Primary Malignant Melanoma of the Esophagus

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Primary malignant melanoma of the esophagus is exceedingly rare. The existence of primary malignant melanoma in the esophagus had been in doubt until the presence of benign melanocytes was demonstrated within the esophagus. Hematogenous and lymphatic metastases are common. The prognosis is poor even after a radical procedure due to early metastasis. We report here two cases of primary malignant melanoma of the esophagus. One is a melanotic melanoma and the other is an amelanotic melanoma.

Key Words: Malignant melanoma, amelanotic melanoma, esophagus

Melanocytes are found in the epithelio-stromal junction in 4–8% of normal esophagus. But primary malignant melanoma arising in the esophagus is an extremely rare lesion that constitutes less than 0.1% of all malignant esophageal tumors. The major criteria for accepting a melanoma as arising in the esophagus have been the presence of junctional change on the mucosa adjacent to the tumor and a typical histologic pattern of a melanoma and melanin within the tumor cells. But amelanotic melanoma has ever been reported. The duration of symptom is short before diagnosis and it is mostly fatal within 1 year regardless of radical resection. We have had the opportunity to examine two recent cases of primary malignant melanoma of the esophagus, so that the cases are described and a review of the literature is presented.

CASE REPORT

Case 1

A 47-year-old man was admitted to Severance Hospital with a 3-month history of mild dysphagia. His family history was unremarkable. He had stopped smoking 16 years before and he drank alcohol 3 to 4 times per week. Notable pigmented skin lesion and lymph node swelling were not found in physical examination. Routine blood and urine tests were unremarkable. Endoscopic sonography showed a 3.0 cm-sized polyloid mass in the lower esophagus which involved the muscle layer of esophagus and there was no lymph node (L/N) enlargement. Chest CT revealed esophageal-wall thickening in the subcarina level and no L/N enlargement in the mediastinum. Endoscopic examination disclosed multiple black-pigmented nodules within the esophagus extending from 35 to 40 cm from the oral incisors (Fig. 1A) and a 3.5 cm-sized black-pigmented polyloid mass in the lower esophagus (Fig. 1B). Transthoracic radical near-total esophagectomy and cervical esophagogastrectomy were performed with macroscopically complete removal of the lesion. Histologically, there were melanin pigments and melanoma cells containing melanin pigment (Fig.

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Fig. 1. Endoscopic finding of case 1. A) Endoscopy revealed multiple black discoloration of the surrounding mucosa. B) A 3.5 cm sized black pigmented polypoid mass in the lower esophagus.

Fig. 2. Microscopic finding of case 1(H&E, × 400). A) Melanoma cells were widespread and the black arrows indicate a melanoma cell which was filled with melanin. B) The small black arrows indicate junctional activity in adjacent mucosa and the medium sized black arrows indicate melanin pigment.

2A) and junctional activities were found in adjacent tumor mucosa (Fig. 2B). The tumor mass was limited within the submucosal layer and there was no L/N metastasis. The patient recovered well and was discharged on the 18th postoperative day. Three months after operation, follow-up CT showed multiple liver metastasis and he died 4 months after operation (Fig. 3).

Case 2

A 39-year-old woman was admitted to Severance Hospital with a 6-month, history of mild dysphagia. Her past history, family history, routine blood and urine test were unremarkable. No pigmented lesions were found in physical examination. Esophagogram revealed a 1.5 cm-sized lobulating mass with central
Fig. 3. Multiple liver metastasis and ascites were found in follow-up abdominal CT of case 1 and the patient died 4 months after operation due to carcinomatosis.

Fig. 4. Endoscopic examination of case 2 revealed a 1.0 cm-sized polypoid mass with central ulceration located 40 cm from the oral incisors and there was no discoloration in surrounding and overlying mucosa.

Fig. 5. Gross and microscopic finding of case 2. A) Grossly, the tumor was located in distal esophagus just above the G-E junction. B) H & E staining (× 400) C) The cytoplasm and nucleus of melanoma cells(arrows) stained with S-100(X 400). D) The cytoplasm of melanoma cells(arrows) stained with HMB-45(× 400).
ulceration in the lower esophagus. Chest CT showed anterior-wall thickening of the esophagus and there was no L/N enlargement. Endoscopic examination disclosed a 1.0 cm-sized ulcerofungating mass within the esophagus located 40 cm from the oral incisors and the overlying mucosa was whitish-gray (Fig. 4). It was diagnosed as poorly-differentiated carcinoma by preoperative endoscopic biopsy. Transthiatal radical near-total esophagectomy and cervical esophagogastrostomy were performed. Histologically, the tumor was limited within the submucosal layer of the esophagus and there were no melanocytes in the adjacent mucosa of the tumor and melanin pigment was not found in melanoma cells. Tumor cells did not contain melanin pigment, but positive for both S-100 protein and HMB-45 antigen by immunohistochemical analysis (Fig. 5). The patient was diagnosed as amelanotic melanoma of the esophagus. She recovered well and was discharged on the 25th post-operative day. At present, she is approximately 4 months out of surgery and is doing well with no evidence of recurrence.

