Anorectal melanoma is a rare malignant neoplasm with variable natural history and nonspecific presentation. We describe the clinicopathologic and prognostic parameters of a series of 18 patients (16 [88.9%] white; 10 [55.6%] male; median age, 64.0 years [interquartile range, 45.8-74.3 years]) with histologically proven anorectal melanoma treated at our institution during a 21-year period between October 1991 and August 2012. Late diagnosis was common (44.5% of patients had stage II disease or worse at diagnosis), likely owing to a delay in presentation, nonspecific presenting symptoms, and frequent incorrect diagnoses (16 cases [88.9%]). Overall disease-specific mortality was 66.7% (12 of 18 patients), with a median time to death of 15.5 months (interquartile range, 7.3-25.5 months). Disease-specific survival was significantly better following wide local excision vs abdominoperineal resection (P = .04), although patients undergoing the former tended to have fewer rectal lesions (P = .04), smaller lesions (P = .02), and a trend toward less advanced stage (P = .06). Larger studies assessing optimal medical and surgical management for anorectal melanoma are needed to improve outcomes.

Anorectal melanomas (AMs) compose fewer than 1% of all malignant melanomas and fewer than 3% of all anal tumors.¹ ² They are usually diagnosed between the sixth and eighth decades of life and may have a female predilection.³ Unlike the relatively good prognosis of local cutaneous melanoma,⁴ the prognosis of AM is very poor.⁵ Because AMs tend to spread through submucosal drainage, the course of the disease is frequently indolent. Symptoms are nonspecific, and as a result patients tend to have large lesions and/or advanced disease at presentation. Therefore, disease recurrence and disease-related morbidity and mortality are high, with 5-year survival rates ranging from 0% to 30%.³⁶⁻¹²

Because of its rarity, the natural history, diagnosis, and optimal treatment of AM are poorly defined.¹³ The aim of our study was to describe the natural history and clinicopathologic characteristics of a series of patients with AM at our institution.

Results

**Patient Presentation**

Eighteen patients (16 [88.9%] white; 10 [55.6%] male; median age, 64.0 years [interquartile range, 45.8-74.3 years]) with a confirmed tissue diagnosis of AM were identified during the 21-year study period (Table 1). The most common presenting symptom was bright red blood per rectum (15 patients [83.3%]), followed by rectal pain (6 patients [33.3%]), change in bowel habits (5 patients [27.8%]), rectal mass (4 patients [22.2%]), nonbloody rectal discharge (2 patients [11.1%]), and anemia and weight loss (1 patient [5.6%]). Overall, presenting symptoms occurred over a median of 3 months (interquartile range [IQR], 2-7 months) prior to patients seeking medical evaluation.
The majority of patients (16 patients [88.9%]) were initially diagnosed incorrectly. Incorrect initial diagnoses included hemorrhoids (8 patients [44.4%]), rectal polyp or benign mass (4 patients [22.2%]), nonmelanotic malignant neoplasms (3 patients [16.7%]; 1 adenocarcinoma, 1 small cell cancer, and 1 gastrointestinal stromal tumor), and perianal abscess (1 patient [5.6%]).

Disease Characteristics and Staging
The disease characteristics of all patients with AM are summarized in Table 1. Overall, 10 patients (55.6%) presented with stage I disease, 5 (27.8%) with stage II disease, and 3 (16.7%) with stage III disease, all based on computed tomographic imaging of the chest, abdomen, and pelvis. Three patients (16.7%) were found to have extranodal disease on preoperative workup, consisting of metastases to the liver and splenic hilum (1 patient), liver alone (1 patient), and periportal lymph node disease (1 patient).

Disease Management
Surgical management included wide local excision (WLE) in 11 patients (61.1%) and abdominoperineal resection (APR) in 7 patients (38.9%). The median tumor size was 3.0 cm (IQR, 1.7-4.5 cm) and the median tumor depth was 5.5 mm (IQR, 4.0-10.0 mm). Among the 7 patients treated initially with APR, 4 (57.1%) were found to have positive lymph nodes, including 2 patients who were classified as having stage I disease on initial workup.

