Anorectal Malignant Melanoma: Report of Two Cases from Buddhachinnaraj Hospital

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Anorectal malignant melanoma is a rare disease and has a uniformly poor prognosis. The following are two reported cases from Buddhachinaraj Hospital. A 55-year-old and a 65-year-old female patients presented with rectal bleeding. Large anorectal masses with regional lymph node involvement were detected initially. They exhibited different histological features which were atypical round cell resembling lymphocytes or were small cell appearance and spindle cell appearance similar to sarcoma. The diagnosis was confirmed by expression of S100 protein and HMB45. Abdominoperineal resection (APR) was the treatment of choice in both patients. The former case died in the fourth month after diagnosis because of distance metastasis and congestive heart failure. The latter case is receiving postoperative adjuvant therapy.

Keywords: *Anorectal malignant melanoma, Histological features, Abdominoperineal resection (APR)*

J Med Assoc Thai 2005; 88(8): 1128-33
Full text. e-Journal: *http://www.medassocthai.org/journal*

Anorectal malignant melanoma or anorectal 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^{R}). 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

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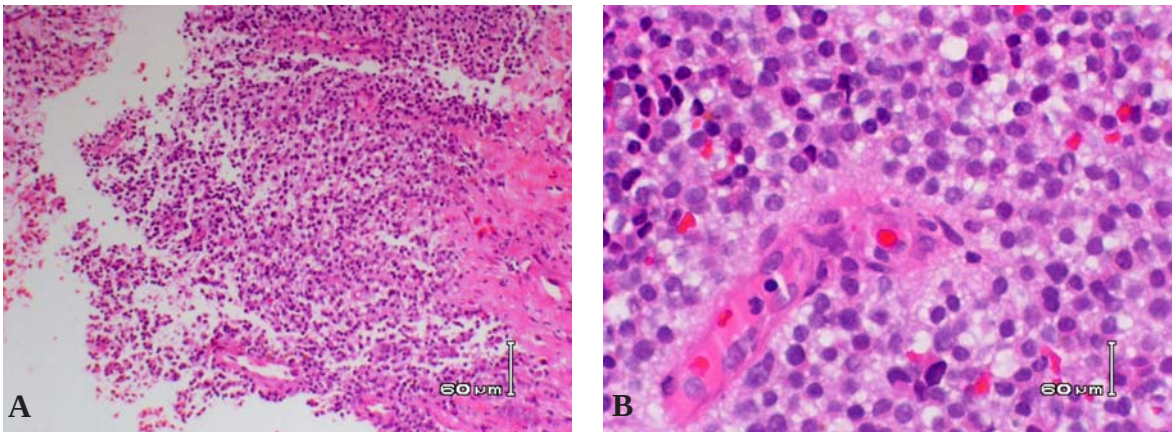

Fig. 1 Biopsied specimen of case 1 shows small round cell appearance, resembling atypical lymphoid cells. A) Low power; B) High power

