Anorectal Malignant Melanoma: Report of Two Cases from Buddhachinaraj Hospital

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Anorectal malignant melanoma is an exceedingly rare disease accounting for 1 to 2% of all anal cancers and approximately 1% of all melanomas(1-3). The prognosis is uniformly poor. The five year survival is less than 10%(4). To the authors’ knowledge, malignant melanomas usually have an unpredictable histological variability which mimic several malignancies. When confronted with an undifferentiated malignant lesion, malignant melanoma is always in differential diagnoses. Herein, the authors report two advanced cases with regional lymph node involvement which exhibit different histological features.

Case Report

Case 1

A 55-year-old female farmer was seen in May 2002 with one and a half months of rectal bleeding and sensation of a mass in the anal canal. She was a healthy woman with no history of chronic illness. Digital rectal examination and Barium enema revealed an irregular lobulated mass about 4 to 5 cm. in length at right lateral aspect of the distal rectum. Multiple liver metastases were detected by ultrasonography of the abdomen. Tissue biopsies were done before definite treatment. The first time, tissue examination was described as acute and chronic inflammation with atypical lymphoid cells (Fig. 1A, 1B). The histological examination of subsequent tissue sampling demonstrated malignant melanoma. The patient had abdominoperineal resection (APR) in July 2002. Two weeks after AP resection with colostomy, she developed congestive heart failure. Pleural effusion and loss of first and second lumbar pedicle were discovered by chest and L-S film, respectively. She received supportive therapy for congestive heart failure and 5 days of chemotherapy (5-FU and Leucovarin®). She did not response to treatment and died in September 2002, 4 months after diagnosis.

Pathology of the APR specimen (Fig. 2A) revealed an ulcerated dark brown mass measuring 12 x 10 cm and 5 cm in thick which was located just...
above the dentate line and had invaded into perirectal surrounding tissue. The histological sections showed surface ulceration and clusters of tumor cells diffusely infiltrating in the intestinal wall and perirectal surrounding tissue. Tumor cells were round and showed hyperchromatic to vesicular nuclei and moderate amounts of clear to eosinophilic cytoplasm (Fig. 2B, 2C). Multinucleation was focally observed. Tumor cells expressed vimentin, S100 protein and HMB45 (Fig. 2D). The immunological studies of leukocyte common antigen (LCA), cytokeratin, NSE, synaptophysin, desmin and CD30 showed negative results. Presence of melanin
diameter at 1 cm above the dentate line. Some of them were deeply pigmented. The histological sections (Fig. 4B) showed infiltration of mucosa and submucosa of the rectum by densely packed sheets of large spindle cells, as previously seen in a biopsied specimen. In addition, some areas of the tumor exhibited large epithelioid cells. The tumor expanded the lamina propria and ulcerated the overlying mucosa. The foci of angiolymphatic tumor embolization were observed. The tumor cells showed strong positively for Masson-Fontana, as well as for S100 protein and HMB-45 (Fig. 4C, 4D), whereas they were negative for AE1/AE3 cytokeratin and epithelial membrane antigen (EMA). One peritumoral lymph node contained metastatic melanoma. The patient is engaged in postoperative adjuvant therapy.

**Discussion**

The anorectal malignant melanoma is an exceedingly rare disease accounting for 1% to 2% of all anal cancers. Approximately 1% of melanomas arise in the anorectal region which represent the third most common site for primary mucosal melanomas, after head and neck and female genitourinary tract and are the most common site for primary gastrointestinal melanomas(1-3). The peak incidence is in the sixth to seventh decades(2,6). The etiology of anorectal melanoma remains unknown. Unlike cutaneous melanoma, the anorectal melanomas do not have a precursor lesion and do not relate to ultraviolet exposure(2,5). The recent study of Cagir et al showed a rising incidence of anorectal melanomas, especially in males younger than the age of 45 years and possible association with HIV infection(6). These tumors commonly arise near the junctions of squamous and columnar epithelia. The pigments was confirmed by Masson-Fontana and bleaching methods. Five out of six mesenteric lymph nodes were positive for metastases.

