Original Article

A Case Series of Anorectal Melanoma in a Single Institution

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Key Words
Anorectal melanoma;
Surgery;
Survival

Purpose. Anorectal melanoma is a rare but aggressive disease comprising approximately 1%-2% of all melanomas. Several case series in Western countries reported about this disease. This study aimed to analyze the symptoms, treatment, and survival of patients with anorectal melanoma in a single center in Taiwan.
Methods. All patients diagnosed with anorectal melanoma in Taipei Veterans General Hospital from 1998 to 2017 were included. We collected data on patient characteristics, symptoms, disease stage, treatment, and overall survival.
Results. Eighteen patients were enrolled, including 6 with anal melanoma and 12 with rectal melanoma. The mean age was 61.8 years at diagnosis. Eight patients (44.4%) were male. The symptoms included bleeding during defecation (72%), bowel habit change (44%), anal pain (22%), pruritus (11%), and anorectal prolapse (11%). At diagnosis, 4 patients had local disease only described as stage I, 5 patients had regional lymph nodes described as stage II, and 9 patients had distal metastasis described as stage III. Fourteen patients underwent surgery, including local excision (n = 6, 33.3%) and abdominal perineal resection (n = 8, 44.4%). Patients with stage III disease had poorer overall survival than those with stage I and II diseases. In stage I and II diseases, there was no disease-free ($p = 0.48$) or overall survival ($p = 0.72$) benefit between local excision and abdominoperineal resection.
Conclusions. Anorectal melanoma is an aggressive disease with rapid local recurrence or distal metastasis even after radical resection, chemotherapy, radiotherapy or immunotherapy. Further study about the ideal multimodality therapy may be needed to improve the outcome of this aggressive disease.
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Melanoma is a rare but aggressive disease. Most melanomas have a cutaneous origin but may also have a mucosal origin in some patients (1.5%).[1] According to previous studies, primary mucosal melanomas behave more aggressively and have poorer prognosis than cutaneous melanomas.[1-3] Primary mucosal melanomas often originate from the head and neck, anorectal and female genital organs, with a distribution of approximately 55%, 24%, and 18%, respectively.[4] The most common melanoma of the gastrointestinal tract is anorectal melanoma (AM), accounting for about 0.4%-1.6% of all malignant melanomas.[4] The incidence of AM is about 2.2-2.7 patients per 10 million population per year in the United States

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and Europe.[1] The symptoms of AM often include bleeding during defecation and perianal pain in some cases, which is often considered as hemorrhoid.[5] Lack of awareness of AM often leads to an advanced stage at diagnosis compared with that of cutaneous melanoma. The treatment of AM often included radical surgical excision such as abdominoperineal resection (APR) or wide local excision. However, which one is better remains controversial.[4,6-8] Nonsurgical treatment includes chemotherapy, immunotherapy, and radiotherapy for metastaticor loco-regional lesions.[9] However, the benefit of these modalities remains unclear in AM, and the prognosis is still poor. For this rare disease, there were many case series published in Western countries for years.[5,8,10-12] This study aimed to analyze the disease in our hospital with 20 years' experience.

Materials and Methods

We enrolled 18 patients who were diagnosed with AM from 1998 to 2017 in Taipei Veterans General Hospital from a pathological report database. We collected data on patient characteristics from medical records and by telephone interview for missing data. Some patients underwent biopsy only, and others underwent surgical excision including APR, local excision, or polypectomy from colonoscopy. A total of 19 patients were initially enrolled, but one patient only underwent biopsy and did not return for follow-up. In 18 included patients, data on characteristics, including age at diagnosis, sex, underlying disease, and symptoms, were collected. All patients had pathological melanoma in the anus or rectum. Staging studies included pelvis computed tomography (CT), chest CT and magnetic resonance imaging (MRI), and positron emission tomography (PET) in some cases. Overall survival and disease-free survival were also obtained from the medical records or telephone interview when the patient did not die in our hospital.

