

Original Article

Anal Melanoma: Outcomes of Current Surgical Approaches

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INTRODUCTION

Anal melanoma (AM) is one of the rarely reported tumors. AMs represent only approximately 0.4–0.6% of all melanoma cases^[1] and 1% of anal malignant tumors.^[2] They are frequently associated with metastatic disease and have been shown to have worse prognoses than cutaneous melanoma. For AMs, the absence of response to local radiation and systemic chemotherapy is the most significant poor prognosis factor.^[3,4] They have a median survival of 24 months and a 5-year survival rate of 10%.^[5]

Melanocytes are located at the anal squamous and transitional zones in the rectum. Most of AMs arise from the dentate line, and 65% of them are located within the anal canal or at the anal verge.^[6]

Treatment strategies for AMs vary from the radical abdominoperineal resection (APR) to the conservative local excision (LE). The role of adjuvant chemotherapy and immunotherapy in the treatment of AM has not been established yet. Also, there is no consensus on which surgical approach is favorable.^[7]

ABSTRACT

Aim: In this study, we aimed to evaluate the clinical characteristics and outcomes of the patients with anal melanoma (AM), who underwent surgical treatment. **Materials and Methods:** This study was conducted in Kartal Training and Research Hospital between January 2010 and December 2017. All patients, who underwent surgical resection with a diagnosis of AM, were enrolled. **Results:** A total of 10 patients were examined, 8 of them were females, and their average age was 69.2 years (range, 47–85 years). Abdominoperineal resection (APR) was performed in five (50%) patients, and local excision (LE) was performed in other five (50%) patients. Three patients (30%) had stage I disease, two (20%) had stage II disease, and five (50%) had stage III disease. All five patients in APR group had stage III disease. In the comparison of the survival period after surgery, the mean survival period of the APR group was 6.2 months (range, 1–16 months) while that of the LE group was 19.6 months (range, 7–43 months). **Conclusion:** LE with adjuvant radiation seems to offer good locoregional control without reducing the survival and may be an option of treatment for patients with small, superficial AM. However, APR should be offered for patients with locally advanced disease or as a salvage following recurrence.

KEYWORDS: *Abdominoperineal resection, anal melanoma, local excision*

In this study, we aimed to evaluate the clinical characteristics and outcomes of the patients with AM, who underwent surgical treatment.

MATERIALS AND METHODS


This study was conducted in Kartal Training and Research Hospital between January 2010 and December 2017. All patients, who underwent surgical resection with a diagnosis of AM, were enrolled. The medical records of the patients were retrospectively examined. Patient demographics, tumor characteristics, surgical methods, pathological records, and overall survival were analyzed. Definition of the extent of disease was based on clinical preoperative assessment in patients undergoing LE and on pathological examination in patients who underwent APR. In the pathology department of our hospital, for

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a definite diagnosis of melanoma, immunohistochemical staining of specimen was performed using S-100, HMB-45 for all cases. Our study was approved by our institution's ethic committee (2018/514/122/7, 30.01.2018).

RESULTS

A total of 10 patients were examined, 8 (80%) of them were females, and their mean age was 69.2 ± 11.3 years (range, 47–85 years). Common symptoms were hematochezia (70%), rectal mass (40%), altered bowel habits (40%), and pain in the anal area (10%) at the first application. Other rare symptoms were tenesmus and fecal incontinence. The interval from the onset of symptoms to the diagnosis of an AM was an average of 11.1 months (range, 3–24 months).

APR was performed in five (50%) patients, and LE was performed in other five (50%) patients. All of the five APR patients were female. Among the five patients who underwent a LE, two patients were males and three patients were females. The mean ages of the two groups were 66.6 ± 11.4 and 71.2 ± 11.9 years, respectively. The interval from the onset of symptoms to the diagnosis of an AM in the APR group was an average of 13.4 ± 5.3 months (range, 3–24 months), and that in the LE group was an average of 8.8 ± 2.8 months (range, 3–14 months). The average tumor size for the abdominoperineal group was 6.3 cm (range, 3.5–14 cm), which was 2.3 cm (range, 1–3.8 cm) for the LE group. In patients with the abdominoperineal group, four of the five operated patients were at the dentate line level, one was below the dentate line. In patients with the LE group, three of the five operated patients were at the dentate line level, two were below the dentate line [Figure 1]. Melanotic discoloration was detected in 7 patients (70%) of the

total 10 patients (3 patients in the APR group and 4 patients in the LE group).

