Case report

Primary malignant esophageal melanoma: Diagnostic and therapeutic manipulations of a Greek patient and review of the literature

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SUMMARY

Primary esophageal melanoma is a rare malignant entity. It has been estimated that since its first description in 1964, no more than 300 cases have been described in the international literature. It represents only 0.1% of all malignant esophageal neoplasms. Amelanotic melanomas represent a minority of all esophageal melanomas. The aim of this presentation is to describe the diagnostic and therapeutic manipulations applied in a patient with amelanotic primary esophageal melanoma. Case report: A man aged 65, was admitted to our department because of dysphagia in solid foods of two months duration. Physical examination revealed nothing important. He was a non-smoker and he denied alcohol consumption. Upper GI barium follow-through showed a feeling defect in the lower third of the esophagus without significant prestenotic dilatation. Upper GI endoscopy revealed the presence of a neoplasm, occupying almost the entire lumen of the esophagus, in an area of at least 5cm. Nevertheless, passing the endoscope through the stenotic lumen of the esophagus could easily be achieved. Histology of tumor samples, revealed the presence of malignant amelanotic esophageal melanoma. Immunohistochemical study showed that the malignant cells were negative in panceratine, cera-tine 7 and AE3 (epithelial indices) and positive to Vimentin S100, HMB45 and MART1. Computed tomography of the whole body showed a small metastatic lesion in the liver, without lymph-node involvement. Skin examination revealed nothing important. Ophthalmological examination was negative. Chemotherapy consisting of Cisplatin 90mg/m2 IV (1st day) and Temodal 150mg/m2 tb po (1st and 5th day), every 25 days (3 cycles) combined with radiotherapy were applied. Four months later satellite lesions in the esophagus, and lung and liver metastases were found. Palliation treatment with Interferon-a, was unsuccessful. After one month Fotemustine was given with little improvement. The patient died after 3 more months. Conclusion: Primary amelanotic esophageal melanoma is a rare neoplasm with dismal prognosis. Modern histochemistry can significantly facilitate the correct diagnosis.

Key Words: Esophageal melanoma, Esophageal tumors, Malignant melanoma

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INTRODUCTION

Primary Esophageal Melanoma (PEM) is a rare malignant entity. It has been estimated that since its first description in 1964, no more than 300 cases have been described in the international literature. Search in the PubMed database of the USA National Library of Medicine reveals numerous publications mainly in the form of case reports as well as scattered reports consisted of small series of 4 to 7 cases mainly of retrospective nature.[1-103]

PEM represents a proportion of only 0.1% of all malignant esophageal neoplasms. It metastasizes via the blood and/or lymph stream. It is a very aggressive malignant neoplasm leading to death in less than one year after diagnosis in the majority of patients. PEM without

melanine (amelanotic PEM) consists of only a small subgroup of the whole pool of PEM.

To the best of our knowledge only three cases of PEM have been described so far in the Greek medical literature with none of them being amelanotic.[17,63]

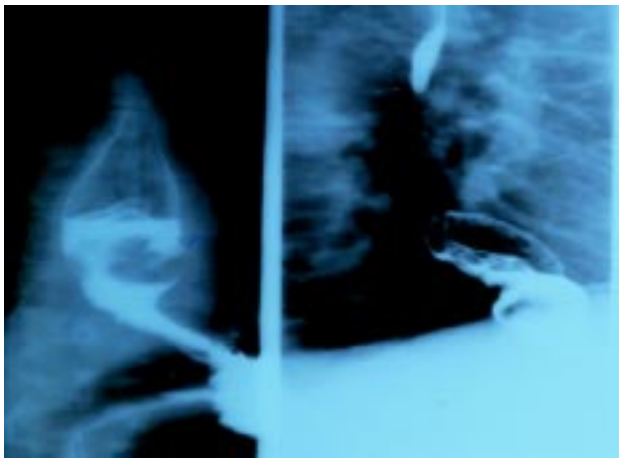

Fig. 1. Barium follow-through. Stenotic area in the lower third of the esophagus

The aim of this presentation is to describe the diagnostic and therapeutic manipulations applied in a patient with amelanotic malignant esophageal melanoma.

Case report

A man aged 65, was admitted to our department because of dysphagia in solid foods of two months duration accompanied by fatigue and loss of 4 Kg of body weight. Physical examination revealed nothing important. He was a non-smoker and he denied alcoholic consumption. Past medical history was unremarkable.

