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Gastrointestinal Malignant Melanoma: A Single Center Experience

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ABSTRACT

Introduction: Malignant melanoma (MM) is a tumor that develops from skin-derived melanocytes and has a poor prognosis. Extracutaneous involvement of MM is also known, and one of these localizations is in the gastrointestinal tract. The study investigated gastrointestinal MM cases diagnosed as primary or metastatic in terms of their clinicopathological findings and survival rates.

Methods: Patients diagnosed with gastrointestinal MM in our clinic between August 2013 and December 2022 were retrospectively evaluated. Data including demographics, physical examination, laboratory and imaging findings, surgical procedures, oncological treatment status, presence of metastasis, histopathological features, and mortality were recorded and analyzed.

Results: The study group consisted of 9 patients: 4 (44.5%) women and 5 (55.5%) men with a mean age of 57.8±13.5 (median: 61, range: 40-75). Surgery could not be performed in four patients because of locally advanced or metastatic disease. Radical surgical interventions were performed in 4 (44.4%) patients who were operable. A second surgical intervention was performed in one patient. The mean duration of hospital stay of surgically treated patients was 6.4±4.3 (median: 5, range: 2-13) days. The mean overall survival in these patients was 40.0±25.7 (median: 40, range: 12-74) months. Three (33.3%) patients who underwent surgery are still being followed up.

Conclusion: In operable cases of histopathologically proven primary or metastatic MM disease, surgical treatment has an important impact on terms of providing local control and improving survival.

Keywords: Melanoma, gastrointestinal tract, neoplasm metastasis, general surgery

Introduction

Malignant melanoma (MM) is a skin-derived malignant tumor that has increased in frequency in recent years and has an aggressive course. MM is the rarest but most deadly type of skin cancer and is most likely to metastasize (1). MM can develop primarily in many organs other than the skin, albeit at a low rate. It may occur in the eye, oropharynx, nasopharynx, anal canal, rectum, small intestine, esophagus, or urinary system (2). The main presenting symptom of patients with primary gastrointestinal MM is bleeding. The diagnosis can usually be made by endoscopic visualization of the lesion. In the gastrointestinal tract, MM can also occur metastatically. Metastatic lesions may present with organ-specific symptoms. Radical surgical treatment of patients diagnosed histopathologically is effective for elimination of the disease and survival. Oncological treatment is also part of the treatment. Surgical treatment is the primary option for patients who develop gastrointestinal metastases.

Methods

All patients who were histopathologically diagnosed with primary or metastatic gastrointestinal MM between August 2013 and December 2022 in the department of general surgery were included. The study was conducted after the approval of the Local Ethics Committee of University of Health Sciences Turkey, Medeniyet University, Göztepe Training and Research Hospital (approval number: 2023/0199, date: 29.03.2023).

The patients' historical records, including demographics, physical examination, laboratory and imaging findings, surgical procedures, presence of metastases, histopathological features, and mortality, were prospectively recorded and retrospectively analyzed. Lesions located in the anorectum were diagnosed endoscopically or via excisional biopsy, whereas lesions located in the liver were diagnosed using

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Table 1. Patient characteristics

		n	%
Gender	Women	4	44.5
	Male	5	55.5
Diagnostic method	Endoscopic biopsy	6	66.7
	Excisional biopsy	1	11.1
	Tru-cut biopsy	2	22.2
Surgical procedure	No	5	55.5
	Yes	4	44.5
Surgical method	Right hemicolectomy, non-anatomical hepatectomy (segment 6), and duodenal wedge resection	1	25
	Abdominoperineal resection	1	25
	Segmentary liver resection	1	25
	Total transanal excision and non-anatomical hepatectomy (segments 4B and 5)	1	25

n: Number of patients

ultrasound- guided percutaneous tru-cut biopsy (Table 1). Magnetic resonance imaging (MRI) and 18-fluorodeoxyglucose positron emission tomography (18-FDG-PET) were used as cross-sectional imaging methods for detecting metastatic lesions.

Postsurgical and oncological follow-ups were conducted via office visits in the surgical outpatient clinic. Survival rates were determined at the end of the long-term follow-up period.

Statistical Analysis

Statistical analysis was performed using standard descriptive statistical methods (mean, median, percentage, minimum, maximum).

Results

The total study group of 9 patients consisted of 4 (44.5%) women and 5 (55.5%) men. The mean age of the patients was calculated to be 57.8±13.5 (median: 61, range: 40-75) years. 4 (44.4%) patients were considered inoperable because of locally advanced or metastatic disease. One patient (11.1%) who was lost to follow-up had to be excluded from the study mandatorily. Chemotherapy was initiated in 4 (44.4%) patients who were considered inoperable (Table 2). Among patients who were candidates for surgical treatment, primary lesions within the gastrointestinal tract were detected endoscopically, as in three patients (33.3%), the lesion was located in the anorectum. In one (11.1%) patient, imaging studies showed that the lesion was metastatically located in the liver, whose primary tumor site was known to be the uvea because she had a history of left eye enucleation 30 years ago.

