Jaw angiosarcoma
First case, with massive intraosseous localization, described in Italian literature

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Angiosarcoma (AS) is a rare non-epithelial malignant neoplasm arising from neoplastic vascular degeneration of endothelial cells. It usually occurs in soft tissue and skin. The incidence, according to American authors, is 1% of all soft tissue sarcomas. About 50% of AS is localized in head and neck region (scalp and face skin) and represents less than 1% of all malignancies of this district; the primitive intra-oral localization is rare, even rarer intraosseous development of AS in jaw bones.

The Authors report a case of a mandibular intraosseous angiosarcoma with different peculiarities: the rarity of the location and mode of occurrence; in addition they have focused on clinical-histopathological and immunohistochemical characteristics.

KEY WORDS: Angiosarcoma, Jaws Introduction, Oral cavity

The case of intraosseous angiosarcoma of the mandible presented by the authors, first described in Italian literature, presents a double feature: the rarity of the location and mode of occurrence. The authors have focused also on the clinical, pathological and immunohistochemical characteristics of the tumor.

Case report
The patient MM, aged 49, was admitted to the UO Maxillofacial Surgery of the «Magna Graecia» University of Catanzaro in March 2011 for the presence of an expansive vegetating lesion of the entire mandibular body in alveolar region 35-38, previously performed within an avulsion of 37 in February of same year. The patient reported a massive bleeding following a dental extraction, which forced him to immediate admission to the nearest emergency center, where it was carried out for an emergency treatment with blood transfusion (three units of blood) and compressive sutures. Resigned in the following days due to increased volume of the lesion, occurrence changes in sensitivity (hypoesthesia) of lips (bottom left) and by the spontaneous bleeding episodes, the patient performed CT-DentalScan which showed large osteolytic lesion interesting to the whole left mandibular region (31 to 38), with erosion of vestibular cortical at the two premolars and molars (region 34-35). The patient, admitted to our unit, also reported...
other concurrent systemic diseases (paroxysmal atrial fibrillation, hypertensive heart disease, diabetes mellitus type II, grade I obesity, hypercholesterolemia, hypothyroidism) in drug treatment with cardiodinamic and metabolic balance very precarious. Locoregional and physical examination showed facial asymmetry due to the presence of swelling in the left hemimandible region. Inspection of oral cavity showed us a lesion of about 3x2, 5x1, 5 cm, corresponding to the premolar-molar area with an elastic consistency, easily bleeding, bad defined margins, light red with bluish patches on the surface and disappearance of the vestibular fornix (Fig. 1). In correspondence with the previous avulsion, and more precisely in reg.35-38, it showed a vegetans lesion, ulcerated and easily bleeding. On neck palpation we found an increase of cervical lymph node volume of level I and II (left side) apparently unharmed other organs and systems explored. Subjected to instrumental tests (neck and SAT ultrasound, OPT, Dental-scan, head and neck CT scan), were shown the involvement of soft tissues at the site of erosion of the cortical left mandibular region and some lymph nodes in the submandibular area with no other lymphadenopathy (Figg. 2, 3, 4). The biopsy report gave as a “malignant mesenchymal tumor type (suspected angiosarcoma)” and, therefore, was a planned surgery-chemotherapy. The advice radiotherapy excluded the radiation treatment.

After stabilizing the patient, hemodynamically, for his other disease he was submitted to surgery. The surgical procedure in the first phase involved the prior ligation of external carotid artery at its origin and therefore the ostectomy left hemimandibolar section from symphysis to condylar base, with removal of paralysional lymph nodes (levels I-II). The minus bone was reconstructed with a metallic endoprosthesis of titanium (picture). Reconstruction with revascularized free flaps (fibula) has not been used and for concomitant peripheral vascular disease and for the patient decision, knowing the risks that its complex pathology of systemic and peripheral disease could result in the immediate future.

