Gingival Metastasis as First Sign of Multiorgan Dissemination of Epithelioid Malignant Mesothelioma

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Introduction: Metastatic malignant mesothelioma to the oral cavity is extremely rare. They are more common in the jaw bones than the soft tissue. Occurrence of the malignant disease typically carries an average survival rate of 9–12 months

Methods: Thirteen patients underwent neoadjuvant chemotherapy and radical pleurectomy decortication, followed by radiotherapy from August 2012 to September 2013. Patients were followed up with computed tomography of the chest and the abdomen every 3 months. All patients were followed up until February 2014.

Results: In January 2014, 11 patients were still alive with a median survival of 11 months, eight patients developed a recurrence and two patients died at 8 and 9 months after surgery. After 1 year from macroscopic radical pleurectomy decortication, a 68-year-old man suffered from gingival mass turned out to be a metastatic deposit of biphasic malignant mesothelioma as first sign of multiorgan recurrence. The patient underwent chemotherapy and local radiotherapy in the oral cavity.

Conclusions: This case points out the relevance of biopsy to all new growing lesions, even in uncommon anatomical sites, whenever a history of mesothelioma is on record.

Key Words: Malignant pleural mesothelioma, Epithelioid histology, Sarcomatoid histology, Pleurectomy/decortication, Gingival metastasis

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Malignant pleural mesothelioma (MPM) is a rare tumor with different histological patterns: epitheliod (60%), sarcomatoid (10–20%), and biphasic (20–30%). MPM often spreads locally to pericardium, diaphragm, and chest wall. Distant metastases are very rare, and the oral cavity metastases are exceedingly rare. The prognosis of MPM is poor with a median survival ranging from 9 to 12 months.[1,2] We present a patient with a history of epithelioid malignant mesotelioma treated by neoadjuvant chemotherapy and pleurectomy decortication, who developed subsequently gingival recurrence as the first sign of multiorgan relapse.

PATIENTS AND METHODS

Thirteen patients underwent neoadjuvant chemotherapy with cisplatin and pemetrexed and radical pleurectomy decortication, followed by radiotherapy on the wound site for malignant pleural mesothelioma from August 2012 to September 2013. Extrapleural dissection from the apex to the diaphragm was performed and decortication was also performed where the visceral pleura was macroscopically involved. Diaphragm was resected only in case on muscle infiltration (n = 3). Macroscopic radical resection was achieved in 10 patients. Patients were followed up with computed tomography (CT) of the chest and the abdomen every 3 months, in case of evidence of local recurrence integrated CT and positron emission tomography (PET/CT) and a biopsy were performed to confirm the recurrence before starting a second line chemotherapy. All patients were followed up until February 2014.

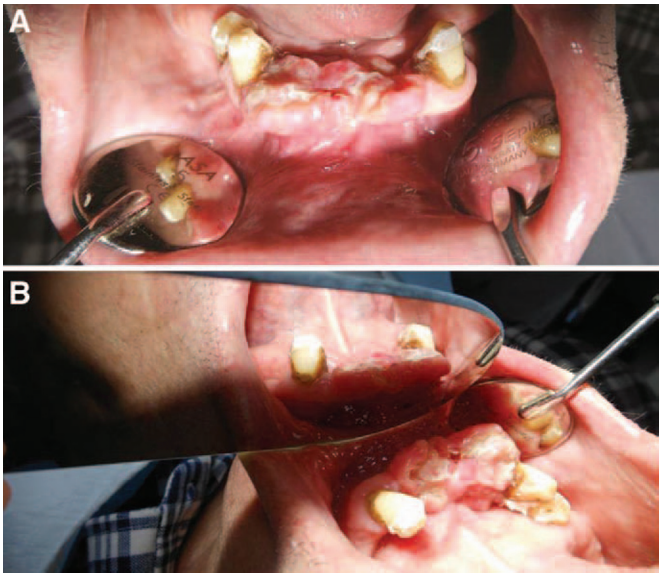

FIGURE 1. Gengival metastasis with erosion of the bone and mucosa.