Results

There were 18 patients diagnosed with AM from 1998 to 2017 in Taipei Veterans General Hospital from the pathological report database. Patient details are presented in Supplement Table 1. Of 18 patients, 6 (33.3%) were diagnosed with anal melanoma, and 12 (66.7%) with rectal melanoma. Eight patients were male (44.4%). The average age at diagnosis was 61.8 years (35-87 years). There were 4 patients (22%) diagnosed with stage I disease with only local lesion, 5 (28%) with stage II disease with lymphadenopathy at the pelvic or inguinal area, and 9 (50%) with stage III disease with distal metastasis at diagnosis. The surgical intervention included biopsy only in 4 patients (22.2%) with stage III disease. Six patients (33.3%) underwent local excision, and 8 (44.4%) underwent radical resection with APR (Table 1). Common symp-

Table 1. Patient characteristics

	All patients	Anus	Rectum	Survival (M)
Patient number	18	6 (33.3%)	12 (66.7%)	
Sex				
Male	8 (44.4%)	1 (16.7%)	7 (58.3%)	
Female	10 (55.6%)	5 (83.3%)	5 (41.7%)	
Age, years	61.8 ± 15.5	60.2 ± 10.0	62.7 ± 18.0	
Stage				
I. Localized	4 (22%)	2 (33.3%)	2 (16.7%)	19.5 (7-52)
II. Regional	5 (28%)	1 (16.7%)	4 (33.3%)	20 (7-38)
III. Distal	9 (50%)	3 (50.0%)	6 (50.0%)	7.6 (1-22)
Treatment				
Biopsy only	4 (22.2%)	1 (16.7%)	3 (25.0%)	
Local excision	6 (33.3%)	3 (50.0%)	3 (25.0%)	
APR	8 (44.4%)	2 (33.3%)	6 (50.0%)	

APR, abdominoperineal resection.

toms include bleeding during defecation (72%), bowel habit change (44%), anal pain (22%), pruritus (11%), and anal prolapse (11%) (Table 2). There were 14 patients (82%) with lung metastasis and 13 (76%) with liver metastasis (Table 3). Patients with stage III disease have poorer overall survival (average survival 7.6 months) compared to those with stage I and II diseases (average survival 19.5 and 20 months) (p = 0.038) (Fig. 1). Three patients with stage I and II diseases underwent local excision, and 6 underwent APR. However, there were no disease-free (p = 0.48) (Fig. 2A) or overall survival (p = 0.72) (Fig. 2B) benefit compared to radical resection or local excision.

Table 2. Symptoms of anorectal melanoma

Symptom	Number	Percentage
Bleeding during defecation	13	72%
Bowel habit change	8	44%
Anal pain	4	22%
Pruritus	2	11%
Anal prolapse	2	11%

Table 3. Patients with anorectal melanoma with distal metastasis

Metastatic location	Initial (n = 9)	At death (n = 17)
Lung	5	14 (82%)
Liver	4	13 (76%)
Pelvis	0	9 (53%)
Brain	0	4 (24%)
Bone	1	7 (41%)
Abdomen (LNs)	3	8 (47%)

LNs, lymph nodes.

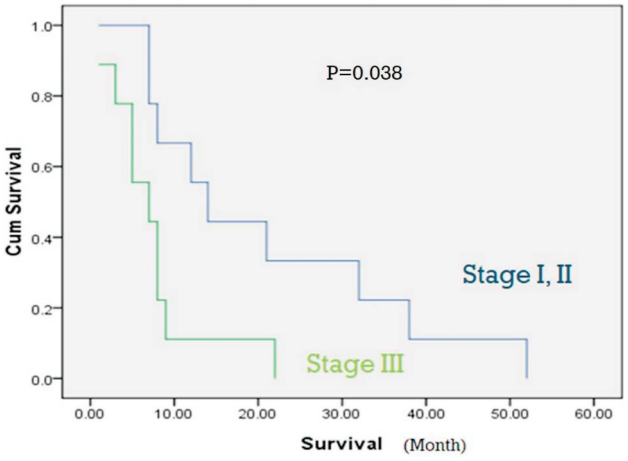

Fig. 1. Overall survival (Kaplan-Meier method) of patients with anorectal cancer with stage I, II, and III disease (p = 0.038).

