[症例報告]Primary amelanotic melanoma of the anorectum : A case report and literature review

Primary amelanotic melanoma of the anorectum: A case report and literature review

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ABSTRACT

A case of anorectal amelanotic melanoma in a 72-year-old female is reported. The patient presented with several episodes of anal bleeding after defecation. Endoscopic examination showed a 1 cm-polypoid tumor with a roughly irregular surface in the right wall of the anorectum about 5 cm from the anal verge. No pigmentation was evident in the tumor. Endoscopic ultrasonography (EUS) revealed the depth of invasion to be limited to the submucosa. Although poorly differentiated adenocarcinoma was suspected by biopsy, it was difficult to classify the tumor as malignant lymphoma or malignant melanoma. Transanal simple excision of the tumor was performed. The tumor appeared homogeneously gray-whitish and was 10×17 mm in size. The tumor was finally diagnosed to be amelanotic melanoma by electron microscopy and immunohistochemistry. The depth of invasion was limited to the submucosa. The tumor was resected with 1 cm-free margins. A few decades ago, abdominoperineal resection combined with or without pelvic and bilateral inguinal lymph node dissection was recommended for the patients who had anorectal malignant melanoma with no distant metastases. However, recent studies have demonstrated that overall survival is related to the tumor size and staging of the depth of invasion, but not the extent of surgical margins. So we didn't perform additional resection. She is now living and well 11 months after operation with no evidence of recurrence of the disease. She comes to the hospital every three months. *Ryukyu Med. J., 15(3)147~151, 1995*

Key words: amelanotic melanoma, anorectum, simple excision

INTRODUCTION

Malignant melanomas have been encountered in many parts of the gastrointestinal tract, and with the exception of those primary in the esophagus and anorectum, they are considered to be metastatic. Although the anorectum represents the commonest site for the development of malignant (amelanotic) melanoma in the gastrointestinal tract, it is an extremely rare condition. To our knowledge, only 15 cases of amelanotic melanoma of the anorectum were reported from 1964 to 1992 in Japan[1]. Because of the rarity of the disease, problems associated with anorectal melanoma such as accurate and timely diagnosis, role of surgical treatment, and sequence or strategy of treatment remain unsettled. We present here an additional case of primary amelanotic melanoma of the anorectum, involving a simple resection, focusing on the role of surgery in the treatment of melanoma.

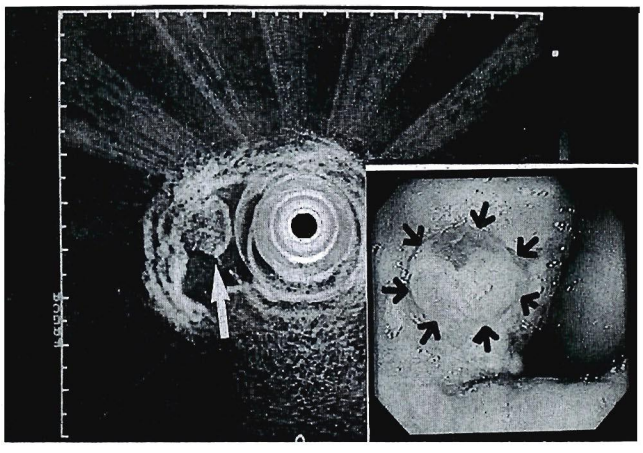

Fig.1 Endoscopic ultrasonography demonstrating a polypoid tumor with no evidence of penetration into the proper muscle layer. Colonoscopy (the inset at the lower right) showing the tumor with no brown to black pigmentation.