DISCUSSION

Primary malignant melanoma of the esophagus is an extremely rare lesion, with about 150 cases reported in the literature, since it was first described by Baur in 1906 (Dematos et al. 1997; Sivak, 1997). When de la Pava et al. established the presence of melanocytes in 4 of every 100 human esophagus at autopsy, its existence was generally accepted (Pava et al. 1963) Ohashi et al. reported that melanocytes were found in the epithelio-stromal junction in 7.7% of normal esophagus specimens examined at autopsy in Japanese and were observed most commonly in the lower esophagus (Ohashi et al. 1990). Mucosal melanoma accounts for 3% of all malignant melanoma in whites, whereas they account for 13% of all malignant melanoma in Japanese (Kato et al. 1987). The tumor occurs most frequently in the 6th and 7th decades (Joob et al. 1995). No association was noted with tobacco or ethanol, nor was there a personal or family history of malignant melanoma (Dicostanzo and Urmacher, 1987). Its manifestations are very similar to those of epithelial carcinomas and are usually of short duration before diagnosis (Dematos et al. 1997). Symptoms appear in 80% of patients, dysphagia being the most common symptom (Sabanathan et al. 1989). More than 90% of tumors are located in the lower 2/3 of the esophagus (Sabanathan et al. 1989; Dematos et al. 1997). The tumor is most often solitary, but multiple lesions have been reported in 12% of cases (Joob et al. 1995). They tend to be large, intraluminal, polypoid, and irregular in appearance, making them easy to identify by esophagogram. Endoscopy is also helpful in demonstrating and localizing these lesions, usually revealing a polypoid and pigmented mass in a majority of cases (Dematos et al. 1997). Endoscopic biopsy specimens are occasionally misdiagnosed as poorly-differentiated carcinoma and only 54.7% of cases are diagnosed preoperatively as malignant melanoma (Joob et al. 1995; Sivak, 1997). Amelanotic melanoma is often misdiagnosed at biopsy as another malignancy due to little melanin pigment and morphologic features (Taniyama et al. 1990). The development of a diagnostic tool using monoclonal antibody HMB-45 makes diagnosis of melanoma easy (Joob et al. 1995). Immunohistochemically, these tumors react to S-100 protein, neuron-specific enolase, and HMA antibody, but not to anticytokeratins or anti-CEA antibody (Dicostanzo and Urmacher, 1987; Joob et al. 1995). In both of our cases, the tumors were situated in the lower esophagus. In endoscopic examination, the former revealed a black polypoid mass with multiple black nodules in surrounding mucosa and it was diagnosed as primary malignant melanoma before operation. The latter disclosed a polypoid mass with central ulceration and the overlying mucosa was whitish-gray. Its preoperative diagnosis was a poorly-differentiated carcinoma and immunohistochemical analysis was not performed for endoscopic specimens. Since gastrointestinal mucosal metastases are found at autopsy in 48% of all patients with malignant melanoma of the skin, the diagnosis of primary malignant melanoma of the esophagus should only be accepted when a very careful examination does not disclose any other primary site (Roesch and Rohner, 1984). Allen and Spitz defined the criteria of primary malignant melanoma: 1) it manifests the characteristic structure of melanoma and contains melanin pigment; 2) melanocytes can be found in
the adjacent epithelium; 3) the tumor is polypoid; 4) it originates from an area of junctional activity within the squamous epithelium (Allen and Spitz, 1953). However, only 40% of esophageal melanomas fulfill this criteria (Dematos et al. 1997). Melanosis, considered as a predisposing factor, has been seen in 23–25% of reported cases of primary malignant melanoma (Ludwig et al. 1981; DiCostanzo and Urmacher, 1987; Sabathan et al. 1989; Muto et al. 1997) while junctional change has been seen in only 40% of reported cases (Muto et al. 1997). Amelanotic melanoma has been reported in 9.4% of primary malignant melanoma of the esophagus (Tanigama et al. 1990). In case one, all of the above described criteria were satisfied. In case two, the tumor cells didn’t contain melanin pigment and were positive for both S-100 protein and HMB-45 antigen by immunohistochemical analysis. Only one of the above criteria, junctional activities, was fulfilled in case two.

The tumors tend to grow in the mucosal and submucosal layer in a lentiginous radial manner and infiltration beyond the esophagus wall is uncommon. Both hematogenous and lymphogenic metastases are common (Dematos et al. 1997). Thirty-to-forty percent of patients have lymph node or distant metastasis at the time of diagnosis (Ribeiro et al. 1996; Dematos et al. 1997). The most common site of metastases is the liver, followed by the mediastinum and mediastinal node, lung, and brain (Chalkiadakis et al. 1985). Malignant melanoma also has a high incidence of cardiac metastases (Chello et al. 1993). Tumors in both of our cases were limited within the submucosal layer and did not have lymph node metastasis. Case one had multiple liver metastasis after operation and the patient died due to hepatic failure and carcinomatosis 4 months after operation. Case two is approximately 4 months out of surgery and the patient is doing well with no evidence of recurrence.

Although some authors have questioned the operative indications for this tumor, surgical resection is the preferred method of treatment and long-term survival can be expected. When surgical resection is elected, a total or near-total esophagectomy should be carried out because of the tendency of the tumor to spread longitudinally (Joob et al. 1995). Some authors have reported a case of melanoma successfully palliated by endoscopic laser therapy (Mohandas et al. 1993). Radiation therapy generally has been reserved for patients with metastatic disease of a poor functional status. Chemotherapy and immunotherapy have no major role in treatment (Joob et al. 1995). In our cases, radical near-total esophagectomies were performed without any other adjuvant therapy.

Despite early stage and a radical surgical approach, this diagnosis portends a poor prognosis. The mean survival after diagnosis is 13.4 months, with a 5-year survival of 4.2% (Chalkiadakis et al. 1985; Dematos et al. 1997). The overall survival was 9.8 months (Sabathan et al. 1989; Muto et al. 1997).

REFERENCES


