 months later verified by a CT scan. Unfortunately, this last CT scan is not available, and only the description in the medical file is available.

In 1993, the 37-year-old patient developed upper abdominal pain and itching again. A CT scan of the abdomen showed recurrence of the tumor in the head of the pancreas. The pancreatic metastasis was radically resected by a pancreaticoduodenectomy (PD) ad modum Whipple. The final pathology was consistent with metastatic malignant melanoma, and

From the *Department of Plastic Surgery, Herlev Hospital, University of Copenhagen, Herlev, Denmark; and †Department of Oncology, Herlev Hospital, University of Copenhagen, Herlev, Denmark.

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Fig. 1. The cosmetic result after excision of cutaneous malignant melanoma on the back reconstructed with a split skin graft.

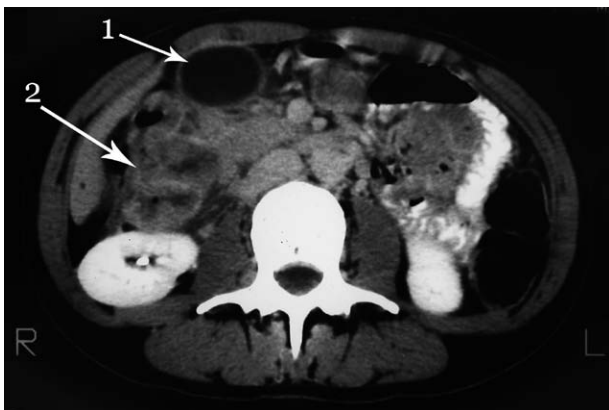


Fig. 2. CT scan of the abdomen identifying the gallbladder (arrow 1) and the malignant melanoma metastasis mass in the head of the pancreas (arrow 2).

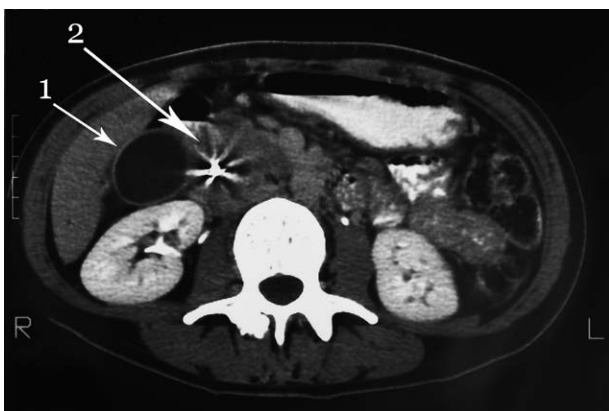


Fig. 3. CT scan of the abdomen after the first cycle of systemic treatment showing the gallbladder (arrow 1) and regression of the tumor in the head of the pancreas (arrow 2). In the center of the tumor, an endoprosthesis is creating artifacts.

the surgical margins and lymph nodes were negative. The postoperative stay was uneventful, and the patient was discharged 2 weeks later.

The patient was followed until December 2000 where the final CT scan was without malignancy.

The patient returned in 2011 with a melanoma on her left arm. A biopsy revealed a malignant melanoma (Clark level IV, Breslow thickness 2.34 mm). The melanoma was excised in 2-cm distance according to standard protocol, and the skin defect was closed directly. A sentinel node biopsy of a lymph node in the left axilla was negative. The 18-month follow-up was without sign of clinical recurrence, and in 2012, a transabdominal ultrasonography was normal. The patient declines further scans.

For this review, a PubMed search was undertaken with the keywords as referred. English written reports with isolated melanoma metastatic to the pancreas published between 1990 and 2012 were included.

DISCUSSION

The treatment of metastatic melanoma consists of surgery, chemotherapy, immunotherapy, and radiation, either in combination or individually. Patients with melanoma who have distant metastases have a median survival of less than 1 year.

Long-term survival of isolated malignant melanoma metastasis to the pancreas is rare according to the literature.^{6,8}

Surgery, when possible, consists of a pancreaticectomy procedure, dependent on the tumor location in the pancreas.

Systemic treatment options for patients with metastatic malignant melanoma have improved substantially the last decade. Immunotherapy with cytokines, such as interferon- α or interleukin-2, has demonstrated response rates of 10–15% in appropriately selected patients with metastatic malignant melanoma. Chemotherapy agents, such as Dacarbazine, Temozolomide, or Cisplatin, are some of the single agents showing response in the treatment of metastatic melanoma. The overall results of chemotherapy describe an overall response rate between 15% and 28%. The long-term remission rate is less than 2%.^{1,5-7}

Ipilimumab has also shown effect on metastatic malignant melanoma. Hodi et al⁸ present a randomized, double-blind, phase 3 study in 403 patients with unresectable metastatic melanoma, showing an improved survival with Ipilimumab.