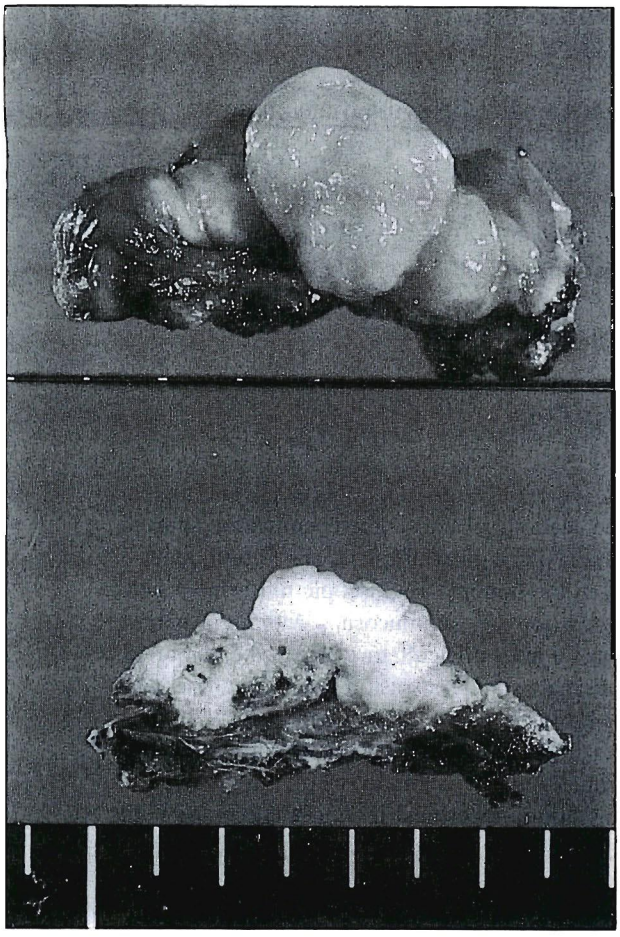

Fig.2 Macrophotographs of the resected tumor revealing an oval polypoid tumor with irregular surface (top) and its cut section showing a solid, whitish tumor (bottom).

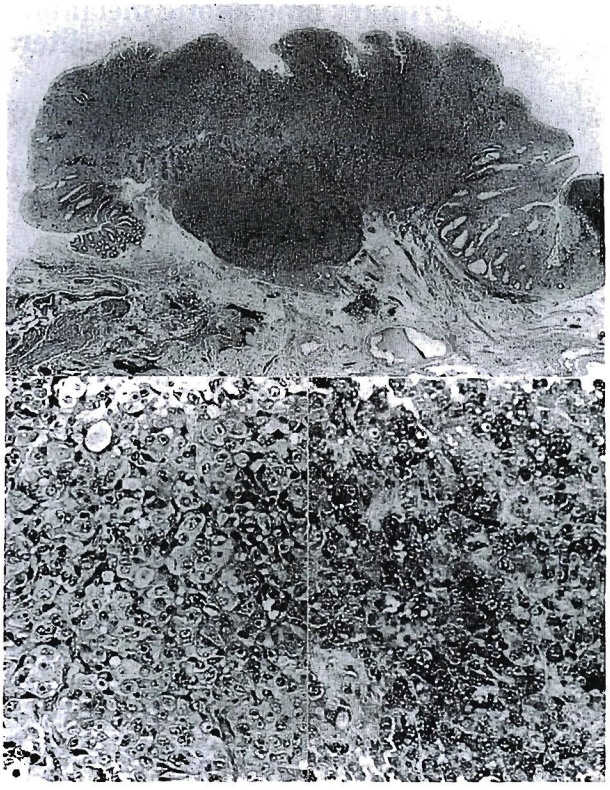

Fig.3 Microphotographs of the tumor revealing a domed polypoid tumor (top) (HE, ×2.5), cuboidal cells in alveolar formations with mitotic figures and no melanin pigment (left, bottom) (HE, ×50) positive immunohistochemical staining for S-100 protein (right, bottom) (HE, ×50).

CASE REPORT

A 72-year-old female was admitted to the Ryukyu University Hospital with a diagnosis of rectal carcinoma for surgical treatment on July 13, 1994. The patient presented with episodes of rectal bleeding at every defecation in May. She was seen at a local hospital, where endoscopic examination revealed a 1 cm-tumor with irregular surface in the right lateral wall of the anorectum about 5 cm from the anal verge, just above the dentate line. On admission, the patient appeared well without any complaint. The physical examination showed no abnormality except for rectal tumor on rectal examination. Her laboratory data including CBC, serum chemistry, tumor markers (CEA, CA-19-9) and urinalysis were within normal limits. Barium enema demonstrated a 1 cm-polypoid tumor in the right wall of the anorectum. Endoscopic study showed a 1 cm-polypoid tumor with a hemorrhagic, roughly irregular surface and with a similar color to the surrounding rectal mucosa. No pigmentation was found in the tumor. Endoscopic ultrasonography (EUS) revealed a polypoid well-delineated tumor mass without penetration into the surrounding tissue (the proper muscle layer) (Fig.1). The depth of invasion was diagnosed to be limited to the submucosa, but not into the proper muscle layer. Although poorly differentiated adenocarcinoma was suspected by biopsy, it was difficult to classify the tumor as malignant lymphoma or malignant melanoma.

