Clinicopathologic Presentation and Natural History of Anorectal Melanoma: A Case Series of 18 Patients

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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.

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.
Abbreviation: IQR, interquartile range.

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Disease Management

Surgical management included wide local excision (WLE) in 11 patients (61.1%) and abdominoperineal resection (APR) in 7 (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. Within the United States there were fewer than 200 cases reported between 1982 and 2012, and fewer than 700 cases are reported in the literature overall. 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.

The optimal treatment approach for AM remains a topic of debate. Currently, no data demonstrate the utility of medical therapy, although a variety of chemotherapy and radiotherapy approaches have been tried. With respect to surgical management, a number of retrospective studies report outcomes following WLE vs APR for AM with no clear survival advantages to one approach over the other. 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

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Study concept and design: Hicks, Pappou, Gearhart, Ahuja, Efron.

Acquisition, analysis, or interpretation of data: Hicks, Pappou, Magruder, Gazer, Fang, Wick, Ahuja, Efro.

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REFERENCES