CASO CLÍNICO

Hypertrophic osteoarthropathy associated to lymphoepithelioma of the nasopharynx: a case report

Osteoartropatia hipertrófica associada a linfoepitelioma de nasofaringe: relato de caso

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ABSTRACT

Malignant neoplasms of the nasopharynx are very rare and has two peaks of incidence: below the age of 30, and between the 4th and 5th decade of life. It is, however, uncommon after the 60 years of age. In rare cases, some patients may present, in the form of paraneoplastic syndrome, hypertrophic osteoarthropathy (HOA). In this case report, we describe a case of HOA from lymphoepithelioma of the nasopharynx in a 77-year-old male patient, representing an extremely unusual condition.

Keywords: Osteoarthropathy, Secondary Hypertrophic. Nasopharyngeal Neoplasms. Patients/Aged.

Introduction

Malignant neoplasms of the nasopharynx are very rare, representing 0.25% of all tumors. Histologically, the epithelial tumors of the nasopharynx account for 85% of cases, and according to the World Health Organization (WHO), lymphoepithelioma is classified as Type III - Undifferentiated carcinoma.[1] Lymphoepithelioma of the nasopharynx is more prevalent among males and has two peaks of incidence: below the age of 30, and between the 4th and 5th decade of life. It is, however, uncommon after the 60 years of age.[2] It presents few clinical manifestations from the beginning, with its most common initial symptom being the appearance of an asymptomatic neck mass.[1] In rare cases, some patients may present, in the form of paraneoplastic syndrome, Hypertrophic osteoarthropathy (HOA), characterized by digital clubbing, periostitis of long tubular bones, polyarthralgia and synovial effusion.[3] Considering the rarity of the occurrence of HOA from lymphoepithelioma of the nasopharynx, the objective of this paper is to present a case report whose condition is uncommon and discuss, by means of a literature review, such association.

Case report

77-years-old patient, male, born in Montes Claros, in northern Minas Gerais/ Brazil, diagnosed in May, 2009 with lymphoepithelioma of the nasophar-

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ynx after work-up for investigation of persistent stuffy nose and sore throat, with pathological examination and immunohistochemistry, staged as T4 N0 M0 at the moment of his admission. He began cancer treatment in Belo Horizonte/MG, with concomitant radiotherapy (16 sessions with 200 cGy a day) and chemotherapy (two weeks with cisplatin, 50 mg IV per week). He then presented grade III of mucositis, making it necessary to temporarily stop the treatment. During this period, the patient was transferred to Montes Claros/MG to pursue the proposed treatment, which was completed in September, 2009. Magnetic Resonance Imaging (MRI) of the Skull/Nasopharynx for response evaluation showed a significant reduction of the lesion in the parapharyngeal space. In April, 2010, new brain MRI showed a complete reduction of that same lesion. The patient was followed up for evaluation of disease control with a consultation every three months, presenting oligosymptomatic caracterized by radiation-induced xerostomia. In July, 2011, the patient began to experience loss of appetite, weight loss, frequent coughing and major discomfort in the lower limbs. Brain MRI was stable when compared to the previous one and Computer Tomography (CT) scan of the chest showed the appearance of nodules located in segments 3 and 6 of the right lung, suggesting secondary implants (Figure 1A, B). A bone scintigraphy was done and revealed heterogeneous images in both femurs and in the proximal half of the tibias, where we found a linear increase in the uptake of the topography of the cortical bone, consistent with secondary Osteartropatia Hypertrophic in both the femurs and the tibias (Figure 2). Biopsy of the suspicious lung lesions was conclusive for epithelial metastatic carcinoma, and the immunohistochemical through the expression of antibodies, such as HE, AE1/AE3 e p63 confirms the diagnosis of epithelial metastatic carcinoma (Figure 3).