Five patients (27.8%) also received adjuvant therapy, including interferon alone in 2 patients (both of whom were treated surgically with WLE), chemotherapy combinations including carboplatin and paclitaxel with either imatinib mesylate (1 patient, following APR) or ipilimumab (1 patient, following WLE), and a peptide vaccine trial (1 patient, following APR).

Outcomes
Patients were followed up for a median of 18.5 months (IQR, 3.8-47.5 months). Two patients (11.1%) were lost to follow-up. Disease recurrence occurred in 11 of 13 patients (84.6%) with initial stage I or stage II disease within 7.0 months (IQR, 2.0-19.0 months). Most recurrences occurred to metastatic sites (9 of 11 patients [81.8%], including liver [5 of 9 patients [55.6%]], regional lymph nodes [4 of 9 patients [44.4%]], lungs [4 of 9 patients [44.4%]], and pelvis [3 of 9 patients [33.3%]]. Of the 11 patients with disease recurrence, 6 (54.5%) underwent repeated resection of local recurrence and 2 (18.2%) underwent extended resection of metastatic disease. Overall disease-specific mortality was 66.7% (12 of 18 patients). The median time to death was 15.5 months (IQR, 7.3-25.5 months). Among patients with appropriately available follow-up data, 5-year survival was 14.3% (2 of 14 patients).

Disease-specific survival was significantly better for patients who underwent WLE vs those who underwent APR ($P = .04$) (Figure). However, patients undergoing WLE had fewer lesions in the rectum ($P = .04$), smaller lesions ($P = .02$), and a trend toward less advanced disease ($P = .06$) compared with those undergoing APR (Table 2).
Discussion

Anorectal melanoma is a rare malignant neoplasm that accounts for fewer than 1% of all colorectal tumors.14 Within the United States there were fewer than 200 cases reported between 1982 and 2012,3 and fewer than 700 cases are reported in the literature overall.15 A review of all patients with histologically proven AM treated at our institution during the past 21 years identified only 18 total cases, consistent with the rarity of the diagnosis.

Our data suggest that patients tend to present with an advanced stage of disease, likely owing to nonspecific presentation and frequent misdiagnoses. Nearly one-quarter of patients had multiple lesions on initial presentation, and nearly half had stage II or stage III disease. The median tumor depth was 5.5 mm, and more than half of the patients (11 patients [61.1%]) had melanomas 4.0 mm or greater in thickness. An advanced stage of disease on initial diagnosis may contribute to the high recurrence rate (84.6%) and poor survival outcomes (14.3% estimated 5-year survival rate) that we observed, which are similar to previously published data.3-7,9-12,14,20-25 In our series, patients undergoing WLE appeared to have longer survival times than those undergoing APR. However, this finding may be a reflection of differences in disease burden rather than surgical management given that patients in the WLE group tended to have fewer lesions in the rectum, smaller lesions, and a trend toward less advanced disease.

The limitations of our study include its retrospective nature, small sample size, and 21-year period. In addition, patients were treated with a variety of treatment regimens that make comparisons of different management strategies difficult. Ideally, a prospective or case-matched clinical trial investigating the efficacy of local vs extended resection for AM is needed to truly understand disease prognosis and optimal treatment strategies, but the low incidence of AM makes such a trial currently impractical.

Conclusions

Anorectal melanoma is a rare and aggressive malignant neoplasm that is often associated with late diagnosis, advanced stage, high metastatic potential, and high mortality. In our small series, use of WLE appeared to be associated with better survival, although the interpretation of this finding is limited by our small sample size and lack of patient standardization. Additional studies assessing optimal medical and surgical management are needed to improve outcomes.