Upper GI barium follow-through showed a feeling defect in the lower third of the esophagus without significant prestenotic dilatation (figure 1), while upper GI endoscopy revealed the presence of a neoplasm, occupying half of esophageal lumen in an area of almost 5cm (figure 2). Despite this, passing the endoscope through the stenotic lesion could easily be achieved.

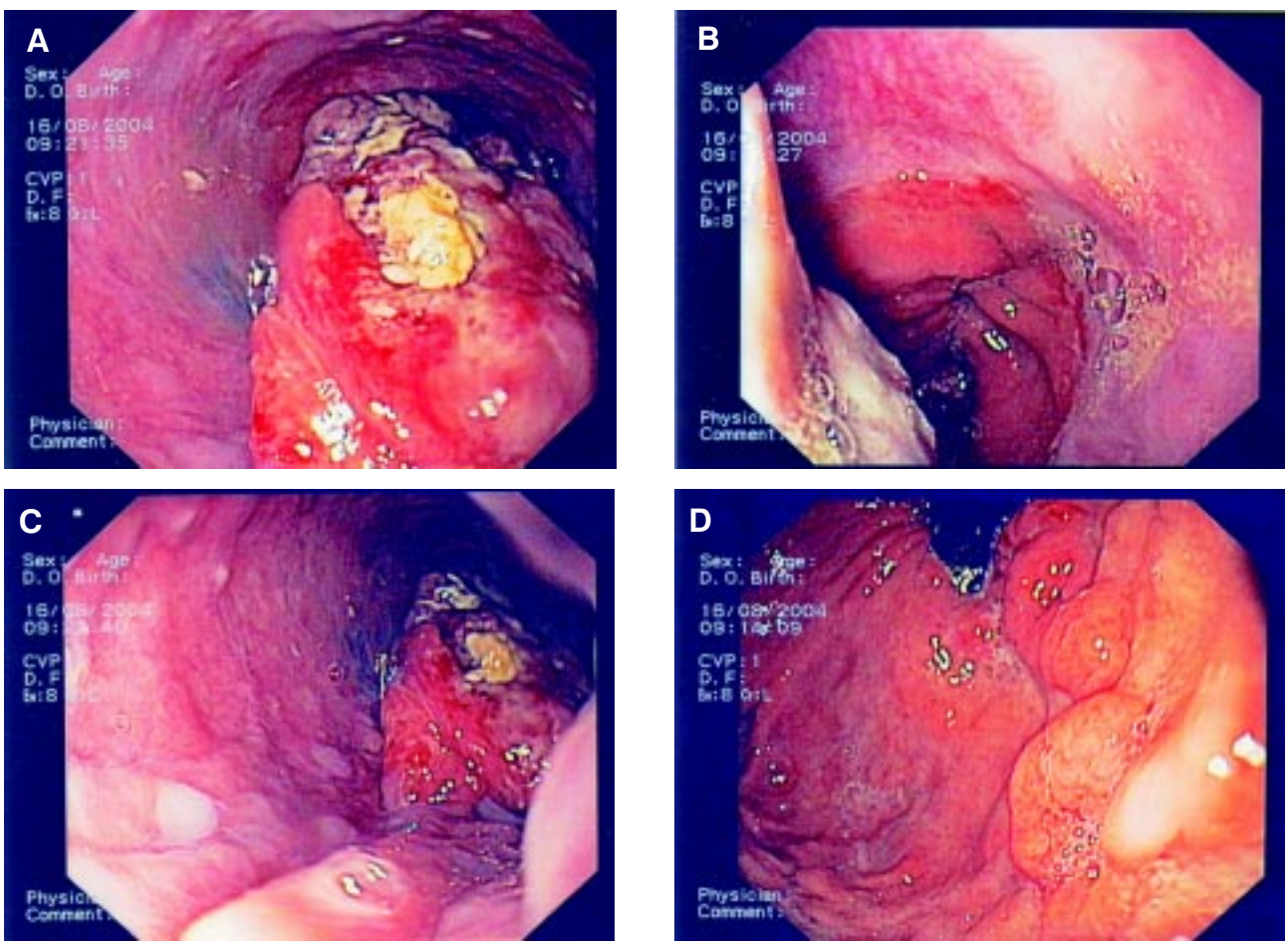

Fig. 2. Endoscopic appearance of melanoma.

Histology revealed the existence of a malignant esophageal melanoma. Immunohistochemical study showed that the malignant cells were negative in the epithelial indices panceratine, ceratine 7 and AE3 and positive to Vimentin S100, HMB45 and MART1 (figures 3 –7).

