Primary giant aggressive amelanotic duodenal melanoma

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ABSTRACT

Primary malignant melanoma of the gastrointestinal tract is extremely rare. A 35-year-old man presented with complaints of abdominal pain and weight loss. Contrast enhanced computed tomography showed a large mass involving the duodenum and the superior mesenteric vessels. Upper gastrointestinal endoscopy demonstrated a large, friable mass along the duodenal wall and biopsy was suggestive of malignant melanoma. A detailed physical examination and whole body imaging (positron emission tomography and computed tomography) did not reveal any other lesion.

The patient underwent a pancreaticoduodenectomy with segmental resection and anastomosis of the superior mesenteric vein as well as a segmental colectomy. His postoperative recovery was uneventful. The histopathology of the operative specimen showed a malignant amelanotic melanoma arising from the duodenum with lymph nodal involvement. He received oral temozolomide. However, he developed liver metastasis at six months and again at ten months, which was managed with radiofrequency ablation both times. He is doing well at 32 months of follow-up review. Multimodality treatment including surgery, adjuvant chemotherapy and salvage therapy appears to be a promising tool for achieving long-term survival in such patients.

KEYWORDS

Primary duodenal melanoma – Gastrointestinal melanoma – Metastatic – Radiofrequency ablation – Pancreaticoduodenectomy – Superior mesenteric venous resection

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Malignant melanomas comprise 1–3% of all malignant tumours of the gastrointestinal (GI) tract.¹ Even though the small intestine is the most common site for GI metastases from cutaneous malignant melanomas, primary malignant melanomas arising in the small intestine are exceedingly rare. We report the case of a man who presented with abdominal pain and weight loss. On evaluation, a duodenal melanoma was diagnosed.

Case history

A 35-year-old man presented with intermittent pain in the epigastrium, which was radiating to the back. It was moderate in intensity, aggravated by food intake and relieved spontaneously. There had been weight loss of around 15kg over the preceding six months. Conversely, there was no associated loss of appetite although oral intake was reduced owing to pain. There was no history of vomiting, haematemesis or melaena. The patient later noticed a lump in his upper abdomen, which gradually increased in size. As the episodes of pain became more frequent, he sought medical advice.

The patient was pale and abdominal examination indicated a large, firm, irregular mass with an irregular surface occupying the epigastrium and right hypochondrium. Ultrasonography of the abdomen revealed a large mass arising

from the region of the duodenum. Subsequent upper GI endoscopy showed a large, friable mass along the duodenal wall and a biopsy was taken. On contrast enhanced computed tomography (CT), a large lesion was noted involving the duodenum and superior mesenteric vessels (Fig 1). Endoscopic ultrasonography to assess the status of the vessels demonstrated a large heteroechoic lesion arising from the fourth layer of the duodenal wall, with the superior mesenteric artery draped over it with a maintained interface. Biopsy indicated a tumour with the histomorphological features of a malignant melanoma, being immunopositive for HMB-45, and negative for S100 protein, CD3, CD20, CD117 and cytokeratins.

A detailed ophthalmological, otorhinolaryngeal and dermatological examination did not reveal any other lesion that could serve as a primary tumour for the duodenal lesion. Whole body positron emission tomography (PET) detected uptake only in the duodenum and peripancreatic lymph nodes. A pancreaticoduodenectomy was arranged.

Intraoperatively, the tumour was found to arise from the second part of the duodenum, involving the pancreatic head, distal common bile duct and right mesocolon. The tumour was situated close to the superior mesenteric vessels and the inferior vena cava was compressed. Nevertheless, the vessels could be separated, except for a 1cm segment of

Figure 1 Computed tomography showing a large, irregular, polypoidal mass arising from the second part of the duodenum

superior mesenteric vein, which was resected and reconstructed with an end-to-end anastomosis. A segment of colon was also excised and a side-to-side anastomosis was fashioned. The pancreatic duct was small (1.5mm) and a duct-to-mucosa pancreaticojejunostomy was performed (Fig 2).