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

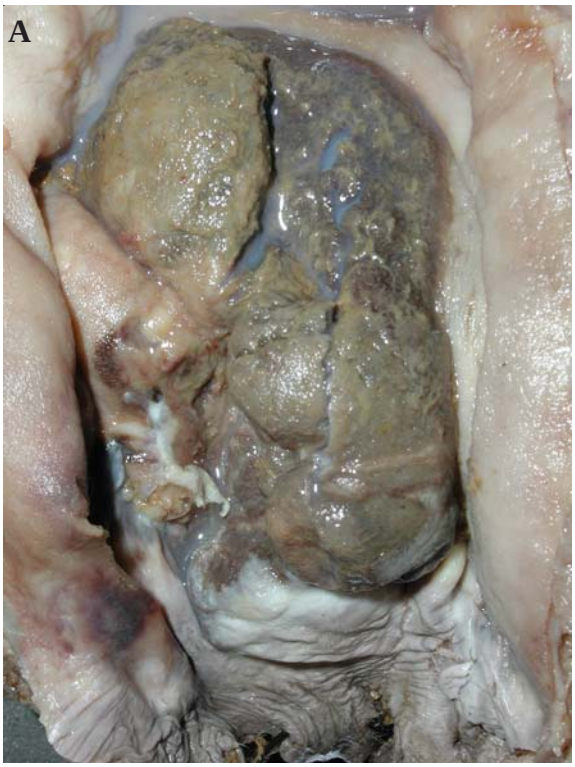

Fig. 2A Gross finding of case 1 reveals large mass with surface ulceration

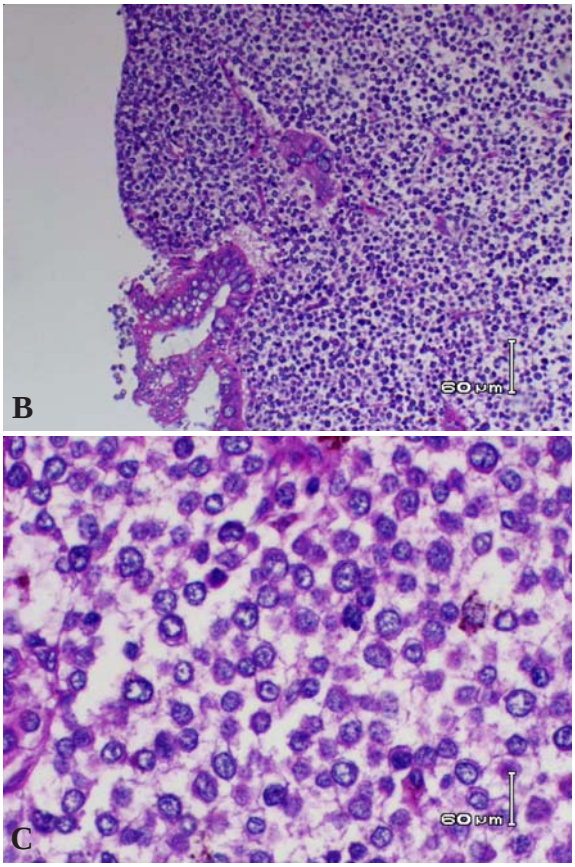

Fig. 2B, C Histologic feature demonstrates small-sized malignant cells

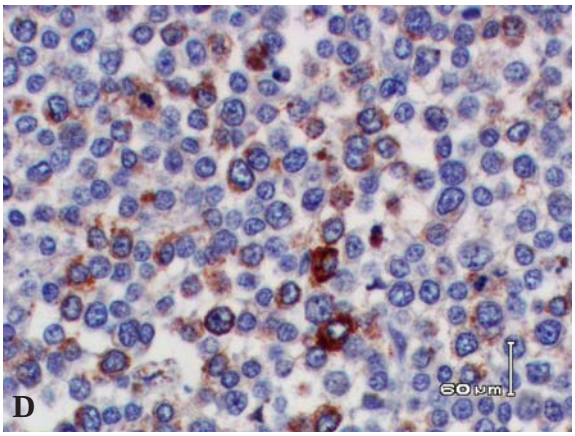

Fig. 2D The tumor stained with HMB45

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 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 propia 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[3,5]. 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

