Uncommon pleural effusion: pleuropulmonary metastasis from primitive neuroectodermal tumor*

Derrame pleural incomum: metástase pleuropulmonar de tumor neuroectodérmico primitivo

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Abstract

Primitive neuroectodermal tumor is an invasive neoplasm with neuronal differentiation, which frequently results in metastasis in various organs. We report the case of a patient with primitive neuroectodermal tumor whose primary site was the axilla. The patient presented with metastases in the lung, pleura, bone, iliac muscle and bone marrow. We highlight the uncommon finding in the pleural fluid cytology.

Keywords: Neuroectodermal tumors, primitive; Neoplasm metastasis; Cytology; Pleural effusion.

Resumo

O tumor neuroectodérmico primitivo é uma neoplasia com diferenciação neural de comportamento invasivo que origina metástases para diversos órgãos. Relatamos um caso de tumor neuroectodérmico primitivo primário em axila com metástases para pulmão, pleura, osso, músculo ilíaco e medula óssea. Enfatizamos o achado incomum da análise citológica do líquido pleural.

Descritores: Tumores neuroectodérmicos primitivos; Metástase neoplásica; Citologia; Derrame pleural.

Introduction

Primitive neuroectodermal neoplasms originate from cells that migrate from the neural crest and are classified according to the degree of differentiation. Therefore, we denominate Ewing sarcoma as a tumor in which the cells are undifferentiated or as primitive neuroectodermal tumor (PNET) those with cells presenting neural differentiation. Histologically, those present as round blue cell tumors, and, from a cytogenetic point of view, those are characterized by presenting translocation t(11;22)(q24;q12) in 85% of the cases.[1]

Primitive neuroectodermal tumors with extraskeletal location are more commonly observed between 10 and 30 years of age, with equal incidence between genders, being rare before 5 and after 40 years of age. Most cases originate in deep soft tissues, particularly in the torso and preferably in the paravertebral region or lower limbs. Approximately 10% of these tumors originate in an identifiable nerve.[2]

It is an invasive neoplasm which can give origin to metastases in several organs (skeleton system, lung, pleura, bone marrow, central nervous system, sympathetic chain, adrenal glands and orbit). Five-year survival in patients with extraskeletal PNET does not exceed 20-30% at most facilities.[3]

In the present article, we report a case of primary PNET in the axilla with metastases to

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Table 1 - Immunohistochemical profile of the tumor cells.

Markers	Result
CD99	Positive
CD45	Negative
AE-1/AE-3	Negative
Chromogranin	Negative
Desmin	Negative
Myogenin	Negative
S-100 protein	Negative
TdT	Negative
Vimentin	Negative

CD99: monoclonal antibody which recognizes the MIC2 protein; CD45: leukocyte common antigen; AE1/AE3: cytokeratin 1 and 3; and TdT: terminal deoxynucleotides transferase.

lung, pleura, bone, iliac muscle and bone marrow, with emphasis in the uncommon finding of the cytological analysis of the pleural fluid.

Case report

A 26-year-old male patient, born in Rondônia, Brazil, sought treatment at our facility. He had a history of smoking but reported having had good health until the onset of a profile of loss of movement of the right upper limb and the appearance of a palpable mass in the right axilla. After four months of progressive worsening, the patient sought treatment in the emergency room.

At physical examination, the patient presented right arm and forearm muscle atrophy, with decreased strength and local sensitivity. A palpable hardened mass present in the area of the right axilla was submitted to biopsy and immunohistochemical analysis. Anatomopathological and immunohistochemical findings were consistent with PNET (Table 1).[4]

With this diagnosis, we initiated a chemotherapy regimen with vincristine, doxorubicin and cyclophosphamide for six months (6 cycles). There was reduction of the tumor mass. However, the patient persisted with loss of movements in the right upper limb and intense pain in the limb, and was submitted to right humeral interscapulo-thoracic resection. Palliative second-line chemotherapy regimen was resumed (topotecan and cyclophosphamide).