Computed tomography of the whole body showed a small metastatic lesion in the liver, without lymph-node involvement. Skin and ophthalmological examination revealed nothing important.

Radiation therapy and chemotherapy was applied. Chemotherapy consisting of cisplatin 90mg/m2 IV (1st day) and temodal 150mg/m2 tb po (1st and 5th day), every 25 days (3 cycles) combined with radiothrapry were applied. Four months later satellite lesions in the esophagus, as well as lung and liver metastases, were found. Palliation treatment with Interferon-a2,3 was unsuccessful. After one month Fotemustine was given with little benefit. The patient died after 3 more months.

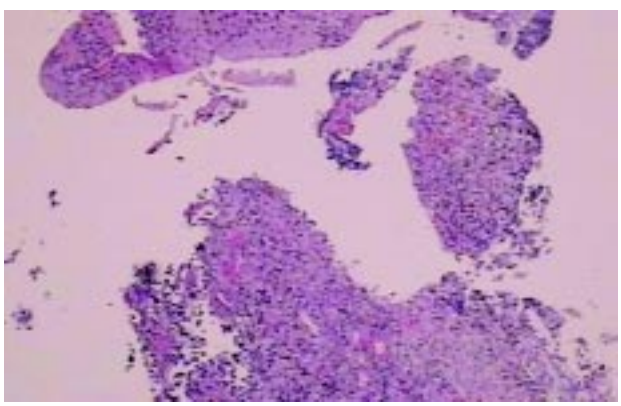

Fig. 3. Normal esophagus and a small part of the malignant neoplasm.

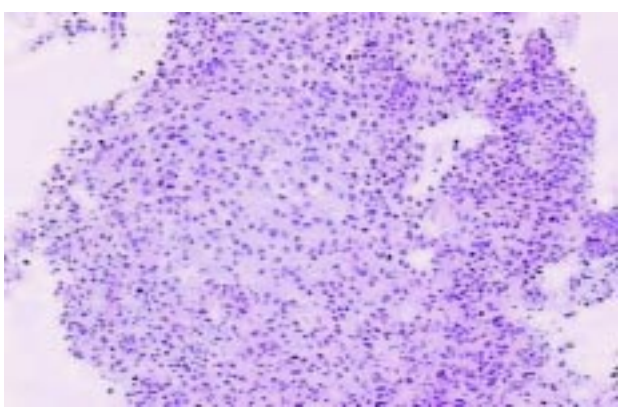

Fig. 4. Poorly differentiated malignant neoplasm.

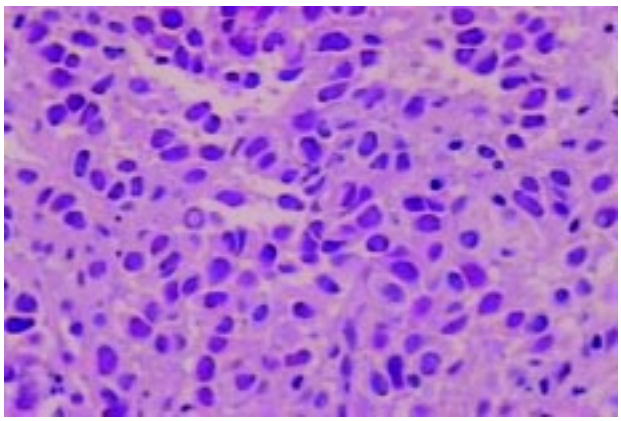

Fig. 5. Endonuclear material suggesting the presence of malignant melanoma.

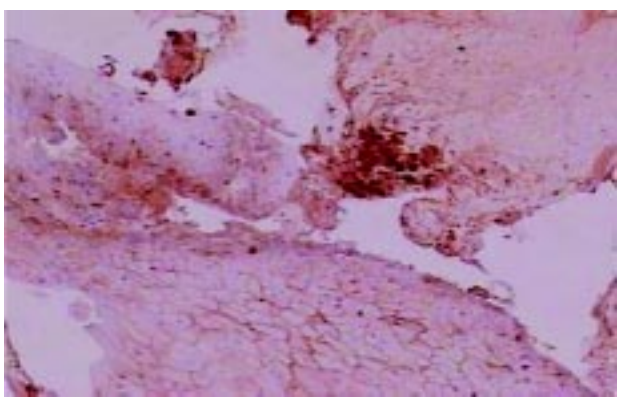

Fig. 6. Immunohistochemistry with S100. Positive only in the site of neoplasm.