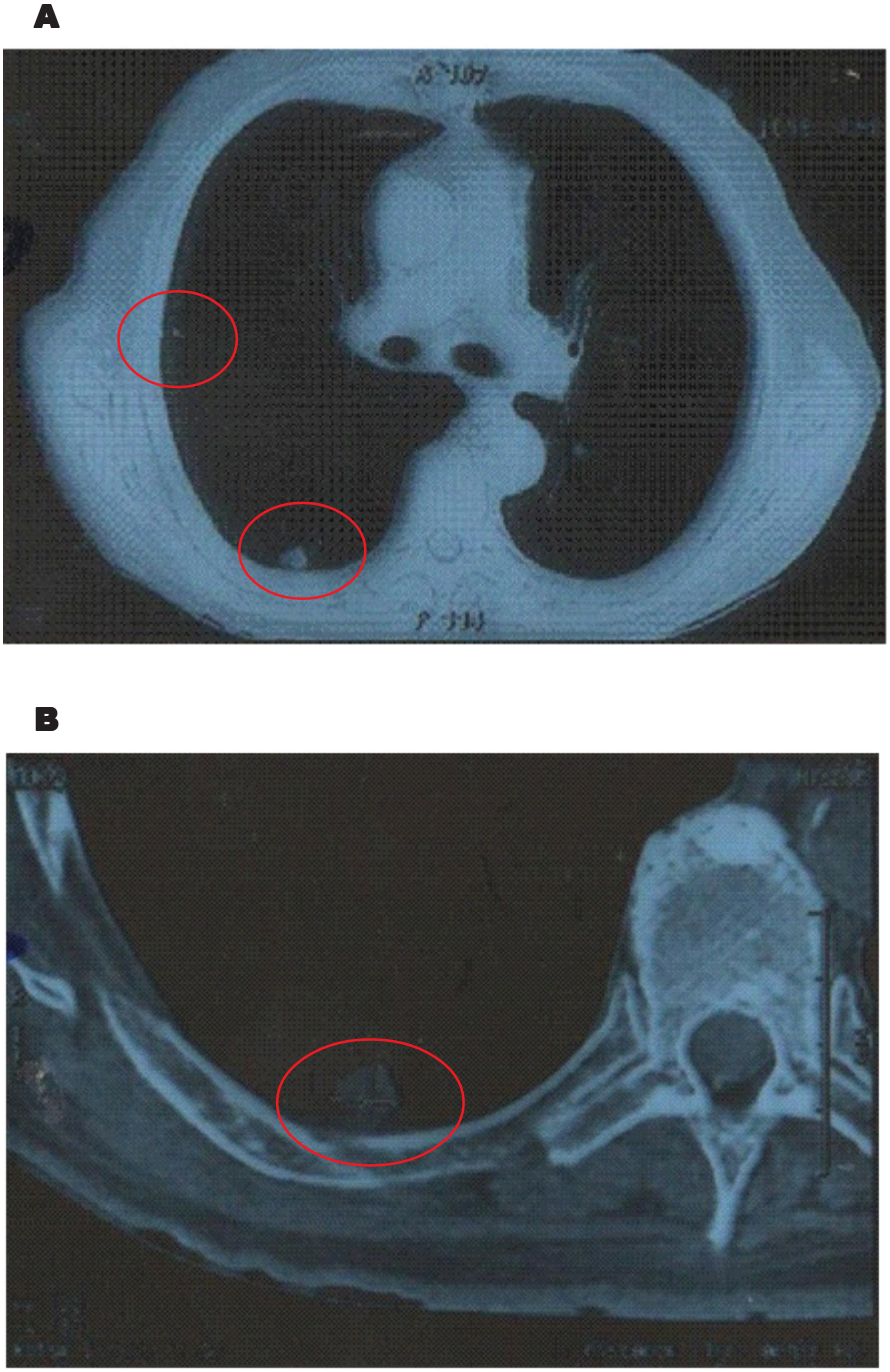

Figure 1 A, B: CT scan identified an nodules located in segments 3 and 6 of the right lung, suggesting secondary implants.