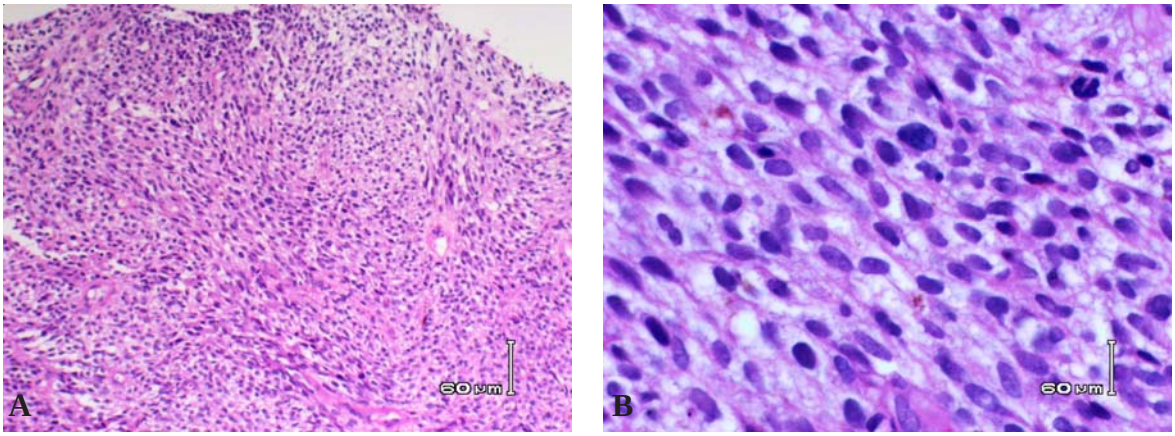

Fig. 3 Tissue biopsy of case 2 reveals bundle of spindle cells mimic sarcoma. A) Low power; B) High power

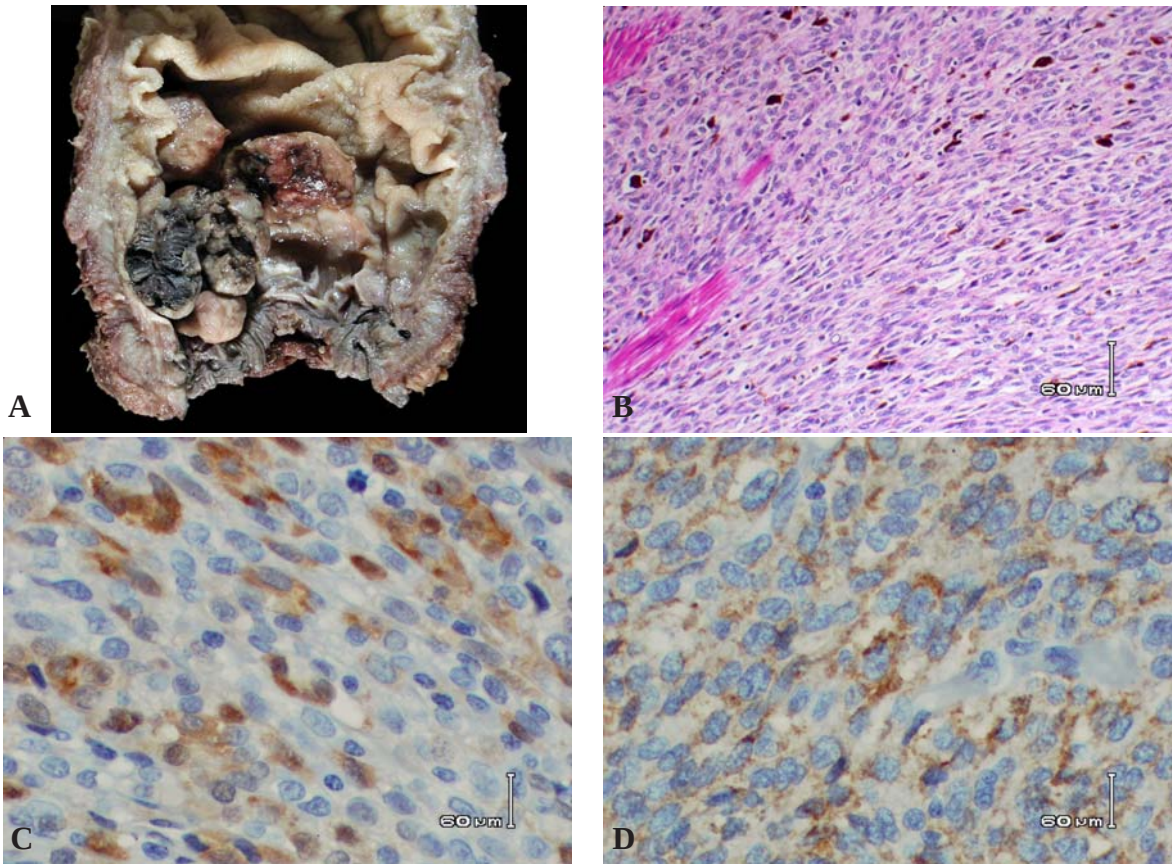

Fig. 4 A) Gross finding of AP resection specimen reveals polypoid pigmented masses just above dentate line; B) Histologic finding of AP resected specimen. Note some tumors contain melanin pigment. Immunohistochemical stains; C) S100 protein; D) HMB45

