Primary Melanoma of the Esophagus with Non-metastatic Dark Lymph Nodes in a Female Breast Cancer Patient

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Abstract. Background: Primary melanoma of the esophagus is a very rare and aggressive neoplasm; only a small number of patients survive more than 1 year after initial diagnosis. Case Report: We describe a case of primary melanoma of the esophagus in a woman with a history of invasive breast cancer. The patient suffered from dysphagic and dyspeptic disorders. The abdomen ultrasonography and the esophagogastroscopy showed a lesion located at the esophago-gastric junction extending to the gastric fundus. Histological and immunohistochemical studies revealed a primary esophageal infiltrating melanoma. A total gastrectomy and regional lymphadenectomy with a partial resection of the distal esophagus was performed. Results: During laparotomic exploration, numerous dark lymph nodes were found. On frozen sections, surprisingly neither malignant cells nor melanin were detected in the lymph nodes. Resection margins were not involved with the tumor. Conclusion: Patient is still alive with no evidence of recurrence at 24 months after surgical treatment, alone.

Mucosal melanoma accounts for 4%-5% of all primary melanomas. Generally, they arise in the mucous membranes located in the gastrointestinal, genitourinary and respiratory tract. De la Pava (1) was the first to identify the presence of melanocytes in the esophageal sub-mucosa. In particular, melanocytes were found in 4% of normal esophagus specimens. Those findings were confirmed in a Japanese subjects, with a reported incidence of 7%-8% (2). Moreover Ohashi et al. (3) observed a 29% incidence of melanocytes in the epithelial stromal junction of esophageal carcinoma surgically removed. Primary melanoma of the esophagus is a very rare and aggressive neoplasm, accounting for 0.1%-0.5% of all malignant esophageal tumors (4-5). Among 250 cases reported to date, only a small number of patients survived more than 1 year after initial diagnosis (6-8). This reflects the aggressive nature of the disease. Moreover, the delayed detection due to the lack of symptoms and the dismal results of treatments, contribute to the poor prognosis of such a neoplasm.

Case report

A 75-year-old, non-smoking and non-alcoholic, Caucasian woman was referred to our hospital on the suspicion of esophageal cancer. She presented with a 4 kg weight loss in the previous 2 months, asthenia, dysphagic and dyspeptic disorders. The patient had previously undergone conservative surgery followed by radiotherapy for invasive breast cancer. An upper gastrointestinal barium examination showed a filling defect at the esophago-gastric junction. Moreover an abdomen ultrasonography was performed, revealing an exophytic mass of 3.5 cm in the epigastric region. Therefore the patient underwent an esophagogastroscopy that showed a grey-red mucosal lesion located at the esophago-gastric junction extending to the gastric fundus. The lesion was not bleeding. Multiple biopsies were obtained. Based on histological and immunohistochemical studies, the diagnosis of primary esophageal infiltrating melanoma was made: tumor cells were intensively positive for immunohistochemical staining (HMB-45+, S-100+) (Figure 1). Physical examination was negative, in particular skin, oral and anal mucosa examination revealed no lesion. Results of routine haematology and blood chemistry tests were all within normal values. The patient underwent staging pre-surgical procedures. A thoracic and abdominal computed tomography (CT) scan showed a vegetant neoplasm at the esophago-gastric junction with no lymph node enlargement. FDG-PET scan showed an uptake in the gastric region, but...
Figure 1. Immunohistochemical staining positive for HMB-45 (magnification 40x).

Figure 2. Resected specimen: smooth grey-red tumoral mass (diameter 5x4x3.5 cm).
Figure 3. Microscopic examination: polypoid-ulcerated primary melanoma with mucosa, submucosa and muscular mucosa infiltration (magnification 2x).

Figure 4. Lymph node microscopic examination: anthracosis, absence of neoplastic cells (magnification 10x).
not in other anatomical sites. A total gastrectomy and regional lymphadenectomy with a partial resection of the distal esophagus was performed. During laparotomic exploration, numerous, dark lymph nodes were found. On frozen sections, surprisingly, neither malignant cells nor melanin were detected in these lymph nodes. In fact, although they appeared dark, this was due to anthracosis and not to metastatic involvement.