Transanal excision of the tumor was performed on July 29. Grossly, the tumor was 6×17 mm in size. When sectioned, the tumor appeared homogeneously gray-white in color and was 10×17 mm in size (Fig.2). Histological examination revealed cuboidal cells in alveolar formations with mitotic figure and no melanin pigment. Immunohistochemical staining was positive for S-100 protein and HMB-45 (human melanoma associated antigen) (Fig.3, 4). Electron microscopy revealed the tumor cells containing melanosomes and premelanosomes (Fig.5, 6). Based on these findings, the tumor was microscopically diagnosed to be amelanotic melanoma. The tumor invaded the submucosa, but not the proper muscle with 1 cm-free margins. Following the pathology report, diagnostic modalities showed no evidence of metastases. She was discharged on August 16, and comes to the hospital every

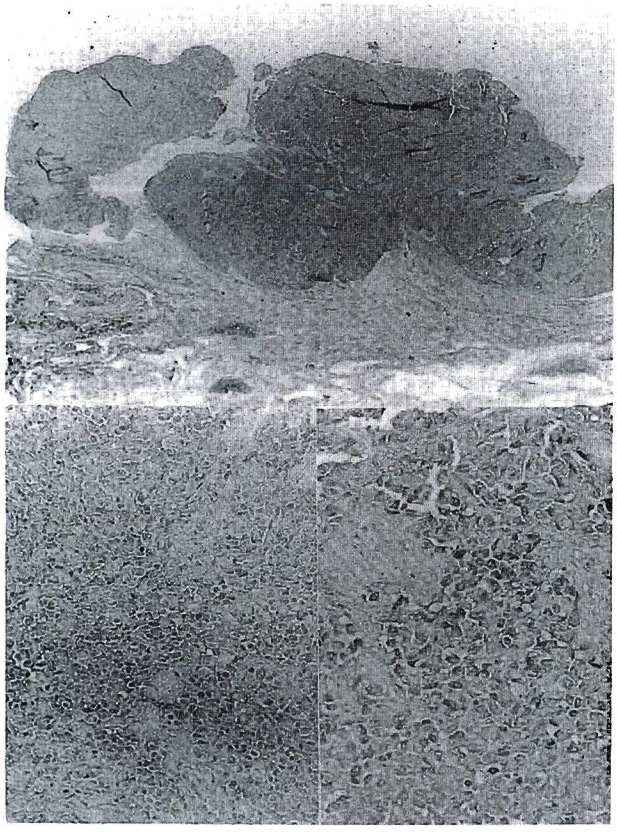

Fig.4 Microphotographs of the tumor showing positive immunohistochemical staining for HMB-45 (human melanoma-associated antigen) (top, ×2.5) (bottom, left, ×25 ; right, ×50).

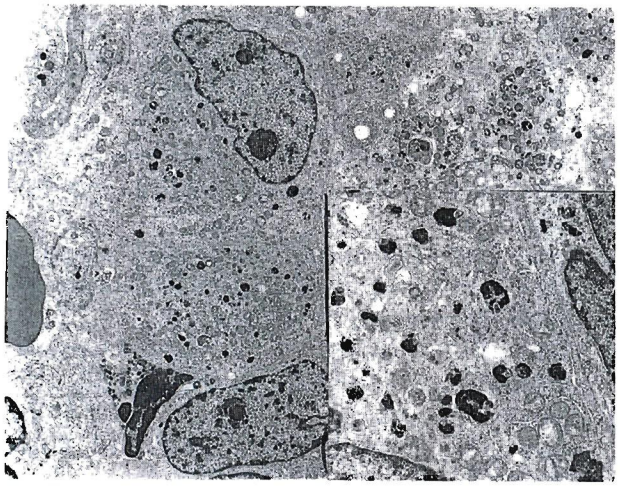

Fig.5 Electron microphotographs of the tumor revealing a tumor cell containing melanosomes and premelanosomes (×2,000). The inset at the lower right showing its magnification (×5,000).

three months. She is now living and well eleven months after operation with no evidence of recurrence of the disease.