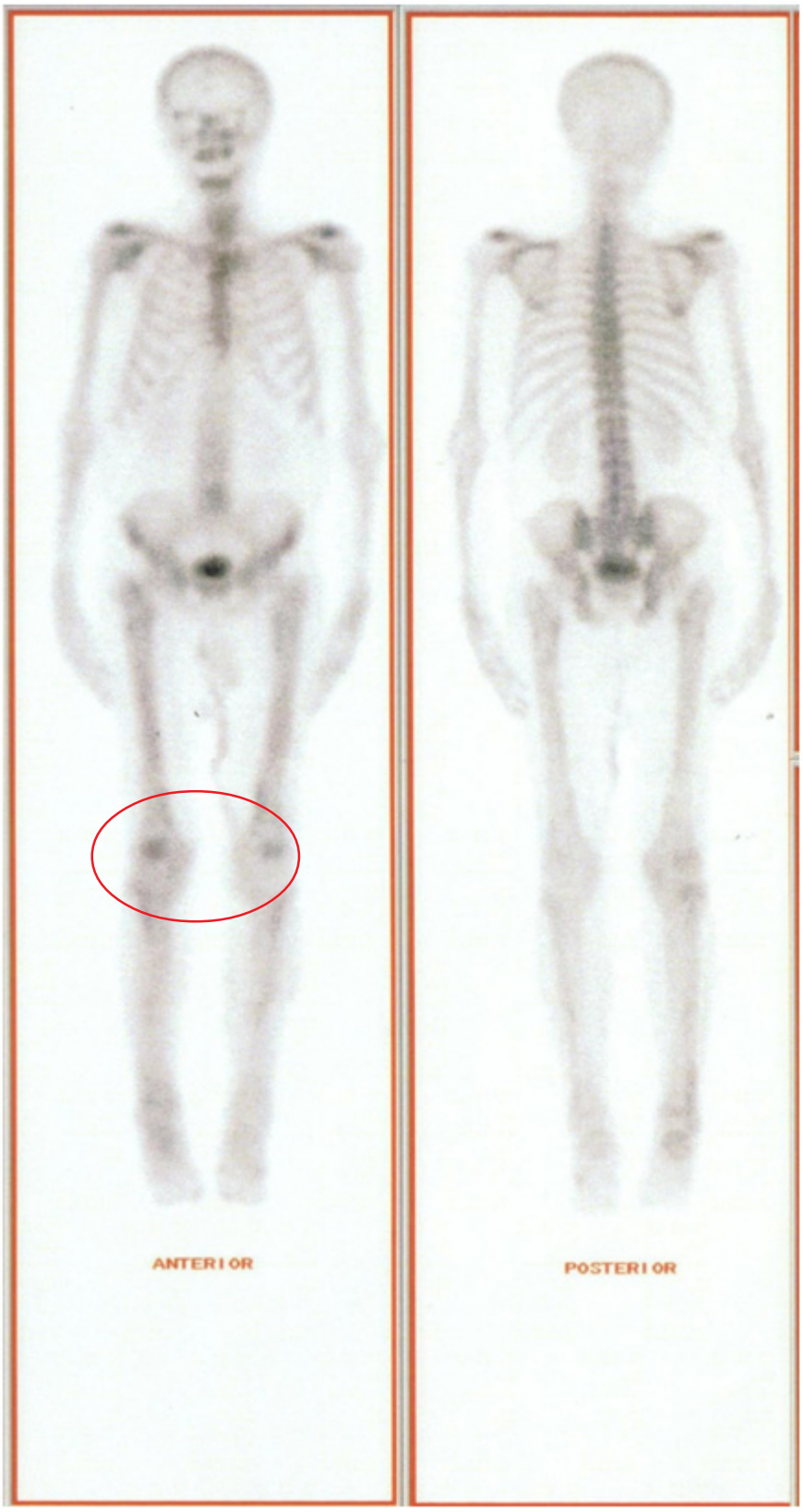

Figure 2: Bone scintigraphy scan showing intense bilateral symmetrical cortical uptake of Tc-99m MDP in tibias and femurs, consistent with hypertrophic osteoarthropathy.