Three (30%) patients had stage I disease, two (20%) had stage II disease, and five (50%) had stage III disease. One (10%) patient with stage II disease had only inguinal nodal metastasis, whereas other had both bilateral inguinal nodes and metastasis in the liver. Five

Table 1: Clinical characteristics of two groups (abdominoperineal resection and local excision)

	APR (n=5)	LE (n=5)
Sex		
Male	-	2 (40)
Female	5 (100)	3 (60)
Age (years)	66.6 (47-78)	71.2 (60-85)
Time to diagnosis (months)	13.4 (3-24)	8.8 (3-14)
Symptoms		
Bleeding per rectum	3 (60)	4 (80)
Pain	1 (20)	
Mass in rectum	2 (40)	2 (40)
Altered bowel habits	4 (80)	
Tumor size (cm)	6.3 (3.5-14)	2.3 (1-3.8)
Related with anal verge		
Dentate line	4	3
Below dentate line	1	2
Melanotic discoloration	3 (60)	4 (80)
Stage		
I		3 (60)
II		2 (40)
III	5 (100)	
Resection margin (cm)	1.7 (1-2)	0.74 (0.2-1)
Overall survival (months)	6.2 (1-16)	19.6 (7-43)

Values are presented as n (%) or value (range). APR=Abdominoperineal resection; WLE=Wide local excision

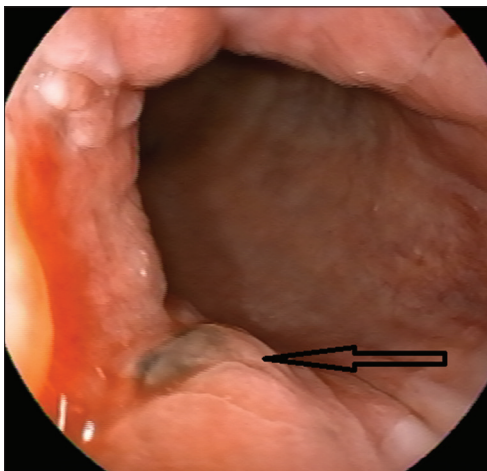


Figure 1: Colonoscopic findings of a patient with anal melanoma

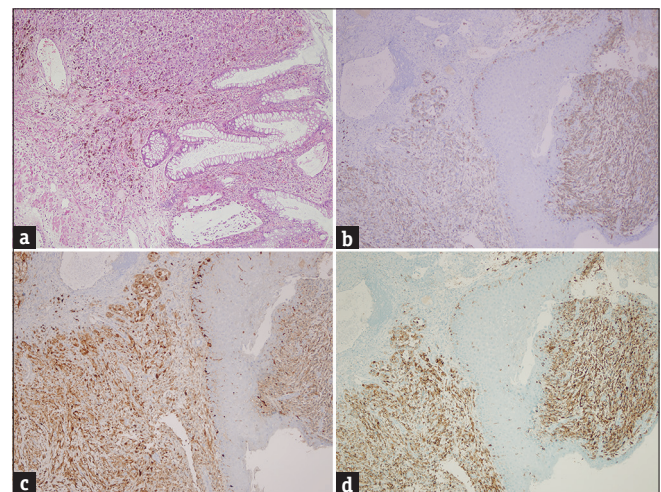


Figure 2: (a) Pathologic finding of anorectal malignant melanoma (H and E, $\times 10$), (b) pathologic finding of anorectal malignant melanoma (HMB-45, $\times 10$), (c) pathologic finding of anorectal malignant melanoma (S-100, $\times 10$), and (d) pathologic finding of anorectal malignant melanoma (melan A, $\times 10$)