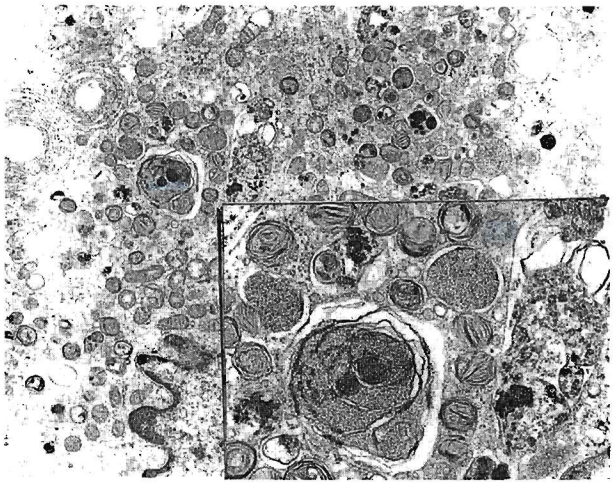

Fig.6 Electron microphotographs of the tumor showing melanosomes and premelanosomes in tumor cells (×5,000). The inset at the lower right showing its magnification (×12,000).

DISCUSSION

Anorectal melanoma is a rare malignant tumor and occurs with a frequency ranging from 0.4-1.6% of all melanomas[2,3]. In clinical practice approximately one melanoma of the anorectum will be seen for every eight squamous cell carcinomas in this location, and one for every 250 adenocarcinomas of the rectum[4,5]. Apparently melanoma of the anorectum is uncommon, and amelanotic, very rare. This is our first case experience of melanoma of the anorectum during the past 20 years. The anorectum is the third commonest site for melanoma, preceded by skin and eyes[6]. Because of the few melanin pigments in, and the morphological features of the tumor cells, the diagnosis of an amelanotic melanoma at preoperative biopsy is often difficult. In Japan, it is reviewed that only 38.5% correct diagnosis of malignant amelanotic melanoma at biopsy had made. In our particular case, it was difficult to distinguish it from undifferentiated carcinoma or reticular fibrosarcoma. Takasu had reported that 23 cases of malignant melanoma was treated for hemorrhoids. It was necessary to perform immunohistochemical staining to detect S-100 protein and HMB-45, and DOPA reaction. The definition of amelanotic melanoma is generally based on the identification of melanosomes by electron microscopy. Nonetheless, problems concerning surgical treatment is controversial.

A few decades ago, abdominoperineal resection combined with or without pelvic and bilateral inguinal lymph node dissection was recommended for the patients who had anorectal melanoma with no distant metastases. Unfortunately, no significant difference was found in survival between the two groups. Subsequently, others recommended local control by surgical treatment and advocated

adjuvant chemotherapy to improve prognosis. However, only 10% of the treated patients survived five years[1,2,7].

Skin melanomas are reported to have no significant prognostic differences in age, sex or anatomic location. Furthermore, it is generally accepted that the appearance and behavior of the primary anorectal melanomas do not differ from those of the corresponding skin melanomas[8]. Thus, we wish to discuss the role of surgical treatment of melanoma in general.

There is a roughly inverse relationship between the tumor size and survival, and its prognosis correlates well with staging of the depth of invasion[1,9]. In our case, the tumor size was 1.7 cm in the greatest diameter, but the depth of invasion was limited to the submucosa of the anorectum. Subsequently, we believed that a simple excision with adequate margin would be useful without inguinal lymph node dissection for the patient.

The role of elective lymph node dissection remains one of the most controversial in the management of patients with melanoma. The results of many studies[11-13] analyzing the effectiveness of elective lymph node dissection are contradictory. The rationale for elective lymph node dissection is based on the hypothesis that melanoma spreads, in a stepwise manner, from the primary to the regional lymph nodes and then to distant sites[12]. The aim of elective lymph node dissection is, therefore, to provide definitive surgical treatment at an early stage in the natural history of the disease. The major prospective randomized studies suggest that there is no overall survival advantage conferred by elective lymph node dissection, but the efficacy of elective lymph node dissection in subgroups of patients with early stage melanoma[14-16]. According to this rationale, we had to perform inguinal lymph node dissection, but not because of no evidence of lymph node enlargement. Another of the important controversies in the management of patients with melanoma is the optimum excision margin for primary melanoma.

Many studies concerning adequate local control after conservative excision of melanoma have been reported[17-20] A 1-cm margin is now widely accepted as adequate for thin (small) melanoma, although the minimum clearance necessary for thicker (larger) lesion remains undefined. Both retrospective and prospective studies have demonstrated that overall survival is related to the biological characteristics of the primary tumor, most importantly thickness (volume or size) at presentation, but not the extent of surgical margins. It is now considered that local recurrence or metastasis can be predicted from the thickness (tumor volume or size) of the melanoma[9,21]. In conclusion, supplementary treatment with radiotherapy has been of no benefit, nor have the various chemotherapeutic agents helped[1,3,20,21]. The patient will require an intimate follow-up to allow early detection and treatment of any local recurrences, regional lymph node metastases or distant metastases that develop.