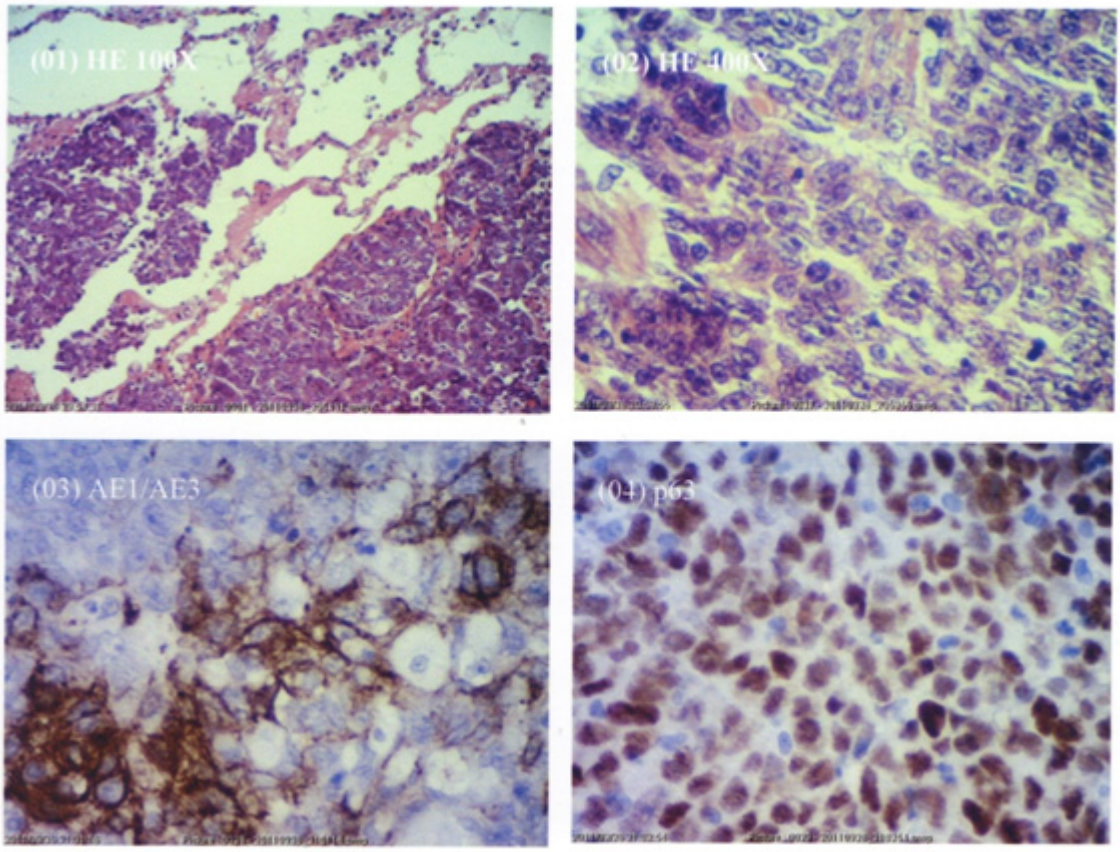

Figure 3: Immunohistochemical analysis showed positivety to HE, AE1/AE3 e p63 confirming the diagnosis of epithelial metastatic carcinoma.

Discussion

Malignant neoplasms of the nasopharynx are rare, amounting to 2% of the head and neck tumors and to 0.25% of all tumors.[1,4] They are more prevalent among males, in a 3:1 ratio when compared to females, and presents two peaks of incidence: young people under 30 years of age, and individuals between the 4th and 5th decade of life.[2] It suggests an association with genetic susceptibility, environmental factors and infection by the Epstein Barr virus (EBV).[4,5]

Epithelial tumors account for 85% of malignant tumors of the nasopharynx, and are divided by the World Health Organization (WHO) according to their differentiation and production of keratin, as: Type I - Carcinoma, Squamous Cell, Type II - Carcinoma nonkeratinized and Type III - undifferentiated carcinomas.[1,6] Type II and Type III have a positive serological profile for EBV, characterized by the detection of viral DNA and viral antigens in tumor cells and high antibody titer in patients affected by the tumor 1.