The diagnosis of MM was confirmed histopathologically in all patients. Histopathological examinations revealed that the melanoma marker antibody (HMB-45) and pan cytokeratin (pan CK) were positive in all (100%) patients. Melanosomal protein (Melan-A) was positive in 5 (55.5%) patients, whereas 7 (77.8%) patients were positive for S100 protein, and the mean Ki-67 value was determined to be 71.7±17.2 (median: 80, range: 50-90) %.

Table 2. Non-operative malignant melanoma cases

Patient#	Age	Gender	Primary tumor location	Metastasis site	The type of biopsy	Surgical procedure	Recurrence/ metastasis	CD45	HMB45	S100	Melan-A	Pan CK	Ki67 (%)	Adjuvant therapy	Survival/ period
1	50	M	Anal canal	Liver	Excisional	No	+	0	+	+	0	-	80	+	Exitus/5 months
2	75	M	Rectum	Liver, lung	Endoscopic	No	+	0	+	+	+	-	80	+	Exitus/3 months
3	61	F	Skin	Liver	Tru-cut	No	+	0	+	+	0	-	-	+	Exitus/7 months
4	53	M	Skin	Liver, bone marrow	Tru-cut	No	+	0	+	-	+	0	50	+	Exitus/2 months

Table 3. Operative malignant melanoma cases

Patient#	Age	Gender	Primary tumor location	Metastasis site	The type of biopsy	Surgical procedure	TNM	HMB45	S100	Melan-A	Pan CK	Ki67 (%)	Adjuvant therapy	Distant metastasis	Survival/ period
1	40	F	Anal canal	None	Endoscopic	1. Total transanal excision (2016) 2. Right hemicolectomy non-anatomical hepatectomy (segment 6) And duodenal wedge resection (2020)	T4NxMx	+	+	No	-	80	+	+	Alive/74 months
2	64	F	Rectum	None	Endoscopic	Abdominoperineal resection	T2bN1bMx	+	+	+	-	-	+	+	Exitus/12 months
3	65	F	Uvea	Liver	Tru-cut	Non-anatomical hepatectomy (segments 4B and 5)	-	+	+	+	-	-	+	-	Alive/40 months
4	74	M	Anal canal	None	Endoscopic	Rectal polypectomy	-	+	+	+	-	50	+	+	Alive/34 months

Figure 1. Right hemicolectomy, nonanatomical hepatectomy, and duodenal wedge resection were performed in this patient, and she is still being followed up with no new findings of recurrence or metastasis. Written informed consent was taken from the patient

Radical surgical procedures were performed for the lesion in 4 (44.4%) patients who were determined to be operable after their initial clinical and radiological evaluations (Table 3). Interventions performed on patients with primary gastrointestinal MM included rectal polypectomy, abdominoperineal resection, and total transanal excision. The patient with liver metastasis underwent non-anatomical hepatectomy. The mean duration of hospital stay in the early postoperative period was 6.4±4.3 (median: 5, range: 2-13) days.

In the patient who was treated with endoscopic polypectomy, local recurrence at the previous polypectomy site was encountered at control colonoscopy in the 4th year which also was confirmed via imaging studies. Right hemicolectomy, nonanatomical hepatectomy, and duodenal wedge resection were performed in this patient, and she is still being followed up with no new findings of recurrence or metastasis (Figure 1).

In the patient who underwent abdominoperineal resection as a radical surgical procedure, liver metastasis developed in the postoperative 3rd month and she died at the 12th month during her adjuvant treatment period.

All (100%) patients who were treated non-operatively died during their long-term follow-ups. Three (33.3%) surgically treated patients are still being followed up. At the end of the long-term follow-up period of the surgically treated patients, the overall survival was found to be 40.0±25.7 (median: 40, range: 12-74) months.

Discussion

MM is characterized by various molecular subtypes and different types of clinical presentations. It is the rarest but most deadly groups of skin cancers with the highest probability of metastasis (1). Although MM is a

primary skin tumor, the lesions are located extracutaneously in 4-5% of cases. It may develop in uveal, ocular, mucosal, anorectal, urinary, or vulvovaginal localizations other than the skin (3). The idea that primary gastrointestinal MM arises from anywhere in the gastrointestinal tract where melanocytes are present is common. However, lesions are predominantly detected in the anorectum (4).

Anorectal MMs detected in the gastrointestinal tract constitute approximately 0.4-1.1% of all MM cases (5). Anorectal MMs may originate from melanocytes located in the anoderm, which is the non-keratinized stratified squamous epithelium below the dentate line, as well as in the transitional zone neighboring the dentate line. In our study, the primary tumor sites within the gastrointestinal tract were detected to be the anorectum in 5 (55.5%) patients. The extraintestinal primary tumor sites were the skin in 2 (22.2%) patients and the uvea in one (11.1%) patient, as these cases had presented with liver metastasis.