REFERENCES

1) Hanba, H., Higashino, M., Hai, M., Osugi, H., Tanimura, S., and Kinoshita, H.: Report of a case of malignant melanoma of the anorectum and review of 154 cases in Japan. Nippon Rinsho Geka Igakkai Zasshi 53: 154-158, 1992 (in Japanese).
2) Pack, G.T., and Orepeza, R.: A comparative study of melanoma and epidermoid carcinoma of the anal canal: A review of 20 melanomas and 29 epidermoid carcinomas. Dis. Colon Rectum 10: 161-176, 1967.
3) Remigo, P.A., Der, B.K., and Fosberg, R.T.: Anorectal melanoma: Report of two cases. Dis. Colon Rectum 19: 350-356, 1976.
4) Morson, B.C., and Volkstaedt, H.: Malignant melanoma of the anal canal. J. Clin. Pathol. 16: 126-132, 1963.
5) Paradis, P., Douglass, H.O.Jr., and Holyoke, E.D.: The clinical implications of a staging system for carcinoma of the anus. Surg. Gynecol. Obstet. 141: 411-416, 1975.
6) Weston, S.D., and Marren, M.: Malignant melanoma of the rectum. J. Int. Col. Surg. 17: 403-416, 1952.
7) Husa.A., and Hocherstedt.K.: Anorectal malignant melanoma. A report of 14 cases. Acta. Chir. Scand. 140: 68-72, 1974.
8) Finne, G., and Ma, C.K.: Alimentary tract. In: Kissane, J.M. (ed) Anderson's pathology. The C.V. Mosby Company, St. Louis, pp1086-1087, 1985.
9) Breslow, A.: Thickness, cross-sectional areas and depth of invasion in the prognosis of cutaneous melanoma. Ann. Surg. 172: 902-908, 1970.
10) McCarthy, W.H., Shaw, H.M., and Milton, G.W.: Efficacy of elective lymph node dissection. Surg. Gynecol. Obstet. 161: 575-580, 1985.
11) Crowley, N.J., and Seigler, H.F.: The role of elective lymph node dissection in the management of patients with thick cutaneous melanoma. Cancer 66: 2522-2527, 1990.
12) Balch, C.M.: The role of elective lymph node dissection in melanoma: rationale, results, and controversies. J. Clin. Oncol. 6: 163-172, 1988.
13) Cady, B.: Prophylactic lymph node dissection in melanoma: does it help? J. Clin. Oncol. 6: 2-4, 1988.
14) Veronesi, U., Adamus, J., Bandiera, D.C., Obvennhovd, I.O., Caceres, E., and Cascinelli, H.: Delayed regional lymph node dissection in stage I melanoma of the skin of the lower extremities. Cancer 49: 2420-2430, 1982.
15) Sim, F.H., Taylor, W.F., Pritchard, D.J., and Soule, E.H.: Lymphadenectomy in the management of stage I malignant melanoma: a prospective randomized study. Mayo Clin. Proc. 61: 697-705, 1986.
16) Drepper, H., Koehler, C.O., Bastian, B., Breuninger.H., Broecker, E-B, and Goehl, J.: Benefit of elective lymph node dissection in subgroups of melanoma

patients. Results of a multicenter study of 3616 patients. Cancer 72: 741-749, 1993.
17) Breslow, A., and Macht, S.D.: Optimal size of resection margin for thin cutaneous melanoma. Surg. Gynecol. Obstet. 145: 691-692, 1977.
18) Cascinelli, N., van der Esch, E.P., Breslow, A., Morabito A., and Bufalino, R.: Stage I melanoma of the skin: the problem of resection margins. Eur. J. Cancer 16: 1079-1085, 1980.
19) Goldman, L.I., and Byrd, R.: Narrowing resection margins for patients with low-risk melanoma. Am. J. Surg. 155: 242-244, 1988.
20) Veronesi, U., and Cascinelli, N.: Narrow excision (1 cm margin): a safe procedure for thin cutaneous melanoma. Arch. Surg. 126: 438-441, 1991.
21) Neades, G.T., Orr, D.J.A., Hughes, L.E., and Horgan, K.: Safe margins in the excision of primary cutaneous melanoma. Br. J. Surg. 80: 731-733, 1993.