Histological examination showed a vascular proliferation with florid complex anastomosed and short intraluminal papillary formations, limits are poorly defined, infiltrative growth aspects, the cells showed mild atypia and a low mitotic activity; and the overlying oral mucosa
appared to us ulcerated with the presence of granulation tissue (Figg. 9-10). Immunohistochemistry gave negative for epithelial markers (cytokeratin-clone AE1/AE3-, p63) and positivity for vascular markers (CD31), confirming the diagnosis of low-grade angiosarcoma (Table I). There were no signs of cancer in the lymph nodes removed. The patient was discharged on the tenth day in good clinical and surgical conditions. The inspections took place on a monthly basis and he is still under control. Two months after surgery (first instrumental control) with ultrasound, head and neck CT scan and total body CT scan showed no signs of local recurrence or metastatic regions in the areas examined (Figg. 11, 12). Currently the patient is undergoing chemotherapy.
Discussion

Sarcomas are a heterogeneous group of malignancies arising from malignant degeneration of cells originated from embryonic mesodermal sheet. Represents only 1% of all the malignant neoplastic diseases with more than 50 different subtypes, which are derivated from different structures as bone, cartilage, muscle (smooth or striated), skin, fat, synovial tissue, blood vessels (blood or lymph), nervous tissue, etc. which leads to a great variety and potential histopathologic ubiquity anatomy of onset. Risk factors for the onset of sarcomas are a previous radiation therapy, exposure to certain chemicals such as vinyl chloride and arsenic, chronic lymphedema, bone infarcts, some syndromes (S. Gardner, S. Li -Fraumeni syndrome, tuberous sclerosis, hereditary retinoblastoma, Neurofibromatosis Type 1), although most cases are unable to identify a unique determining cause. The most relevant prognostic factor for sarcomas is, without doubt, the histological grading; the first grading proposed grading was done in 1939 by Broders (for the fibrosarcoma); Russell in 1977 gave an important contribution in the drafting of TNM sarcomas with a large study of over 1000 cas-
es 10. There are three common types of systems used for grading sarcomas (NWT, NCI, FNCLCC) ranging from 2 to 4 classes of grading. NWT: a 2-degrees (high and low) easy for surgery, but with an ambiguous statement in respect of intermediate grading type of sarcomas; NCI system assigns a grade from 1 to 3, it is considered the best approach for predictability response to therapy and survival rate; the FNCLCC system presents 4 degrees, but for most sarcomas, this system does not add anything more to NCI for the minimum difference between grades 1 and 2.

The main criteria used for classifying the various grading systems, and variously estimated between them, are the histologic type, cellularity, the mitotic index and tumor necrosis, depth of tumor site. In the classification of sarcomas, defined as “generally high-grade” will include: synovial sarcoma, angiosarcoma, rhabdomyosarcoma, Ewing sarcoma, malignant fibrous histiocytoma, osteosarcoma extraosseous, and in those defined as “generally low-grade” myxoid liposarcoma, well-differentiated liposarcoma, dermatofibroma protuberans, desmoid sarcoma, other sarcomas such as fibrosarcoma, leiomyosarcoma, often need a more careful evaluation of the grading in relation to this case. The frequency of occurrence for site we can highlight sarcomas is higher against the extremities (50%), the trunk and peritoneum (40%), however is extremely lower than incidence in head and neck region (10%) 7,12, demonstrating a high range differentiation: smooth or striated muscle (leiomyosarcoma, rhabdomyosarcoma), adipocyte (liposarcoma), cartilage (chondrosarcoma), bone (osteosarcoma), fibroblast (dermatofibrosarcoma), endothelial (angiosarcoma), etc.

From all of those Sarcomas who have a relative preference for the district are the head and neck rhabdomyosarcoma in children, cutaneous angiosarcoma and sinusal hemangioendothymomas (the latter is specific for this anatomical region) The angiosarcoma (AS) is a rare non-epithelial malignant neoplasm arising from neoplastic vascular endothelial (angiosarcoma), angiosarcoma and lymphangiosarcoma, they are different but prognosis and therapeutic approach are the same, and therefore often included in a single denomination of angiosarcoma 1-3,13.

It can occur at any anatomical site, typical is the skin and abdominal viscera. According to American authors, the angiosarcomas constitute only 1% of all soft tissue sarcomas with a prevalence of 2-3 cases every 100000 people. Most patients with this disease died of lung metastasis or local extension. About 50% of all AS is localized in head and neck region at the level of scalp and face skin 14, and represents less than 1% of all malignancies of this district 8,15,16, but with a high morbidity and mortality 17-19. The oral cavity in angiosarcomas comprise less than 5% of the total cases reported in literature for this this neoplasm (19).

The first described case in 1923 by HJ Banks-Devis was an hemorrhagic angiosarcoma of the maxilla 20. Sites of involvement in oral cavity are lips, tongue, mouth floor, cheeks palate and mandible 18. Intraosseous development of AS is occasionally rare in humans and animals is allowed (though not uncommon in dogs) therefore the sites of greatest bone involvement are the femur and tibia, followed by the pelvis, spine and upper limb bones.