V-raf murine sarcoma viral oncogene homolog B1 (BRAF) inhibitor therapy, such as Dabrafenib, has shown response in BRAF (= v-raf murine sarcoma viral oncogene homolog B1) mutated metastatic

Table 1. English Written Reports with Isolated Melanoma Metastatic to the Pancreas 1990–2012

No.	Authors	Year of Publication	No. Patients	Sex	Age at Surgery	Interval: Years from Primary Melanoma to Metastasis	Primary Site of Melanoma	Tumor Location in the Pancreas	Surgery and Systemic Treatment	Follow-up (mo)	Status at Follow-up
1	Nikfarjam et al ⁵	2003	1	Male	55	13	Ocular	Head	Total pancreatectomy	7	ANED
2	Crippa et al ⁹	2006	1	Female	36	2,6	Skin	Head	PPPD	14	DOD
3	Eidt et al ⁴	2007	1	NR	NR	4	Skin	NR	PPPD Postoperative chemotherapy	76	ANED
4	Goyal et al ¹	2010	1	Female	73	22	Skin	Head	PPPD	3	DOD
5	He et al ¹⁰	2010	1	Male	39	5	Ocular	Tail	DP and splenectomy Postoperative chemotherapy	25	DOD
6	Portale et al ³	2011	1	Female	43	7	Skin	Tail	DP and splenectomy	84	ANED
7	Current	2013	1	Female	37	5	Skin	Head	PD Radiotherapy and immunotherapy	264 (22 y)	ANED

ANED, alive; no evidence of disease; DOD, dead of disease; NR, not reported.

melanoma patients. Hauschild et al¹² present studies where BRAF inhibitor therapy has shown objective response rates of 70–80% in patients with metastatic melanoma, and as palliative therapy, the treatment seems to be valuable.

We report a case with a unique long-term survival after a pancreatic melanoma metastasis 22 years following a combination of immunotherapy, radiotherapy, and surgery. Studying the English literature, only 6 other cases with isolated malignant melanoma metastasis to the pancreas were identified (Fig. 1).

In the reviewed cases, the interval from primary malignant melanoma to pancreatic metastasis varied from 2.6 to 22 years, and the long-term survival from treatment to latest follow-up was 3–264 months with the present case (no. 7, Table 1) achieving by far the longest survival.

Of the 7 cases, 5 cases, the present case included, originated with cutaneous malignant melanoma and 2 as ocular malignant melanomas.

Our patient had the metastasis located in the head of the pancreas and received a PD, whereas the other 3 cases with metastasis location in the head of the pancreas received either a total pancreatectomy or a pylorus preserving PD (PPPD). In the 2 cases where the metastasis was located in the tail of the pancreas, the patients received a distal pancreatectomy (DP) and splenectomy. Eidt et al⁴ do not describe the location of the metastasis in the pancreas.

Based on the cases presented in Table 1, there is no obvious correlation between primary site of the melanoma, tumor location in the pancreas, the surgical treatment modality, and the long-term survival of the patient.

According to the literature, the PPPD procedure is growing increasingly popular compared with a traditional PD.¹³ In a PPPD, the pylorus and thus normal gastric emptying are preserved. It shows similar long-term survival as a PD (which is a PD and hemigastrectomy), but patients benefit from improved recovery of weight after a PPPD. Therefore, the PPPD is recommended when the tumor does not involve the stomach and when the lymph nodes along the gastric curvatures are not affected. When the tumor is located in the body or the tail of the pancreas, the surgical procedure should be a DP with splenectomy, as described in 2 cases reported by He et al¹⁰ and Portale et al.^{3,13}

Our presented case received treatment with interleukin-2 and interferon- α and radiotherapy before surgery. Two cases (Eidt et al⁴ and He et al¹⁰) received adjuvant therapy and with a resulting relative long-term survival of 76 and 25 months. Unfortunately, no specific data concerning this adjuvant chemotherapy are presented in the articles. The 4 other cases did not receive any systemic treatment: 2 were

reported dead after 3 and 14 months after treatment with PPPD, and 1 patient had a total pancreatectomy and was reported alive with no evidence of disease after 7 months. The last patient was treated with a DP and splenectomy and was alive with no evidence of disease 84 months after surgery. Furthermore, only our patient received radiotherapy. Radiotherapy for metastatic melanoma is generally associated with improved local and regional control rates without any survival benefit.¹¹

CONCLUSION

The available material is too small to make any conclusions, but the reviewed cases may point to a role for systemic therapy in the treatment of isolated melanoma metastatic to the pancreas and maybe also for radiotherapy.

The current case shows that even after malignant melanoma metastasis to pancreas, long-term survival is possible.

Anne K. Larsen

Department of Plastic Surgery
Herlev Hospital
University Hospital of Copenhagen
Herlev Ringvej 75
Herlev 2730
Denmark
E-mail: annekristinelarsen@yahoo.com

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