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CASE STUDY

Ewing's Sarcoma: A Rarity in Sinonasal Region☆

Sarcoma de Ewing: una rareza en la región nasosinusal

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Case Report

A 54-year-old man was presented in ENT to consult 2 months of progressive nasal obstruction and to epistaxis accompanied by progressive periorbitary and cheek swelling. He was a diabetic and hypertensive patient with a poor general state, submitted to a radical prostatectomy in 2007, followed by chemotherapy (QT) and radiotherapy (RT) to treat a prostate carcinoma with bone, liver and lung metastases.

Rhinoscopy revealed a crispy neoformation that obstructed the left nasal cavity, without nasopharynx extension. Patient had a left periorbital and cheek swelling and no palpable cervical lymphadenopathy.

The paranasal sinuses CT scan showed a large soft tissue density lesion completely filling the left maxillary sinus and nasal cavity, without bone erosions (Fig. 1). There were present cerebral metastases.

The histopathology revealed at microscopy fragments of nasal mucosa infiltrated by neoplasm composed of small cells with scanty cytoplasm, hyperchromatic and rounded nuclei, arranged in towel and sometimes in Homer-Wright rosettes type, with numerous mitotic figures. Immunohistochemistry was positive for CD99, vimentina, CAM 5.2 and chromogranin (Fig. 2). Synaptophysin, neuron specific enolase (NSE), neurofilament protein, S100 protein, GFAP, CK7, LCA and PSA were negative. The anatamopathological result was compatible with a soft tissue sinonasal Ewing's sarcoma.

The patient underwent medical treatment with topic and systemic corticotherapy and systemic antibiotic. He was proposed for palliative care due to its poor general condition, advanced tumor stage and presence of a metastatic prostate tumor. He died three months after diagnosis.

Discussion

Ewing's sarcoma (ES) is a highly malignant small round cell tumor of mesenchymal origin.[1,2] This was first described by Ewing in 1921.[2,3] Ewings sarcoma (ES)/primitive neuroectodermal tumor (PNET) are closely related family of small round cell sarcomas with varying degrees of neuroectodermal differentiation.[1–3] PNETs show neuroectodermal differentiation, whereas ES lack them as assessed by light microscopy, immunohistochemistry, and electron microscopy.[3]

These tumors can arise from bone (skeletal type) or occasionally from soft tissues (extra skeletal type).[3] The skeletal type is more frequent and occurs in long bones of the extremities.[2] The extra skeletal form has the same histological, immunohistochemical and molecular features of skeletal ES and affects soft tissue of lower limbs, paravertebral tissues, chest wall, retroperitoneum and rare in head and neck region (2%–7%).[2,3] Mandible and maxilla are the most common sites affected in the head and neck region and involvement of the paranasal sinuses is very rare.[1–3] Few cases of extra skeletal ES have been published in world literature.[2]

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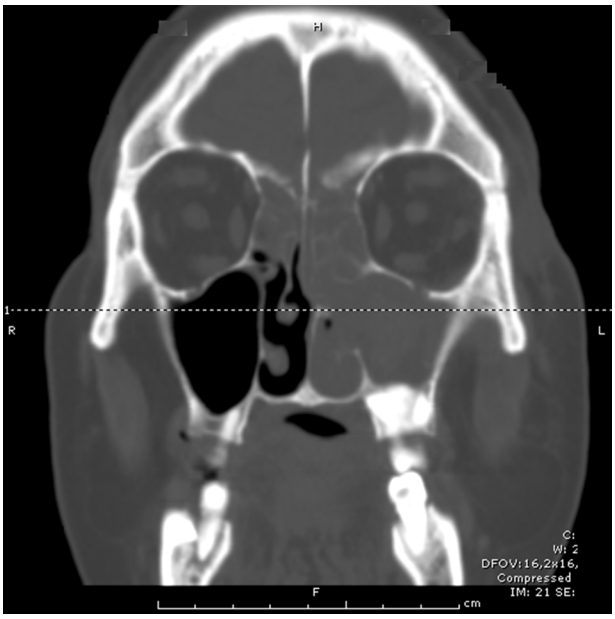

Figure 1 SPN CT image of the left Ewing sarcoma (coronal view).

