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Malignant melanoma of the gastro-intestinal tract: A case series

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ABSTRACT

Background: Resection of gastrointestinal (GI) metastases of malignant melanoma (MM) offers a significant survival benefit. No adjuvant therapy has been shown to be effective in the treatment of these metastases.

Methods: All resections of MM affecting the GI tract at a UK University teaching hospital between October 1999 and January 2013 were identified from a pathology database. Demographic, investigative, operative and outcome data were retrieved from hospital records. Survival analysis was performed.

Results: Thirty patients were identified (median age 62.7 years). 3 patients underwent a second operation at a later date to resect further metastases. 6 patients (20.0%) presented with no identifiable cutaneous lesion. The average time to GI metastases was 52.0 months (range 4.9–139.8 months) for those with an identified cutaneous primary ($n = 24$). Two patients with initial cutaneous lesions with Breslow's thickness < 1 mm developed GI metastases.

Common presenting symptoms included abdominal pain ($n = 8$, 27.6%), GI bleeding ($n = 5$, 17.2%) and symptoms of GI tract obstruction ($n = 4$, 13.8%). CT scan was the most commonly performed investigation (96.6%). Over half of resections (54.5%, $n = 18$) included small bowel resection. Mortality at 2 and 5 years was 66.4% and 73.1%. Of the 3 patients who underwent a second resection of GI metastases, one is still alive after 26 months of follow up; 2 patients died after 32.8 and 18.6 months.

Conclusions: Clinicians should have a low threshold for investigating GI symptoms in patients with a history of malignant melanoma even in the case of early-stage primary disease. Re-resection should be considered in patients presenting with further GI metastases.

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1. Background

Melanoma is the most common tumour to metastasise to the gastro-intestinal (GI) tract. These tumours are commonly metastases from a cutaneous or less frequently, an ocular primary lesion. Rarely malignant melanomas (MM) of the GI tract can be primary tumours.

The superficial spreading sub-type of MM is most likely to metastasise to small intestine although all are capable of such spread [1]. Amersi and colleagues implicated chemokine receptor-9 (CCR9), which contributes to enhanced motility of melanoma cells, and its ligand CCL25 in the preferential metastasis of MM to this location [2].

The existence of primary intestinal melanoma remains a contentious subject with some authors stating the aetiology of GI tract MM as unknown or regressed primary lesions. Plausible theories attribute the origins of primary melanoma of the small intestine to schwannian neuroblast cells [3], melanoblastic cells of the neural crest [4], or amine-precursor uptake and decarboxylation (APUD) cells via neoplastic transformation [5].

Up to 60% of patients with MM will have evidence of GI metastases at autopsy yet only 1–4% of all patients with MM will have clinical manifestations of GI tract involvement during their lifetime [6].

Acute presentations include intestinal obstruction (including intussusception [7]), massive GI haemorrhage and less commonly, perforation. Sub-acute presentation commonly includes symptoms of anaemia (including occult GI haemorrhage), cramping/chronic abdominal pain and an abdominal mass [8]. Less frequent presentations include obstructive jaundice caused by obstructing lesions within the biliary tree [9].

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Standard CT scan is commonly used to locate MM spread intra-abdominally although 18F-2-fluoro-2-deoxy-D-glucose-positron emission tomography (FDG PET) CT scan has been shown to have a higher sensitivity and accuracy in the detection of visceral metastases, including extra-intestinal metastatic disease [10,11]. Conventional endoscopy for proximal and distal portions of the GI tract offers the possibility of biopsy. Less readily available capsule endoscopy allows non-invasive examination of the small bowel mucosa although difficulties exist in locating lesions and an inability to biopsy lesions.

Systemic chemotherapy regimens show no benefit to overall survival and are not recommended for treatment of GI tract metastases of MM [12]. Surgery is carried out for acute intra-abdominal emergency such as obstruction or haemorrhage, yet the criteria for surgery in minimally symptomatic/asymptomatic metastases is less well defined.

Most case series for GI tract metastases of MM have come from Australia and US populations. We therefore undertook an analysis of all resections for MM GI tract metastases at a large university teaching hospital in the UK to see if some common conclusions could be drawn.