**Case 2**

A 65 year-old female patient presented with intermittent rectal bleeding in January 2003. A rectal mass was detected by digital examination and proctoscopic finding. The initial biopsy was taken, revealing infiltrative malignant spindle cells tumor in interlacing fascicles (Fig. 3A, 3B). Their nuclei were elongated, hyperchromatic and showed anisonucleosis. Some viable tumor cells as well as necrotic cells contained melanin granules. The diagnosis of malignant melanoma was confirmed by histochemical and immunohistochemical stainings. The patient had abdominoperineal resection in March 2003.

Pathology of the APR specimen (Fig. 4A) showed 5 fungating masses, ranging from 1 to 2 cm in diameter.
Fig. 4  A) Gross finding of AP resection specimen reveals polypoid pigmented masses just above dentate line; B) Histologic finding of AP resected specimen. Note some tumors contain melanin pigment. Immunohistochemical stains; C) S100 protein; D) HMB45

melanocytes are thought to be initial cells which have undergone malignant transformation\(^{10}\). Anorectal melanomas are assumed to be a disease of Caucasians\(^{10}\). In the authors’ search, there were more than 80 Asian cases, which were published\(^{7-11}\). The presented cases are the fourth and fifth reported cases in Thailand (Table 1).

Patients with anorectal melanoma may complain of anal discomfort, pain, constipation, rectal bleeding, or a protruding mass. The latter may be confused with hemorrhoids, which delay the initial diagnosis\(^{2,12}\). The most common presenting symptom is rectal bleeding\(^{1-3,8,12}\). The growth pattern of anorectal melanomas is similar to the other mucosal melanomas, which have a rapid and progressive vertical phase\(^{5}\). Then the initial gross findings usually exhibit large polypoid masses, which are variable in color\(^{2,11}\). In a review of 85 patients from the Memorial Sloan-Kettering Cancer Center, the median tumor size was 3.3 cm and the median depth of tumor invasion was 7.5 mm\(^{3}\).

Like cutaneous melanomas, anorectal melanomas exhibit considerable variability in cell size and shape, both from tumor to tumor and within a given tumor\(^{2,3}\). As a result of these facts, the histology often mimics other malignancies. In the presented first case, the small size of cells caused confusion with other small cell tumors e.g. malignant lymphoma, some small round cell sarcomas, and even small cell carcinomas. The second case disclosed the tumor with a majority of spindle cell features that had to be distinguished from spindle cell sarcomas, gastrointestinal stromal tumor (GIST), and spindle cell carcinoma. The epithelioid cells may mimic epidermoid carcinoma or malignant lymphoma. The histochemical and immunohistochemical studies are very useful in establishing the correct diagnosis\(^{2,3}\).

Primary anorectal melanoma must be differentiated from metastatic melanoma. Complete physical examination and history of previous or existing
melanoma are necessary. The lesions arising near the junctions of squamous and columnar epithelia have been recognized as an important key when distinguishing primary melanoma from metastatic melanomas \((2, 3, 10, 12)\).

The anorectal melanomas usually present with early dissemination of disease. The reasons are probably delay in diagnosis and high vascularization of the anorectal region \((2, 3, 12)\). The mean survival time is only 15 months. Only 5 to 10% of patients with anorectal melanoma will be alive five years after diagnosis \((4, 15)\). The prognosis seemed to be related to tumor size and thickness. In most series, none of the patients with a tumor more than 2 mm thick were alive at 5 years \((4)\). Conversely, sporadic cases with prolonged survival of more than 10 years have been documented \((17, 18)\). The factor for predicting long term survival is unknown but may be correlated with the initial depth of tumor invasion or with absence of distant metastases at the time of diagnosis \((12, 17, 18)\). However, there are some cases, which do not relate to tumor thickness \((17, 18)\). Surgery is considered to be the definite treatment \((1, 3, 4, 15)\). Wanebo et al reviewed their series of 36 patients and found that patients treated with abdominoperineal resection (APR) versus a more conservative procedure by local excision had no difference in survival \((16)\). Chemotherapy and immunotherapy have no benefit in primary anorectal melanoma \((31)\). For the metastatic melanomas, there are many trials for treatment of metastatic cutaneous melanoma but not for metastatic anorectal melanoma. The reason is the rarity of the diseases. Thus, the trials are adopted from those of metastatic cutaneous melanoma, unless more recruited anorectal melanoma cases. Some chemotherapeutic agents e.g. dacarbazine and cisplatinum have been used to treat metastatic cutaneous melanoma. The combination of interferon, interleukin-2, and cytotoxic drugs, termed “biochemotherapy” or “chemoimmunotherapy” showed improved tumor response rates over chemotherapy alone \((12)\).