Discussion

Mucosal melanoma is a rare subtype of melanoma that accounts for < 1.5% of all melanomas.[1] Mucosal melanoma often develops in the head and neck and anorectal and female genital organs.[1] We obtained all cases of AM from 1998 to 2017 from a single institution. The incidence of AM is 1.6-2.3 higher in women

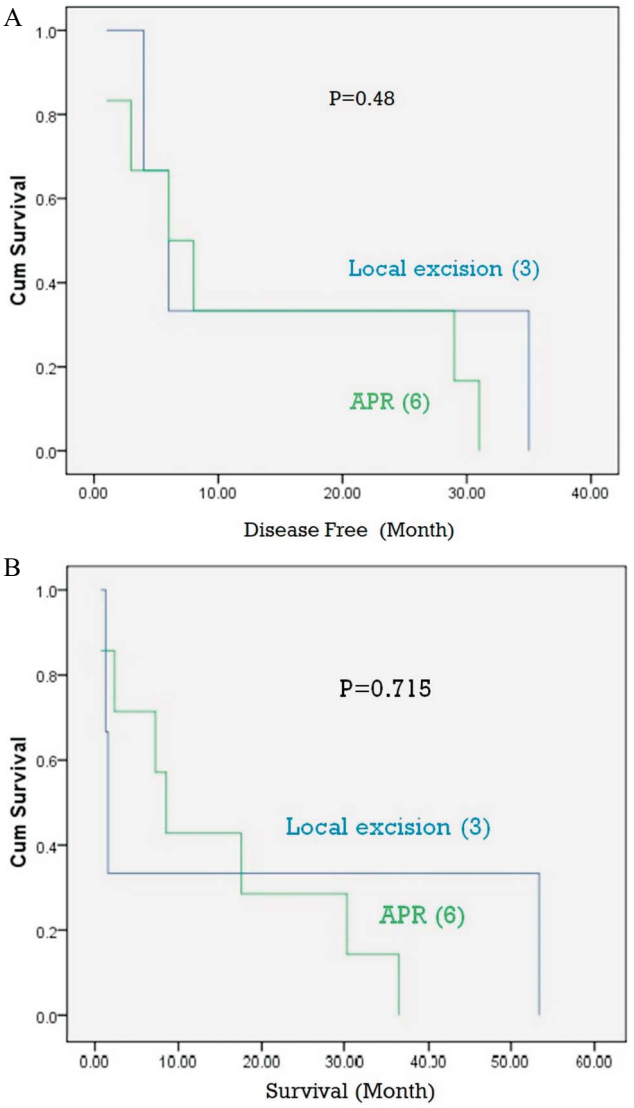

Fig. 2. (A) Disease-free survival (p = 0.48) and (B) overall survival (p = 0.715) patients with stage I and II anorectal melanoma who underwent local excision and abdominoperineal resection (APR).

than in men.[4,5,12,13] In our study, 10 patients (55.6%) were female. The median age at diagnosis is approximately 60-70 years in some studies[1,4,9] and was 61.8 years at diagnosis in our population. AM is an advanced disease, and 50% of patients (9/18) have distant metastasis at initial diagnosis. The symptoms and signs of AM were similar to that of hemorrhoid, such as bleeding during defecation, anal pain, or bowel habit change, which may cause delay in diagnosis. The surgical interventions for AM included local excision and radical resection, such as APR. Some studies showed that compare to local excision, APR had better local control in stage I or II disease but had no overall survival benefit.[6,7,14] In our study, APR had no benefit in overall survival ($p = 0.72$) or disease-free survival ($p = 0.48$) compared to local excision in stage I and II disease.

AM is a rapidly progressive disease. Some studies reported that it takes approximately 1.5 years from diagnosis to develop systemic disease.[12] In our 9 patients with stage I and II diseases, it took approximately 13 months for distal metastasis to develop. When it progresses to a systemic disease, life expectancy is often less than 1 year (6.6 months in our population). The survival of patients with AM with stage I, II, and III disease was 19.5 months, 20 months, and 7.6 months, respectively. Distal metastasis often presents in the liver and lung according to a Netherlands case series.[5] We also have similar results.