The lymphoepithelioma, classified as Type III, is considered a variant of the planocelular type, in which there is intense lymphoid infiltration in the fibrous stroma of the tumor, with a predominance of T cells compared to B cells.[1,5,6] This tumor has few clinical symptoms from the beginning, and patients' complaints are reported according to the location of the primary tumor, its size and growth speed. The most common early symptom is the appearance of an asymptomatic neck mass, in the corner of the lower jaw or at the tip of the mastoid. Other symptoms include nasal congestion, sore throat, epistaxis, facial pain and headache.[1,5]

At the moment of diagnosis, over 80% of the patients have lymph node involvement, a consequence of the poor anatomical barrier of the parapharyngeal space and communication of the lymphatic vessels to the midline of the nasopharynx.[1,4] In addition to the lymph nodes, it spreads to the lungs, mediastinum, bones and liver.[5]

Some patients may rarely present a paraneoplastic syndrome, Hypertrophic osteoarthropathy

(HOA), a condition characterized by digital clubbing, periostitis of long tubular bones, polyarthralgia and synovial effusion, most prominent in the large joints.[3,7,8] OAH can be classified in primary, when it's not associated with any medical condition; and secondary, which can be divided into pulmonary causes such as cystic fibrosis, primary or metastatic carcinoma, and non-lung, such as cyanotic congenital heart disease, liver cirrhosis, intestinal polyps, among other pathologies.[3,7]

Although the pathophysiology of HOA remains controversial, there are two different theories attempting to explain it.[7,8] The neurological theory, sustained by vagal nerve stimulation, is supported by the regression of the syndrome after vagotomy.[7,8,9] The humoral theory, proposed by some authors, is based on the presence of factors in the venous circulation, such as megakaryocytes, which are usually removed or fragmented by the lungs.[9,10] Based this theory, it is proposed that, in diseases with right-left shunts, such megakaryocytes are not fragmented and reach to circulation, affecting sites distal activating endothelial cells, and finally inducing digital clubbing.[8,11]

However, in a pulmonary vascular bed altered by some causative factor, such factors are not fragmented, which leads to the imprisonment of microthrombi in the vascular nail beds. In addition, megakaryocytes are capable of producing a growth factor derived from platelets, which explains the phenomena of tissue expansion, increased blood flow and the stimulation of the proliferation of fibroblasts.[8,11]

OAH caused by pulmonary metastases from extrathoracic malignancies is a rare condition.[12] In 1939, the first case of an association of carcinoma of the nasopharynx and OAH was reported, and since then, there are very few publications about this association.[13]

The development of HOA in patients with nasopharyngeal lymphoepithelioma may be the harbinger of metastatic spread to the chest, showing a progression of the disease.[7,14] For this, a differential diagnosis must be made between HOA and associated bone metastasis.[8,14,15] The most sensitive tool to distinguish these two pathologies is the bone scintigraphy, since the symmetrical and linear concentration of the radiotracer - "parallel tract sign" - in the projection of the cortex of long bones is typical of the HOA.[8,11,14]

Besides the treatment of nasopharyngeal lymphoepithelioma with chemotherapy and radiation therapy, some authors suggest vagotomy for the treatment of OAH.[7] But with a poor prognosis, most patients with nasopharyngeal lymphoepithelioma evolve to death.[1]

In summary, this case illustrates the association of HOA with lymphoepithelioma of the nasopharynx in a 77-year-old male patient, representing an extremely unusual condition. Future researches including the actual biology of the tumor of this association may contribute to ensuring more effective therapeutic conditions for it, since it still has a poor prognosis.

RESUMO

Neoplasias malignas de nasofaringe são muito raras e apresentam dois picos de incidência: antes dos 30 anos e entre a 4ª e 5ª década de vida. No entanto, é incomum após os 60 anos de idade. Em raros casos, alguns pacientes apresentam na forma de síndrome paraneoplásica a Osteoartropia Hipertrófica (OAH). Este relato de caso, nós descrevemos um caso de OAH associada a linfoepitelioma de nasofaringe em um paciente de 77 anos, representando um condição extremamente incomum.

Palavras-chave: Osteoartropatia Hipertrófica Secundária. Neoplasias Nasofaríngeas. Pacientes/Idoso.

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