Table 2. Clinicopathologic Characteristics of Patients Undergoing Wide Local Excision vs Abdominoperineal Resection

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>WLE (n = 11)</th>
<th>APR (n = 7)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (IQR), y</td>
<td>64 (48-74)</td>
<td>64 (45-75)</td>
<td>.89</td>
</tr>
<tr>
<td>Male, No. (%)</td>
<td>7 (63.6)</td>
<td>3 (42.9)</td>
<td>.73</td>
</tr>
<tr>
<td>Duration of symptoms, median (IQR), mo</td>
<td>4.5 (2-7.5)</td>
<td>2 (1-8)</td>
<td>.28</td>
</tr>
<tr>
<td>Correct initial diagnosis, No. (%)</td>
<td>2 (18.2)</td>
<td>0</td>
<td>.23</td>
</tr>
<tr>
<td>Location, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perianal</td>
<td>4 (36.4)</td>
<td>0</td>
<td>.04</td>
</tr>
<tr>
<td>Anal canal or anorectal</td>
<td>6 (54.6)</td>
<td>3 (42.8)</td>
<td></td>
</tr>
<tr>
<td>Rectum</td>
<td>1 (9.1)</td>
<td>4 (57.1)</td>
<td></td>
</tr>
<tr>
<td>Multiple lesions present, No. (%)</td>
<td>2 (18.2)</td>
<td>2 (28.6)</td>
<td>.11</td>
</tr>
<tr>
<td>Tumor size, median (IQR), cm</td>
<td>2.5 (0.6-3.2)</td>
<td>4.5 (2.7-5.0)</td>
<td>.02</td>
</tr>
<tr>
<td>Tumor depth, median (IQR), mm</td>
<td>9.0 (4.5-12.0)</td>
<td>4.5 (4.0-7.4)</td>
<td>.21</td>
</tr>
<tr>
<td>Tumor stage, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>9 (81.8)</td>
<td>3 (42.9)</td>
<td>.06</td>
</tr>
<tr>
<td>II</td>
<td>0</td>
<td>3 (42.9)</td>
<td></td>
</tr>
<tr>
<td>III</td>
<td>2 (18.2)</td>
<td>1 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Resection status, No. (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>7 (63.6)</td>
<td>4 (57.1)</td>
<td>.87</td>
</tr>
<tr>
<td>R1</td>
<td>2 (18.2)</td>
<td>2 (28.8)</td>
<td></td>
</tr>
<tr>
<td>R2</td>
<td>2 (18.2)</td>
<td>1 (14.3)</td>
<td></td>
</tr>
<tr>
<td>Follow-up time, median (IQR), mo</td>
<td>15 (4-16)</td>
<td>43 (3-53)</td>
<td>.17</td>
</tr>
<tr>
<td>Recurrence, No. (%)</td>
<td>5/7 (71.4)</td>
<td>6/6 (100)</td>
<td>.35</td>
</tr>
<tr>
<td>Time to recurrence, median (IQR), mo</td>
<td>13.2 (6.1-33.3)</td>
<td>2.5 (2.0-10.8)</td>
<td>.07</td>
</tr>
<tr>
<td>Mortality, No. (%)</td>
<td>6 (54.5)</td>
<td>6 (85.7)</td>
<td>.04*</td>
</tr>
<tr>
<td>Time to death, median (IQR), mo</td>
<td>13.5 (1.5-57.3)</td>
<td>11.5 (3.2-15.3)</td>
<td>.75</td>
</tr>
</tbody>
</table>

Abbreviations: APR, abdominoperineal resection; IQR, interquartile range; WLE, wide local excision.

* Patients lost to follow-up or with stage III disease at initial diagnosis are excluded.

* By log-rank test.
Anorectal Melanoma

Brief Report Research

ARTICLE INFORMATION
Accepted for Publication: September 3, 2013.
Published Online: May 21, 2014.

Author Contributions: Drs Hicks, Pappou, and Magruder contributed equally to this work. Drs Hicks and Pappou had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

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Conflict of Interest Disclosures: None reported.

Previous Presentation: This work was presented as a poster presentation at the 2013 Annual Meeting of the American Society of Colon and Rectal Surgeons; April 29, 2013; Phoenix, Arizona.

REFERENCES