2. Methods

A single-centre retrospective review of cases of MM affecting the GI tract was conducted between October 1999 and January 2013. Our unit's pathology database was searched for all resections involving the GI tract, excluding hepatic metastases, with a final diagnosis of malignant melanoma.

Information was collected regarding the primary melanoma where appropriate including histopathological staging and location. Information on GI melanoma was collected including presentation, investigation, surgical resection(s) and follow up. Patients were excluded from subsequent analysis if they didn't undergo resection of GI metastases.

Patient survival was calculated from the date of GI resection to date of death. If the patient was still alive according to NHS records, survival time was from date of GI resection to date of study analysis. Survival curves were plotted using SPSS version 19 (IBM Corp., Armonk, NY) and significant differences between survival curves was tested using the log-rank Mantel–Cox test. Internal audit approval was sought prior to data collection.

3. Results

The 30 patients identified comprised of 22 males and 8 females (see Table 1). The median age at operation was 62.7 years (range 24.4–77.6 years). Of the 30 patients, 27 (90.0%) underwent one operation to resect GI metastases. Three (10.0%) had a second operation at a later date to resect further GI metastases.

A primary cutaneous lesion was identified in 24 cases (80.0%) with the remaining 6 patients (20.0%) presenting with GI tract involvement as the first site of disease. Details of the lymph node status of the primary lesion were not available. The median time to GI metastases was 43.0 months (range 4.9–139.8 months) for those with an identified cutaneous primary ($n = 24$). There was a trend towards increased time to GI metastases with early stage primary disease but this did not reach statistical significance ($P = 0.08$, Kruskal–Wallis, see Table 2).

The most common presenting symptoms were abdominal pain ($n = 8$, 27.6%), GI bleeding ($n = 5$, 17.2%), and GI tract obstruction ($n = 4$, 13.8%). Other complaints included an abdominal mass, symptoms of anaemia and altered bowel habit. Seven patients (24.1%) did not complain of any symptoms. One patient who

Table 1

Demographic details of cohort, initial melanoma, investigation and operative resections performed.

		<i>n</i> = 30	%
Gender	Male	22	73.3
	Female	8	26.7
Age	<50	9	30.0
	>50	21	70.0
Primary cutaneous lesion	Identified	24	80.0
	GI tract first presentation of disease	6	20.0
Breslow thickness ^a	<1	2	8.3
	1.01–2	8	33.3
	2.01–4	8	33.3
	>4	6	25.0
Clark's staging ^a	1	1	5.0
	3	2	10.0
	4	13	65.0
	5	4	20.0
Presenting symptoms ^{a,b}	Pain	8	27.6
	GI bleeding	5	17.2
	GI tract obstruction	4	13.8
	Anaemia	2	6.9
	Abdominal mass	2	6.9
	Altered bowel habit	2	6.9
	Abdominal distension	1	3.4
	Jaundice	1	3.4
Asymptomatic	7	24.1	
Investigations ^c	CT scan	28	96.6
	PET CT	5	17.2
	Endoscopy	2	6.9
	Ultrasound	3	10.3
	MRI	1	3.4
Extra-GI metastases ^a	Present	20	69.0
	Absent	9	31.0
Operation	Small bowel resection alone	13	39.4
	Large bowel resection alone	7	21.2
	Small bowel resection and other visceral resection	3	9.1
	Small and large bowel resection	2	6.1
	Partial/complete resection of stomach	2	6.1
	Whipple procedure	1	3.0
	Other combinations	5	15.2

^a Where *n* is less than 30, information was not available for the remaining patients.

^b Several patients experienced more than one symptom.

^c Several patients underwent more than one investigation.

presented with obstructive jaundice secondary to a pancreatic metastasis went on to have a Whipple's procedure.

3.1. Imaging

The majority of patients ($n = 28$, 96.6%) underwent a conventional CT scan. The five patients (17.2%) who were imaged with PET-CT underwent this investigation in addition to conventional CT scan. Seven patients (24.1%) were imaged with more than one modality.

3.2. Operative procedures

A total of 33 operative resections were performed resulting in complete excision of intra-abdominal metastases with clear

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