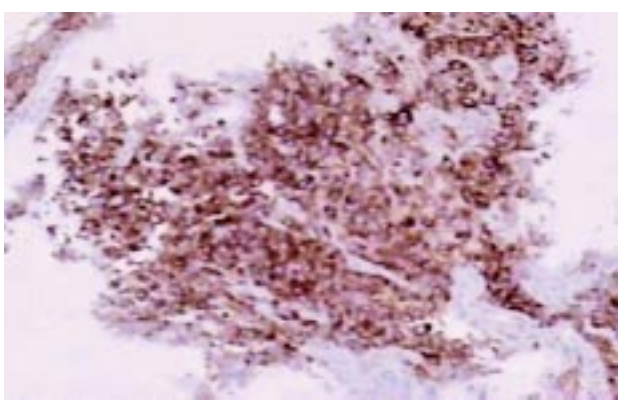

Fig. 7. Immunohistochemical staining with MART-1 (melanoma index): Confirmation of diagnosis of melanoma.

DISCUSSION

Primary esophageal melanoma is a very rear neoplasm. So far, a small number of series of cases of PEM

(mainly retrospective studies), have been described. Therefore, it is quite difficult to obtain safe conclusions concerning the clinical behavior of the disease as well as response to medical or surgical treatment. On the contrary, there is an abundance of case reports from nearly all countries.

In the majority of cases PEM is located in the middle or lower third of the esophagus. At the time of diagnosis the size of the tumor and the depth of penetration into the esophagus wall are quite significant (6.2 and 1.86cm respectively).[83]

It is of interest that almost one third of all PEM are of amelanotic type, a fact that makes the endoscopic diagnosis almost impossible. In the majority of cases (as in our case) distant metastases can be detected.

Histological diagnosis presents a many difficulties. In many cases the initial diagnosis is of esophageal carcinoma. Poor response to medical treatment is the main cause leading to revision of the initial histological diagnosis. Differential histologic diagnosis includes lymphoma, undifferentiated adenocarcinoma and sarcoma. Quite often histological differentiation from esophageal squamous carcinoma is difficult[4]. Clinicians must bear in mind the possibility of anthracosis, a situation in which histiocytes are filled with an abundance of a black material.[102]

PEM becomes positive for specific immunohistochemical staining specific for malignant melanomas. A large number of antigens (melanoma-associated antigens-MAGEs) have been described and divided into two subgroups. Subgroup I consists of antigens expressed only on malignant tumor cells, or on stem cells the so-called cancer/testis antigens.[103]

Various proteins or peptides have been used in clinical studies in the form of immunotherapy offering quite promising results. It seems that many of these substances (family of MAGE) play a significant pathophysiological role during embryogenesis, genesis of stem cells, apoptosis etc. This group plays also an important role in the process of immunosurveillance of some tumors. In our case the correct diagnosis was based on the positivity of the tumor on the special immunohistochemical staining.

Endoscopic ultrasonography and fine needle aspiration help significantly in making the correct diagnosis.[74]

There is no clear therapeutic guidance at the moment, probably because of the lack of the existence of a large series of patients. In early cases esophagectomy is the therapeutic procedure of choice. In such cases five-year survival exceeds 35%.[7]

Chemotherapy offers no satisfactory therapeutic results. Some people apply postsurgical chemotherapy with dacarbazine, nimustine & vincristine (5 courses)[90] although the results are not satisfactory. Others consider chemotherapy as completely unsatisfactory and they do not recommend it.[8] In our case chemotherapy offered no benefit, despite the fact that it was applied early after diagnosis.

Palliative radiotherapy generally offers no significant benefit. However, postsurgical radiotherapy using heavy ions has currently been tried aiming to preserve the surrounding healthy tissues.[88]

Endoscopic stenting can be tried in unoperable cases.[92,93] Placement of a stent does not exclude the concurrent use of radiotherapy.[92]

Endoscopic injection of interferon-beta into the tumor in conjunction with systemic chemotherapy[89] and endoscopic tumor destruction in conjunction with interferon are quite interesting.[91] Both therapeutic modalities produced significantly increased survival rates.

Survival of patients with PEM is disappointing. Mean survival rate after diagnosis does not exceed the limit of 20 months.[81] However better survival rate could be anticipated in the group of patients operated on for PEM.

In conclusion, amelanotic malignant esophageal melanoma is a rare neoplasm with dismal prognosis. Modern histochemistry significantly facilitates the correct diagnosis, especially in cases of amelanotic malignant esophageal melanoma.

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