Results

Macroscopic examination of the resected specimen revealed a smooth grey-red tumoral mass (diameter 5x4x3.5 cm) (Figure 2). Microscopic examination of the lesion showed a polypoid-ulcerated primary melanoma, with epithelioid cells and poor melanic pigmentation infiltrating the mucosa, submucosa and muscular mucosa (Figure 3). Moreover, the adjacent gastric mucosa showed melanocytic hyperplasia. At 8 mm from the primary melanoma, a second neoplastic lesion in the esophageal mucosa was found. In the 33 esophago-gastric junction lymph nodes, little and great gastric curvature lymph nodes, no neoplastic cells were observed (Figure 4). Resection margins were not involved with the tumor. No post-operative complications were reported; the patient was discharged 12 days after surgery in good condition and neither radiotherapy nor chemotherapy was administered. The patient is still alive with no evidence of recurrence at 24 months after surgery.

Discussion

Non-cutaneous melanomas are generally very aggressive neoplasms. In particular, prognosis of esophageal melanoma is extremely poor even with aggressive therapy. We report the case of primary malignant melanoma of the esophagus in a breast cancer woman survivor. The first report of primary esophageal melanoma with histological examination was provided by Garfinkle and Cahan (9). Among esophageal tumors, it accounts for 0.1%-0.2% of cases (10). About 90% of esophageal melanomas were located in the middle or distal third of the esophagus, probably due to the higher incidence of normal melanocytes found in this tract. Generally, gross specimens are polypoid and black pigmented. Of all the malignant melanomas of the esophagus 10%-25% were found in the amelanotic form and generally the colour of the lesion ranged from red to white (11). Moreover, in a review by Sabanathan (12), the presence of satellitesis was noted in 12% of cases. Cutaneous melanoma frequently spreads to the gastrointestinal tract, but metastatic esophageal localization is more rare than primary localization: only about 4% of patients who died of metastatic melanoma were found to have metastases to the esophagus (13).

These data are concordant with our findings, in fact melanoma was found in the third distal esophagus, in the proximity of the esophago-gastric junction, with a second neoplastic distant lesion. Early diagnosis is very difficult due to the lack of symptoms until the neoplastic mass reaches a great size. Generally patients suffer from non-specific symptoms, thus often the diagnosis is delayed. A gastrointestinal barium examination represents the first radiological approach. Usually an intraluminal esophageal mass is shown. It is important to perform an upper endoscopy, which allows a biopsy of the tumor. Because of the high rate of patients with metastatic spread at time of diagnosis, accurate staging is required to avoid unnecessary aggressive treatment. Commonly involved sites are: loco regional and distal lymph nodes (paraesophageal, supraclavicular and celiac lymph nodes), the liver, lungs and bones. An appropriate preoperative staging requires a chest and upper abdomen CT scan for the definition of loco-regional and distant disease (14). A useful tool available for the detection of metastases is FDG-PET imaging. In fact, in about 40% of cases of resectable metastatic cutaneous melanoma, the use of FDG-PET is associated with a change in the planned surgical and medical management and this could also be particularly important in patients with esophageal melanoma (15).

Surgery is the mainstay of therapy. Some authors advocated a great margin of resection and in resectable patients the only way to obtain longer survival is a total or subtotal esophagectomy (16). In our case, we pursued an aggressive surgical approach, considering the absence of patient comorbidity. Systemic therapy for metastatic melanoma includes chemotherapy and immunotherapy. Unfortunately, even with the most active drug, dacarbazine, the response rate is only 20%-25% and long-term survival is poor (17). Furthermore, there is no clear benefit of the addition of interferon alfa-2b or interleukin-2 (18). However in 1998, Naomoto et al. (19) reported a case of primary esophageal melanoma successfully treated with surgery and peri-operative chemo-hormone therapy. In addition Suzuki et al. (20) demonstrated a complete response with chemoendocrine therapy in a patient with recurrence in the upper mediastinum. The therapeutic approach to melanoma of the esophagus should be considered on an individual basis, evaluating the patient’s conditions and extent of disease.

References


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