Table 2: Details of the 10 patients treated by surgery

Age/Sex	Location*	Size (cm)	Depth	Treatment	Resection margin (cm)	Adjuvant chemotherapy	Adjuvant radiotherapy	OS	Dead
70/Female	DL	3.5	MP	APR	2	No	No	1	Yes
82/Female	BDL	2	M	LE	0.5	Yes	Yes	17	Yes
65/Female	BDL	5	PR	APR	1	Yes	Yes	5	Yes
62/Female	DL	2.2	M	LE	1	Yes	Yes	9	Yes
47/Female	DL	5.5	M	APR	1.5	No	No	3	Yes
60/Female	BDL	1	M	LE	0.2	Yes	Yes	7	No
73/Female	DL	14	PR	APR	2	Yes	Yes	16	Yes
85/Male	DL	3.8	MP	LE	1	Yes	Yes	43	No
70/Male	DL	2.5	MP	LE	1	Yes	Yes	22	Yes
78/Female	DL	3.5	MP	APR	2	Yes	Yes	6	No

*Related with anal verge. DL=Dentate line; BDL=Below dentate line; M=Mucosa; SM=Submucosa; MP=Muscularis propria; PR=Perirectal tissue; OS=Overall survival; APR=Abdominoperineal resection; WLE=Wide local excision

patients with stage I disease and stage II disease were in LE group. Among the stage III disease patients, three had metastasis in the liver, one had in the lung, and one had both liver and lung metastasis. All five patients in APR group had stage III disease. In the APR group, 60% of the patients (three out of five patients) received postsurgical adjuvant chemoradiotherapy while in the wide excision group, 100% of the patients (five out of five patients) did [Table 1]. Histopathological examinations revealed melanization in 70% of all cases [Figure 2].

In the comparison of the survival period after surgery, the mean survival period of the APR group was 6.2 months (range, 1–16 months) while that of the LE group was 19.6 months (range, 7–43 months). Detailed information of 10 patients treated by surgery were also tabled [Table 2].

DISCUSSION

Melanoma of the anal region is an extremely rare neoplasm with a poor prognosis. It is thought to arise from melanocytes in the mucosa around the anorectal junction. The rare nature of this entity is represented by the limited number of cases described in the medical literature. AM is mostly seen in the sixth decade, with a female predominance.^[8] Typical symptoms (bleeding, pain, perianal mass) are characteristic of hemorrhoids.^[9] There are very limited studies describing rare symptoms like tenesmus and fecal incontinence.^[10] In our study, 80% of patients were female and the most common symptom was hematochezia (70%). The mean age of our patients was about 69. Mean duration from onset of symptoms was 7.8 (1–36) months in Choi *et al.* study in patients via AM. Late diagnosis remains major obstacle for bad prognosis.^[10] This time frame was 11.1 months (3–24) in our present study.

A mass is usually palpated on digital rectal examination. Proctoscopy usually reveals a

hemorrhoid-like pigmented lesion near the anorectal junction, on which a biopsy must be performed. The histopathologic findings are similar to those of melanomas of other origins. To accurately diagnose an AM and to avoid misdiagnosis of patients with anal tumors, hematochezia, pain in the anal area and other symptoms of hemorrhoids, or other benign diseases in the anal area, pathohistological tests should be performed. Immunohistochemical staining using markers useful for the diagnosis of melanoma HMB-45 and S-100 is recommended. After the histologic diagnosis of AM, a complete staging and search for possible distant metastases (colonoscopy, computed tomography of the abdomen and thorax, MRI of the pelvis and brain), as well as ruling out primary sites (skin and retina), are mandatory.^[11]