Oral intake was commenced on postoperative day 5 but still supplemented by tube feeding, which was discontinued on day 7. Final histopathology results confirmed a large mass (13cm × 12cm × 8cm) arising from the first and second part of the duodenum, suggestive of malignant melanoma, and infiltrating the pancreas with nodal involvement (2/12 nodes positive). All margins were negative. The patient received oral temozolomide as adjuvant chemotherapy. Follow-up CT at six months showed a metastatic lesion in segment VIII of the liver. This was managed successfully with radiofrequency ablation (RFA) but recurrence developed in the same segment after four months, requiring repeat RFA. The patient had regular follow-up appointments every three months. He is doing well at 32 months following surgery without any further evidence of recurrence despite the early aggressive behaviour of the tumour.

Discussion

Malignant duodenal tumours can be primary or secondary to tumours elsewhere. The most common primary tumour involving the duodenum is an adenocarcinoma; others include lymphomas, leiomyomas, neuroendocrine tumours and GI stromal tumours. A duodenal melanoma is an extremely rare entity, with only 14 cases reported in the literature; 9 were metastatic lesions and 5 were primary. The cases with a primary melanoma are summarised in Table 1.²⁻⁶ Two of these patients had a pancreaticoduodenectomy,^{2,5} and two underwent resection and anastomosis.^{3,4} The last case was managed with supportive therapy owing to the poor performance status of the patient, who died three weeks later.⁶ The long-term follow-up of three of the four patients who had surgery has been positive²⁻⁴ despite metastasis in one.⁴

Our case differs from the cases above in terms of the patient's demographic profile, clinical presentation, course

Figure 2 Specimen of pancreaticoduodenectomy with combined segmental resection of the superior mesenteric vein and segmental colectomy

and outcome. He was a young man, unlike the other patients, who were aged 52–67 years. He presented with a large, palpable mass, suggesting that the mass had caused few symptoms until it had grown to a considerable size. This is in contrast to duodenal adenocarcinomas, which usually become symptomatic early in the course of the disease.

In most reported cases, melanoma presents with a painful abdomen and upper gastrointestinal haemorrhage, unlike duodenal adenocarcinoma, which presents with obstructive jaundice, gastric outlet obstruction and occult blood loss in the stool. Our patient had a large lesion with involvement of the superior mesenteric vein and transverse colon. GI mucosal melanomas have been reported to pursue an extremely aggressive course and have a poorer prognosis than other forms of melanoma. This is in part due to a delayed diagnosis because of their location and the rich vascular and lymphatic supply of the region.⁷

There are several theories regarding the origin of primary malignant melanoma in the small intestine. It has variously been postulated that malignant melanomas arise from multipotent neural crest cells, which migrate into the bowel and differentiate into specialised cells,^{8,9} or from amine precursor uptake and decarboxylation cells.¹⁰ In addition, melanoblasts (which are thought to exist naturally in the small bowel) may serve as precursors to malignant melanoma.⁸ Still others believe that primary malignant melanomas do not exist in the small intestine and that lesions found there represent metastasis after regression of the cutaneous primary tumour.^{1,9,11}

Several criteria have been proposed for the diagnosis of primary intestinal melanoma. Sachs *et al* suggested that a biopsy proven intestinal melanoma at a single site in the absence of extraintestinal disease, with a disease free survival of at least 12 months after diagnosis, was compatible

Table 1 Comparison of clinical, operative and postoperative variables for all published cases of primary duodenal melanoma

Variables	Korkolis, 2008 ²	Li, 2012 ³	Suganuma, 2013 ⁴	Bendic, 2013 ⁵	Coban, 2014 ⁶	Present case
Age / sex	55 M	60 M	67 M	52 M	63 F	35 M
Location	D2–D3	D2	D4 – jejunum	D2	D2	D2–D3
Presentation	Pain / haematemesis	Pain / melaena	Dyspnoea / fatigue	Weakness / jaundice	Pain / haematemesis	Pain / lump
Investigation	Upper GI endoscopy / CT	Upper GI endoscopy / CT	Upper GI endoscopy / CT / endoscopic ultrasonography / PET	Upper GI endoscopy / CT	Upper GI endoscopy / CT	Upper GI endoscopy / CT / endoscopic ultrasonography / PET
Metastasis	No	No	Stomach, left adrenal gland	No	No	No
Preoperative diagnosis	No	No	Yes	No	Yes	Yes
Management	Pancreaticoduodenectomy	Excision	Duodenojejunectomy, partial gastrectomy, left adrenalectomy	Pancreaticoduodenectomy	Non-operative; died after 3 weeks	Pancreaticoduodenectomy
Postoperative course	Uneventful	Not known	Not known	Not known	Not known	Uneventful
Histopathological findings						
Size	5.5cm × 4cm × 5cm	2.5cm × 1.5cm × 1cm	6.2cm × 4.6cm	1.4cm	Not known	13cm × 12cm × 8cm
Pigmentation	No	No	No	No	Yes	No
HMB-45	Yes	Yes	No	Not known	Yes	Yes
S100	Yes	Yes	Yes	Yes	Yes	No
Lymph nodes	Yes	Yes	No	Yes	Not known	Yes
Adjuvant therapy	Interferon α -2b	Refused	Dacarbazine, vincristine, nimustine	Not known	Not known	Temozolomide
Recurrence	Not known	Not known	Not known	Multiple liver metastases at 2 months	Not known	Distant recurrence at 6 and 10 months, treated with radiofrequency ablation
Survival	Alive at 14 months	Alive at 46 months	Alive at 36 months	Died at 6 months	Died at 3 weeks	Alive at 32 months