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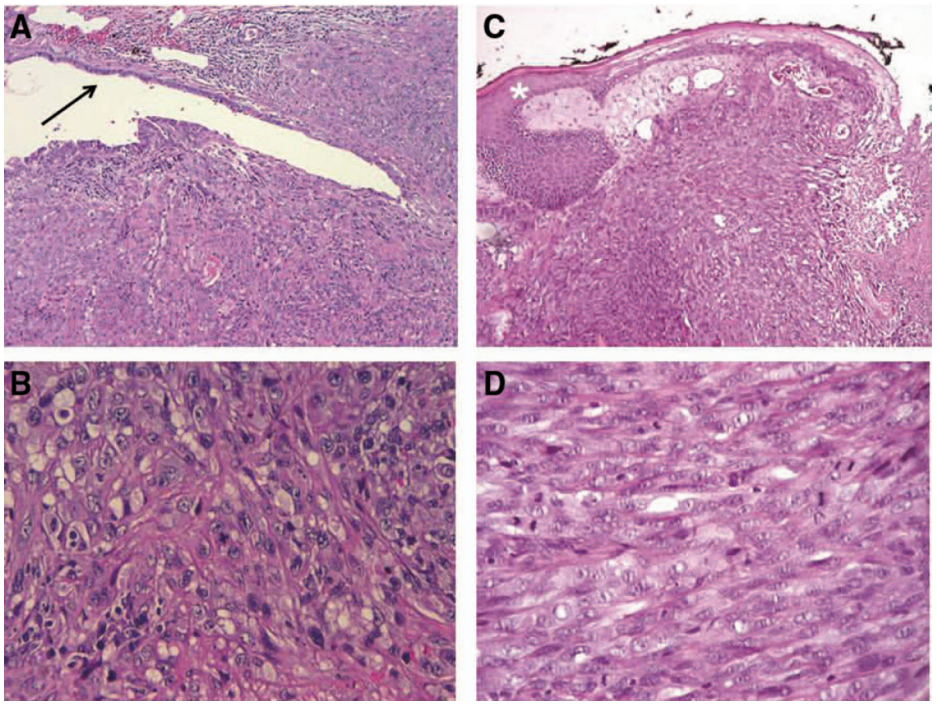

FIGURE 2. A-B, Epithelial mesothelioma infiltrating the visceral pleura and lung parenchyma underneath, the arrow showed the bronchial epithelium; *C-D*, sarcomatoid mesothelioma ulcerating the gingival mucosa (*).

RESULTS

At the last follow-up in January 2014, 11 patients were still alive with a median survival of 11 months (range 6–17 months), two patients died at 8 and 9 months after surgery for local recurrence. Five patients did not show any local or distant recurrence, seven patients showed local recurrence in the pleural cavity and only one patient presented with distant metastasis at 12 months from surgery.

A 68-year-old patient was referred from his private dentist with a painless growth of the attached gingival in the buccal region of teeth 42, 41, 31, 32 (Fig. 1). This lesion had been present for 4 weeks and recurred after a local excision 2 weeks later. The lesion eroded the mandibular bone anteriorly.

Histological examination showed a biphasic malignant mesothelioma with pleomorphic appearance, which exhibited immunoreactivity for mesothelial markers (WT1 and calretinin), lack of carcinoma markers (claudin-4 and BerEp-4), and a Ki-67 labeling index of 95%. The metastatic tumor strongly differed from the one documented in the pleura that was epitheliod in appearance and showed Ki-67 labeling index of 60% (Fig. 2).

One year before, this patient underwent neoadjuvant chemotherapy with cisplatin and pemetrexed, which resulted in a partial response after four cycles. Subsequently, the patient underwent pleurectomy decortication with macroscopic radical resection. The patient recovered well from the operation with no postoperative complications. Local radiotherapy to the site of the chest drainage was also performed to reduce the risk of local relapse.

Orthopantomogram of the lower jaw revealed erosion of the bony architecture. PET/CT confirmed local recurrence in the left side hemothorax nearly the thoracic incision with distant recurrence in adrenal glands, and mandibular region (Fig. 3). At the physical examination a right mandibular lymphadenopathy and a solid nodule in the left hemithorax were also present.

DISCUSSION

MPM is an aggressive tumor with a poor prognosis, although multimodality treatment could improve survival. MPM frequently recurred locally in the chest or in the abdomen. Distant metastases of MPM are uncommon, with the oral cavity and jaws, especially gingival mucosa, being involved in 1% of all metastases. Adrenal gland metastases from mesothelioma are exceedingly rare. A literature review showed only 11 case of metastatic MPM to the oral cavity, and only four cases to the gingival mucosa more frequent in men after 60s.[3–6] These oral lesions often show clinical characteristics similar to hyperplastic reactive lesions or primary oral squamous cell carcinoma.

In a series of 171 cases of malignant pleural mesothelioma published by Falconieri, at autopsy, distant metastases were found in 54% of patients, the most often involved organs were the liver, the adrenals and the kidney, metastase to the pancreas, stomach, bone, and brain were dected in less than 6% of patients, there was no evidence on metastasis in the oral cavity.[7] This is the first documented case with gingival metastases as the first sign of relapse and simultaneous extrathoracic multiorgan dissemination.

Our case showed also a change in the histopathological appearance with pleomorphic and biphasic features, and a shift of Ki-67 labeling index from 60% in the primary pleural lesion to 95% in the gingival metastasis (Fig. 3). Probably, chemotherapy, and operation selected a sarcomatoid subtype, which has hematogenously metastatized like sarcomas. Hashimoto et al. suggested that hematopoietic areas in the mandible favor early deposition of tumor cells.[8,9]