Historically, the primary mode of treatment for anorectal melanoma has always been surgery. In the absence of randomized studies, there exists conflicting reports in literature regarding the optimal surgical procedure.^[8,12] Treatment strategies have varied, from the radical APR to the conservative LE. Locally, limited tumors should be resected, if possible using LE. Best hope for survival is offered by early detection and complete surgical removal. However, it is usually delayed because of occult site of recurrence and unspecific symptoms of diagnosis.^[13] Larger tumors or tumors with sphincter infiltration often require APR with curative intent. Lymph-node metastasis (LNM) remains major risk factor for impaired prognosis. Bilateral involvement of nodes is worse prognostic factor in melanomas.^[14] However, studies showing the importance of LNM are lacking. Limited studies are nonhomogen.^[15] Inguinal lymph node dissection has no advantage on general survival like radical APR with total mesorectal excision.^[16] The reason for that could be complex drainage of lymph

nodes.^[17] Until today, more than 10 different lymphatic routes in anal canal were found.^[18]

There is no value in a prophylactic lymph node dissection during a Wide Local Excision (WLE), even when there are clinically positive nodes, also because locoregional recurrence of Anal Melanoma (AM) occurs more at the inguinal lymph nodes than at the pelvic lymph nodes.^[19] Neither APR nor WLE affect any of the inguinal lymph nodes, so they do not offer an advantage in controlling locoregional recurrence.^[20]

Perez *et al.* published recently presence of perirectal and inguinal LNM at the same time.^[15] Due to limitation of mesorectal excision in APR following resection of perirectal LNM, patients with perirectal lymph node involvement may benefit from radical curative surgery. In the case of distant metastases, palliative surgery is needed for metastasectomy and in cases of incontinence or refractory pain.^[10] In our study, APR was performed in 5 patients, and LE was performed in 5 patients among 10 patients.

Available data suggest no significant difference in survival among patients managed with APR and LE. Because APR is associated with high rates of morbidity and colostomy-associated decrease in the quality of life, many authors advocate LE if negative margins are achievable.^[21] The relative benefit of these procedures, however, is unclear. Some studies suggest an improved survival after APR.^[22] But several studies have reported cases of long-term survival with treatment consisting of only local surgical excision.^[7] Prognosis of patients in early stages limited to mucosal involvement and treated via adjuvant radiotherapy is much better compared to cases via deeper involvement.^[21] Mean survival in cases with stage I received LE is 44 months compared to patients in advanced stages with 22 months.^[4] There was no statistical difference. In 80% of our cases, received LE involvement was limited to mucosa. In APR group, 60% was limited to muscularis propria and 40% to perirectal space. Mean survival was 19.6 months (7–43) in cases received LE, whereas it was 6.2 months (1–16) in APR group.

The impact of chemotherapy and radiation on the treatment of anorectal melanoma remains unclear.^[12] In our study, 60% of the patients received postsurgical adjuvant chemoradiotherapy in the APR group, while in the wide excision group, 100% of the patients did.

The overall 5-year survival rates in patients with AM range from 4% to 31% even if radical surgery and chemotherapy are performed, while median survival varies from 16 to 28 months.^[23] The prognosis is poor, with overall survival rate <20% in 5 years.

Age >60 years and lesions >1 cm in diameter have been identified as prognostic factors.^[24] In our study, the mean survival rates of patients who underwent localized excision gave better results because patients with LE had lower stages than patients with APR. However, a larger patient database is required to further evaluate the role of abdominoperineal and local resection, which will only be possible by a multicenter study, given the rarity of this disease.

CONCLUSION

In our experience, the use of adjuvant chemoradiotherapy seems to hold promise in achieving good locoregional control in AM. However, a larger patient database is required to further evaluate the role of adjuvant chemoradiotherapy, which will only be possible by a multicenter study, given the rarity of this disease. Till then, the local treatment of anorectal melanoma should be individualized for each patient.

The findings of this study suggest that stage of disease is the most important determinant of prognosis in AM. LE with adjuvant chemoradiotherapy should be considered in selected patients with small tumors which are suitable for LE. However, an APR should be offered for all advanced, deeply infiltrating lesions where LE is not possible or as a salvage following local recurrence.

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Conflicts of interest

There are no conflicts of interest.

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