Gastrointestinal MMs can be seen at any age, but it is reported that they are usually seen in the age of 50-60 yr (6). In our study, the mean age of the patients was calculated to be 57.8±13.5 (median: 61, range: 40-75) years. With the understanding of the disease and its molecular and immunological aspects, more effective treatment modalities have emerged recently (3).

The endoscopic appearance is not the same for every patient and may vary. Gastrointestinal metastatic lesions may also be misleading. Polypoid or excavated lesions may be observed, and although the color may be helpful in recognizing the lesion, some lesions may be amelanotic, and biopsy should be performed from suspicious lesions (7). Patients with gastrointestinal metastatic MM may present with nonspecific symptoms, such as abdominal pain or constipation, primarily depending on the affected location. Tumor-related gastrointestinal obstruction and active bleeding cases due to MM have also been reported (8). Bleeding is the most typical symptom in primary anorectal MM and should be considered in the differential diagnosis of hemorrhoids because of its localization and appearance. Endoscopic or excisional biopsies of the lesions observed on anorectal examination also contribute to the diagnosis. Gastrointestinal system MMs are mostly detected by the detection of cavitary, infiltrating, or polypoid lesions in endoscopic examinations performed to investigate gastrointestinal bleeding confirmed by the histopathological examination of the specimens of these lesions (9). In our study, all gastrointestinal primary lesions were histopathologically confirmed to be MMs according to their endoscopic biopsies.

Immunohistochemical positivity of HMB-45 facilitates the diagnosis of the disease (10). The presence of another immunohistochemical marker, S-100, is also important for definitive diagnosis, which is positive in most cases (11). In the present study, HMB-45 and pan CK were positive in all (100%) patients, whereas 7 (77.8%) patients were positive for S100 protein.

MM can metastasize to many organs and are among the most common carcinomas that metastasize to the gastrointestinal tract. However, it has also been reported that these tumors have a specific affinity for the small intestine, especially the jejunum and ileum (12). The clinical diagnosis of primary or metastatic MM disease may not be easy in the presence of non-specific or mild complaints. The interval between the surgical procedure for the primary lesion of MM and the metastatic disease may also be a confounding factor in the diagnosis. Distant metastases of MMs are mostly diagnosed within the first 3 years, but some cases report metastatic disease 15 years after initial treatment (13). Metastatic disease can be detected at the time of admission in approximately 4% of patients diagnosed with primary skin-related MM (7). MMs can also occur in the gastrointestinal tract, typically with liver metastases (4). Multifocal gastrointestinal mucosal melanomas are also usually of metastatic origin (14). In our study, most metastatic cases presented with liver metastases followed by lung and bone marrow metastases, as the primary tumor sites were primarily the gastrointestinal tract, especially the anorectum, followed by the skin and uvea. All 4 (44.4%) patients who were decided to be inoperable consisted of metastatic cases. Among surgically treated cases, only one (11.1%) patient presented with liver metastasis, which was considered operable according to pre-operative clinical evaluations.

In primary or metastatic gastrointestinal MM cases, imaging such as MRI, CT, or 18-FDG-PET/CT may be useful in identifying possible lesions or metastatic melanoma sites and can also be used during follow-up, especially in advanced disease (12). In lesions located in the anorectal region, pelvic MRI is important to determine the depth of the tumor and to have an idea about lymphatic involvement, therefore, to evaluate operability and determine the treatment method.

Radical surgery plays an important role in treating primary or metastatic MM of the gastrointestinal tract. Surgical intervention not only provides local control of the disease but also contributes to the elimination of possible bleeding or obstruction focus. In operable cases, there is an increase in the quality of life and survival of patients whose lesions can be resected by radical surgery (15). Before deciding on radical surgery for the disease, the comorbidities, age, general condition, and disease burden of the patients should also be considered. In this study, all (100%) patients who were treated non-operatively died during their long-term follow-ups. On the other hand, among surgically treated cases, one (11.1%) mortality occurred and three (33.3%) patients are still being followed up, revealing the survival benefit of surgical treatment as the median overall survival of these patients was found to 40 (range: 12-74) months.

Study Limitations

The limitations of our study can be considered as being a single-center study including a limited number of cases. However, given that primary or metastatic gastrointestinal MM is a rare presentation of this particular disease, we believe that the results of our series may shed light on the treatment outcomes of this entity.

Conclusion

The possibility of MM in primary or metastatic lesions detected in gastrointestinal system evaluations should be kept in mind, and should be considered in the differential diagnosis in histopathological examination. For treating histopathologically proven primary or

metastatic MM disease, surgical treatment plays an important role in providing local control of the disease in operable cases. There is an increase in patient survival with radical surgical procedures. Oncological treatment also maintains its place as a part of the multidisciplinary management of MM cases.

Ethics Committee Approval: The study was conducted after the approval of the Local Ethics Committee of University of Health Sciences Turkey, Medeniyet University, Göztepe Training and Research Hospital (approval number: 2023/0199, date: 29.03.2023).

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