In head and neck primary intraosseous localization is more exceptional (the first case describ was in 1948 with involvement of the petrous portion of temporal bone) 22 and even more rare is in intraosseus maxillary bone 2,3,14,18,19,22,23, and among these those with mandibular localization. All ages, sex and nationality may be affected by this disease even though the highest incidence occurs around the fifth decade of life. The etiology of this disease remains unknown although several hypotheses have been examined 8,24. Clinically, the intraoral angiosarcomas (of soft tissue) are usually described as a circular or oval bluish nodules, often ulcerated surface, not very mobile on superficial palpation, lazy but capable of spontaneous bleeding as in the case report described 3. In fact, the lesion presented with a bluish-red knots of the hemi-mandibular body with extension to the left buccal mucosa, bleeding for easy opening and closing mouth movements.

Often, their recognition is difficult, both entering the differential diagnosis with other vascular neoplasms such as malignant epithelioid hemangoendothelioma, Kaposi's sarcoma, malignant melanoma with benign processes including inflammatory disease 25. For the diagnosis of angiosarcoma remains fundamental histopathological examination, the tumor cells are often positive for CD31, CD34 and vWF (it is the most specific vascular markers but is positive only in the minority of angiosarcomas), while CD31 is positive in more than 90% of angiosarcomas (relatively high specificity and sensitivity), especially for the poorly differentiated forms, where these can not be present, additional markers are needed, such as nuclear markers Fli-126.

The treatment of choice for this type of disease is a wide surgical resection of the tumor 2,16,24, with or without chemotherapy and / or radiotherapy 2,27. Elective lymph node dissection is not indicated except in presence of a clinical evident involvement 2. In the case presented by the authors the lateral-cervical lymph node exision in level I was performed for the presence of unstructured submandibular lymph nodes ipsilateral to the lesion, even by an intraoperative clinical evidence of lymph nodes impairment. Our surgical behavior is also derived from the consideration that the lymph node metastasis indeed occurs in 3% of cases of localization in bone and 10% instead of the localization in soft tissue angiosarcomas for head and neck district distant metastases (28% of cases) involves, in order of frequency the lung, bones, CNS, and liver 5.
Il caso clinico descritto dagli Autori è da ritenersi particolare per essere, da un punto di vista patogenetico, a partenza endo-ossea in un segmento scheletrico della testa-collo ancora più particolare, cioè la mandibola. Lo sviluppo intraosseo degli AS è eccezionalmente raro sia negli umani che negli animali domestici (anche se non infrequente nel cane).

Come nel nostro caso, per la diagnosi di angiosarcoma rimane fondamentale l’esame istopatologico. Il trattamento di elezione per questo tipo di patologie è l’ampia resezione chirurgica della neoplasia, associata o meno a chemioterapia e/o radioterapia. La dissezione elettiva dei linfonodi non è indicata, se non in presenza di coinvolgimento clinicamente evidente. La metastatizzazione linfonodale infatti avviene nel 3% dei casi di localizzazione ossea ed invece nel 10% delle localizzazioni dei tessuti molli.

References


Commento e Commentary

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L’angiosarcoma intraosseo mandibolare rappresenta una localizzazione di estrema rarità, per cui riteniamo doverosa la comunicazione di tale evenienza alla comunità scientifica. Nelle classificazioni delle lesioni osteolitiche primarie della mandibola l’angiosarcoma intraosseo non viene quasi mai citato, esponendo lo specialista a possibili errori diagnostici e di trattamento. Anche un accertamento fondamentale come l’esame bioptico può presentare dei rischi di emorragie difficilmente controllabili. Questo articolo offre alcuni interessanti spunti per il dibattito interdisciplinare sulle patologie neoplastiche della mandibola.

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Intraosseus mandibular angiosarcoma is an exceptional evenience; therefore it deserve a mention to the scientific community. Seldom is intraosseus mandibular angiosarcoma citated within osteitic mandibular lesions causing a lack of knowledge that may expose specialists to a misunderstanding of the proper diagnosis and treatment. In those cases, even a biopsy examination may provoke serious bleeding.

This paper provides a starting point for discussion about the management of this disease and represents an in-depth contribution on the head and neck pathology. In particular, about the possibility of the selective embolization of the neoplasm after arteriographic examination in order to handle hemorrhagic risk. Moreover, great attention has been focused on the proper management of the oncologic resection and reconstruction; in fact prognostic outcomes and quality of remaining life should be always considered, even if microsurgical reconstruction appear to have become routine.