CT = computed tomography; GI = gastrointestinal; PET = positron emission tomography

with a diagnosis of primary intestinal melanoma.⁹ This was based on the surmise that a stage IV melanoma would generally be multifocal and the patient would be unlikely to survive for more than a year. Blecker *et al* proposed that primary malignant melanoma can be diagnosed if there is no evidence of a cutaneous melanoma (current or past), an atypical melanocytic cutaneous lesion or extraintestinal metastatic spread but there is evidence of intramucosal lesions in the intestinal epithelium.¹²

Our case fulfils the criteria of both Sachs *et al* and Blecker *et al* for diagnosis of a primary malignant melanoma.^{9,12} Although our patient did develop hepatic metastatic disease at six months, this possibly represented metastasis from the advanced duodenal primary tumour; it responded well to treatment, which is unlikely in a case of metastasis from an untreated occult primary tumour.

Clinically, a primary GI malignant melanoma would be suspected when the patient has no obvious primary skin

lesions or other extraintestinal disease, especially in the ocular system. The anorectum is the most common site for primary malignant melanomas of the GI tract and should always be examined. Diagnosis of GI melanoma is often delayed and patients usually present with advanced disease. As already alluded to, this results from the lack of specific symptoms in early disease and only when the disease is extensive do patients present with symptoms, often as an emergency. An abdominal mass is identified at presentation in about 10% of patients.^{13,14} Our patient presented with pain, an abdominal mass and severe pallor, and despite the size of the mass, there were no symptoms of gastric or biliary obstruction.

Diagnosis is primarily by means of upper GI endoscopy, which shows the lesion; the lesion may or may not be pigmented. The final diagnosis is made on the basis of a histopathological examination. PET is useful for identifying occult primary and metastatic melanoma lesions. The

sensitivity and specificity of PET for melanoma ranges from 79–92% and 86–90% respectively.^{15,16} In our case, the lesion was non-pigmented and the initial suspicion was of a GI stromal tumour. However, the typical pathological features and presence of immunohistochemical markers confirmed the diagnosis.

The treatment of choice for melanoma is surgical excision as other methods (adjuvant radiotherapy, chemotherapy and immunotherapy) are experimental and have not been shown conclusively to offer definitive treatment with a survival benefit. The median reported survival for small bowel melanoma is 49 months.² The longest reported survival in a patient with a primary melanoma is 21 years and multiple resections were required for dealing with metastasis.¹⁷

Tumours larger than 5cm in the second part of the duodenum generally preclude surgical resection owing to the involvement of large vessels. Nevertheless, given the young age of our patient, we attempted surgery encompassing vascular and multivisceral resection as this was his only chance of cure. Despite its large size, metastatic liver lesions within 6 months and an apparent aggressive behaviour early in its course, the tumour responded well and the patient continues to be disease free at 32 months. In the absence of significant literature elucidating the biological behaviour of these tumours, it is probably worthwhile to offer aggressive management to such patients.

Conclusions

To our knowledge, this is the first case report in the literature of a primary giant amelanotic malignant melanoma. It was treated by means of a surgical procedure with vascular and multivisceral resections. Despite early postoperative recurrence, the patient is disease free at 32 months. Multimodal treatment including surgery with adjuvant and salvage therapies appears to be promising for achieving long-term survival in these patients.

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