This study has some limitations. First, this is a retrospective and single-institution observational study. We enrolled only 18 patients diagnosed with AM in our institution. Further multicenter study may be needed for a comprehensive evaluation in the Taiwanese population. Second, each patient underwent different treatment modalities, including surgery, chemotherapy, radiotherapy, or further immunotherapy, and there is a relatively small sample size. We did not analyze the effects of conservative treatment of chemotherapy, radiotherapy, or further immunotherapy.

There are many case series that discussed AM in Western countries. However, there are few studies that reported this disease in Taiwan. We collected data of 18 patients who presented in our hospital in 20 years. It seems that this disease is still advanced and rapid aggressive. Further studies may be needed to improve the care of patients with AM.

Conclusions

AM is an aggressive disease with rapid local recurrence or distal metastasis even after radical resection, chemotherapy, or immunotherapy. There was no significant benefit of APR and local excision in overall and disease-free survival. Further study may be needed to improve the outcome of this disease.

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Supplement

Supplement Table 1. Detailed patient characteristics

No.	Sex	Age	Location	Symptoms	Initial stage	Surgical method	Disease-free survival	Survival (M)
1	Male	46	Rectum	Pain	2	APR	2	8
2	Male	78	Rectum	Bleeding	1	Local excision	6	7
3	Male	87	Rectum	Bleeding, constipation	3	Local excision	-	1
4	Male	72	Anus	Bleeding, constipation	1	Local excision	35	52
5	Male	65	Rectum	Bleeding, tenesmus	3	Biopsy	-	9
6	Female	82	Rectum	Bleeding, prolapsed mass	2	APR	29	32
7	Female	71	Anus	Bleeding, constipation	1	APR	3	7
8	Female	49	Anus	Tenesmus	3	Local excision	-	8
9	Female	51	Anus	Itching	3	Biopsy	-	3
10	Male	35	Rectum	Bleeding	2	APR	31	38
11	Female	68	Rectum	Bleeding	1	APR	6	12
12	Female	63	Anus	Bleeding	2	APR	Lost	14
13	Male	46	Rectum	Bleeding, anal pain	2	APR	8	21
14	Male	36	Rectum	Bleeding, pain, obstruction	3	Biopsy	-	22
15	Female	68	Rectum	Bleeding	3	Local excision	-	8
16	Female	79	Rectum		3	APR	-	5
17	Female	55	Anus	Pain, prolapsed mass	2	Local excision	4	7
18	Female	62	Rectum	Bleeding, obstruction	3	Biopsy	-	5

APR, abdominoperineal resection.

原　著

肛門直腸黑色素癌單一機構病例分析

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主旨　肛門直腸黑色素癌是一個罕見卻非常惡性的疾病，1-2% 的黑色素癌發生在肛門直腸，有許多西方國家針對此疾病做過案例統計，此篇研究主要分析近 20 年台灣單一醫療機構的肛門直腸黑色素癌的案例分析。

方法　我們從台北榮民總醫院的病理資料庫蒐集自 1998 至 2017 所有的肛門直腸黑色素癌的病患資料，其中包含病人基本資料、症狀、初始的分期、初步治療以及預後。

結果　一共有 18 位肛門直腸黑色素癌病人。6 位之腫瘤長在肛門而 12 位於直腸，平均發病年齡於 61 歲，女性的比例高於男性 (55.6% vs. 44.4%)，大部分的病人症狀包含血便、排便習慣改變、肛門疼痛、搔癢或肛門異物脫垂。其中有 4 位疾病診斷時為第一期，5 位為第二期，這兩期平均存活時間約 20 個月。但有一半的病人 (9 位) 於診斷時已經是第三期且其平均存活時間只剩 7 個月。肺部以及肝臟為最常見之轉移器官。一共有 14 位病人接受手術治療，包含了 6 位接受局部切除以及 8 位接受腹部會陰聯合切除。但對於第一、二期的病人，接受局部切除或腹部會陰聯合切除對於其預後存活或腫瘤局部控制並沒有達到顯著的差異。

結論　肛門直腸黑色素癌仍是一非常惡性且致命的疾病，廣泛的手術切除或局部切除對預後並沒有太大的影響，我們需要針對此疾病有更深入的了解。

關鍵詞　肛門直腸黑色素癌、手術治療、存活。