### Conclusion

The anorectal malignant melanoma is a rare and aggressive tumor, probably due to delay in diagnosis. Colonoscopy with biopsy and histological examination is an investigation for diagnosis. The immunohistochemistry enables us to confirm the diagnosis and to exclude epithelial or lymphoid malignancies. The AP resection is a reasonable approach in patients because some of them have unexpected long-term survival.

### References

3. Tomicic J, Wanebo HJ. Mucosal melanomas. Surg

### Table 1. Reported cases of Anorectal Melanomas in Thailand

<table>
<thead>
<tr>
<th>Authors</th>
<th>First case</th>
<th>Secondcase</th>
<th>Third case</th>
<th>Fourthcase</th>
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<tr>
<td>Age (years)</td>
<td>Kraikiat K(^{(9)})</td>
<td>Ammawat K(^{(10)})</td>
<td>Kittipornpeddee V(^{(11)})</td>
<td>Present case</td>
<td>Present case</td>
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<tr>
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<td>Female</td>
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<tr>
<td>Symptom</td>
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<td>Rectal bleeding</td>
<td>Painful mass and rectal bleeding</td>
<td>Mass and rectal bleeding</td>
<td>Rectal bleeding</td>
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<td>24</td>
<td>2</td>
<td>1 and a half</td>
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<td>Size of mass (cm)</td>
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<td>3</td>
<td>NA</td>
<td>12 x 10 and 5 cm in thickness</td>
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<td>Metastasis (at diagnosis)</td>
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<td>NA</td>
<td>Regional lymph node and Liver</td>
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<td>Survival (months)</td>
<td>14</td>
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Note: NA, Data not available
มะเร็งชนิดเมลาโนมาที่เกิดขึ้นบริเวณรอยต่อระหว่างลำไส้ตรงและทวารหนัก: รายงานผู้ป่วย 2 รายในโรงพยาบาลพุทธชินราช พิษณุโลก
จุลินทร สบางโข, สมรภูม หงษ์, สมมาศ กันเงิน, สุชาติ พรเจริญพงศ์, องอาจ เลิศขจรสิน

มะเร็งชนิดเมลาโนมาที่เกิดขึ้นบริเวณรอยต่อระหว่างลำไส้ตรงและทวารหนักนั้นพบได้น้อยมาก และมีพยากรณ์โรคที่ไม่ดี รายงานผู้ป่วยหญิงอายุ 55 ปี และ 65 ปี ของโรงพยาบาลพุทธชินราช พิษณุโลก ซึ่งมาจากภาพถ่ายจากการตรวจจากทวารหนัก จากการตรวจพบมีก้อนเนื้องอกที่บริเวณรอยต่อระหว่างลำไส้ตรงและทวารหนักและมีการกระจายของเนื้องอกไปยังต่อมน้ำเหลืองตั้งแต่ในระยะแรก การตรวจชิ้นเนื้อทางพยาธิวิทยาพบลักษณะทางฮีสโตโลยี่ของเซลล์เมลาโนมาที่แตกต่างกัน มีทั้งเซลล์เมลาโนมาขนาดเล็กกลมคล้ายเซลล์เม็ดเลือดขาวชนิดลิมโฟซัยด์และเซลล์เมลาโนมารูปร่างคล้ายกับมะเร็งชนิดซาร์โคมา การย้อมพิเศษทางอิมมูฮีสโตเคมมิสตรีช่วยในการวินิจฉัยมะเร็งปฐมภูมิชนิดเมลาโนมาผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยรายแรกได้รักษาด้วยการผ่าตัด APR ผู้ป่วยรายที่ 2 ได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR ผู้ป่วยทั้ง 2 รายได้รักษาด้วยการผ่าตัด APR