Eight months after the surgery, the patient presented local recurrence (right axilla) and metastasis to the lung. He evolved with progressive dyspnea and pain at the left coxofemoral joint. Physical and radiological (chest CT) examination evidenced voluminous right-

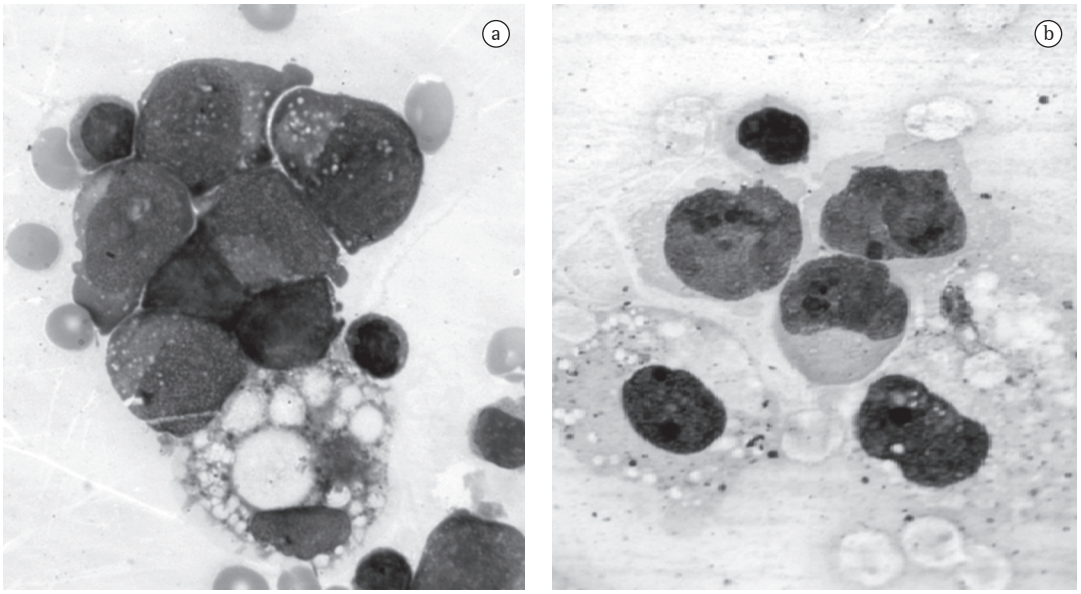

Figure 1 - Pleural fluid cytology. In A, neoplastic cells disposed in cohesive groups. Leishman staining, magnification ×1000. In B, neoplastic cells stained by the *silver staining nucleolar organizing regions* (AgNOR) technique, magnification ×1000.

sided pleural effusion, with numerous pleural nodules. The effusion was drained, and the pleural fluid analysis showed characteristics of exudate (proteins: 4.2 g/dL and lactate dehydrogenase: 2,456 UI/L)(Figure 1). The tomography study of the abdomen and pelvis showed tumor metastasis in bone and right iliac muscle. Bone marrow aspirate showed bone marrow infiltration. At this writing, the patient was still under treatment with palliative chemotherapy.

Discussion

PNET is an extremely aggressive tumor that affects principally the deep soft tissues. The differential diagnosis between the tumors of the childhood round cells and those of the adolescence includes Ewing's sarcoma, neuroblastoma, lymphomas, rhabdomyosarcoma and PNET. These subtypes are differentiated through immunohistochemical reactions, cytogenetic and molecular biology studies. The degree of neural differentiation in the PNET is generally subtle, and it is often detected only through immunohistochemistry. Those tumors frequently present positivity to neural markers, among those, neurospecific enolase, Leu-7 (CD57), synaptophysin, chromogranin and S-100 protein. The detection of positivity of those markers is more evident in case the tumor presents well-defined Homer-Wright or Flexner-Wintersteiner rosettes or an ultrastructural pattern of neural differentiation.

PNETs are generally positive for CD99 (sensitivity > 95%), although this marker is not specific and can also appear in lymphoblastic lymphoma, synovial sarcoma, some neuroendocrine carcinomas and, more rarely, in alveolar rhabdomyosarcoma.

In the present case, only CD99 was positive. However, the clinical status and the morphological and structural aspect of the tumor cells were fundamental for the diagnostic definition.

The patient reported in our study evolved to metastasis to the bone, iliac muscle, bone marrow, lung and pleura. Although pleural effusion is a relatively common radiological finding when the tumor is located in the chest wall (Askin tumor), we highlight the fact that the characteristics of the pleural fluid are rarely known, and the identification of neoplastic cells in the pleural fluid is uncommon.

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