melanocytes are thought to be initial cells which have undergone malignant transformation[3]. Anorectal melanomas are assumed to be a disease of Caucasians[2]. 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[3]. Then the initial gross findings usually exhibit large polypoid masses, which are variable in color[2,3]. 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

Table 1. Reported cases of Anorectal Melanomas in Thailand

	First case	Secondcase	Third case	Fourthcase	Fifthcase
Authors	Kraikiat K[9]	Ammawat K[10]	KittipornpeddeeV[11]	Present case	Present case
Age (years)	81	51	68	55	65
Sex	Male	Female	Female	Female	Female
Symptom	Painful mass	Rectal bleeding	Painful mass and rectal bleeding	Mass and rectal bleeding	Rectal bleeding
Duration of symptoms (month)	12	24	2	1 and a half	1
Size of mass (cm)	4	3	NA	12 x 10 and 5 cm in thickness	1-2 (5fungating masses)
Metastasis (at diagnosis)	Regional lymph node	NA	NA	Regional lymph node and Liver	Regional lymph node
Therapy	AP-resection	Polypectomy	AP-resection	AP-resection	AP-resection
Survival (months)	14	NA	NA	4	NA

Note: NA, Data not available

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[3]. 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.

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มะเร็งชนิดเมลาโนมาที่เกิดขึ้นบริเวณรอยต่อระหว่างลำไส้ตรงและทวารหนัก: รายงานผู้ป่วย 2 ราย ในโรงพยาบาลพุทธชินราช พิษณุโลก

จุลินทร สำราญ, สมรมาศ กันเงิน, สุชาติ พรเจริญพงศ์, องอาจ เลิศขจรสิน

มะเร็งชนิดเมลาโนมาที่เกิดขึ้นบริเวณรอยต่อระหว่างลำไส้ตรงและทวารหนักนั้นพบได้น้อยมาก และมีพยากรณ์โรคที่ไม่ดี รายงานผู้ป่วยหญิง อายุ 55 ปี และ 65 ปี ของโรงพยาบาลพุทธชินราช พิษณุโลก ซึ่งมาพบแพทย์ด้วยอาการเลือดออกจากทวารหนัก จากการตรวจพบมีก้อนเนื้องอกขนาดใหญ่ที่บริเวณรอยต่อระหว่างลำไส้ตรงและทวารหนักและมีการกระจายของเนื้องอกไปยังต่อมน้ำเหลืองตั้งแต่ในระยะแรก การตรวจชิ้นเนื้อทางพยาธิวิทยาพบลักษณะทางฮีสโตโลยี่ของเซลล์เมลาโนมาที่แตกต่างกัน มีทั้งเซลล์เมลาโนมาขนาดเล็กกลม คล้ายกับเซลล์เม็ดเลือดขาวชนิดลิมโฟซัยด์และเซลล์เมลาโนมารูปร่างรีเรียงตัวคล้ายกับมะเร็งชนิดซาร์โคมา การย้อมพิเศษทางอิมมูฮีสโตเคมมิสตรีช่วยในการวินิจฉัยมะเร็งปฐมภูมิชนิดเมลาโนมา ผู้ป่วยทั้งสองรายได้รับการ รักษาโดยการผ่าตัด APR ผู้ป่วยรายแรกเสียชีวิต ในเดือนที่ 4 ภายหลังจากการวินิจฉัยโรค เนื่องจากมะเร็งแพร่กระจาย และภาวะหัวใจล้มเหลว ส่วนผู้ป่วยรายที่สองกำลังอยู่ในระหว่างการรักษาเพิ่มเติมภายหลังการผ่าตัด