It usually affects individuals less than 20 years old, with a male preponderance.[2,3] Although the exact etiology remains unknown, majority has a specific gene sequence *t*(11:22)(q24:q12) i.e., fusion between the 5′ end of the EWS gene from chromosome band 22q12 with the 3′ portion of the 11q24 FLI1 gene, a member of the ETS family of transcription factors.[1–4] This EWS/ETS fusion protein blocks the differentiation of pluripotent marrow stromal cells. Rest of the 10%–15% cases have *t*(21;22)(q22;q12) fusing EWS to a closely related ETS gene, ERG from chromosome band 21q22. In less than 1% of cases, *t*(7;22), *t*(17;22), *t*(2;22) and inv(22) have been found that give rise to fusions between EWS and the ETS genes like ETV1, E1AF, FEV, and ZSG, respectively. Mutations associated with P53 or P16/p14 ARF have high aggressive behavior and poor hemotherapeutic response.[3]

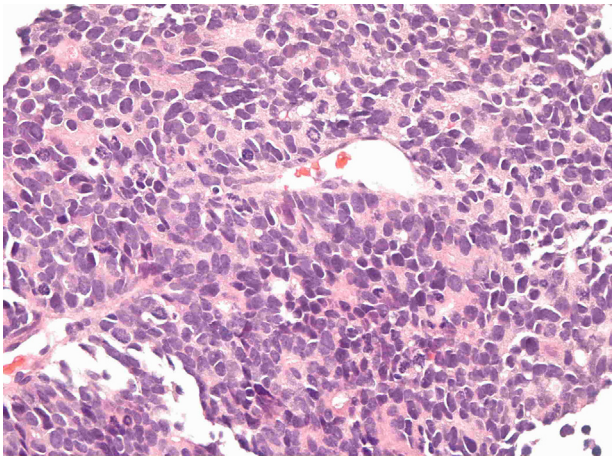

Figure 2 Ewing's sarcoma (light microscopy, hematoxylin and eosin).

The clinic depends on the location of the tumor. Sinonasal tumors only provide sinus symptoms such as nasal obstruction and epistaxis, in very advanced stages, thus delaying its diagnostic.[5]

Imaging exams, particularly computerized tomography (CT) are important for the diagnosis, however ES images are not specific. In this patient, the CT scan pointed more to a benign lesion with associated sinusitis than a malignant lesion, because there were no bone erosions suggestive of malignancy.

The definitive diagnosis is made by histology of the lesion.[3,5] At microscopy the ES are tumors composed of small round cells, with round nuclei, containing fine chromatin, scanty clear or eosinophilic cytoplasm with poorly defined limits, containing PAS positive intracytoplasmic glycogen granules.[3,5] The essential diagnostic test is for the specific immunocytochemical CD99/013 marker. This is a surface protein detected by AC013 although is not specific for ES/PNET is found in almost all ES and PNETs and combination with other markers like FLI1, HNK1 and CAV1 gives more accurate diagnosis and helps to avoid erroneous diagnosis. This test has a sensitivity of 98%.[1]

The differential diagnosis involves a wide variety of small round cell tumors like poorly differentiated neoplasms of the sinonasal region as olfactory neuroblastoma, lymphoma, undifferentiated carcinoma, sinonasal melanoma, acute leukemia, embryonal rhabdomyosarcoma, sinus mesenchymal chondrosarcoma, osteosarcoma small cell and small neuroendocrine cell carcinoma.[2,3] In Table 1 are listed some the characteristics of these tumors.

In our case synaptophysin, neuron specific enolase (NSE), neurofilament protein, S100 protein, GFAP, CK7, LCA and PSA were negative, ruling out the chances of small cell carcinoma, poorly differentiated sinonasal carcinoma, olfactory neuroblastoma or lymphoma.

ES metastasizes in about 18% of cases, most often to the lungs (57%), bone (34%), brain and spinal cord, and rarely to the ganglia.[3] In this case, the concomitant presence of another metastatic prostate tumor did not allowed to distinguish the origin of metastases.

The prognosis depends on the age of the patient, anatomic location, tumor size and stage, being better in younger patients, with axial disease, small tumors (<8 cm diameter), with volume less than 100 ml and absence of metastasis at diagnosis. Bone metastases have better prognosis than lung metastases.[2,3,5] The 5-year survival of patients with metastases at diagnosis is around 22% versus 55% in patients without metastases.[2,3,5]

Therapeutic options are surgery, chemotherapy (QT) and/or radiotherapy (RT).[5] Local control of the tumor with surgery and/or RT is subsequently followed by metastatic treatment with QT.[3,5] The most effective treatment for these tumors is surgery followed by QT/RT. In cases where surgery is not possible due to the extension of the tumor or patient's co-morbidities, the QT/RT is a valid option.[3,5] Combination chemotherapy (vincristine, doxorubicin, cyclophosphamide and actinomycin) is more effective than monotherapy.[5,6] RT is reserved for patients in whom surgical excision was incomplete or not held because of the morbidity. Local control is achieved in 85% of cases with a 5-year survival rate of 55%–60%.[2]