Histiocytic Sarcoma of Nasal Cavity: A Case Report

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Received: 24 Apr. 2017; Accepted: 30 Apr. 2017

Abstract- Histiocytic sarcoma is a rare hematopoietic malignancy that originates from histiocytes, and may involve lymph nodes and extranodal sites such as the spleen, head and neck, skeleton, liver, breast, bone marrow, mediastinum, pancreas, skin, lung, kidney, central nervous system, testis, gastrointestinal tract, and uterus. The involvement of the nasal cavity is considered extremely rare. The prognosis is poor, even with chemotherapy, and the survival time is usually two years. We report the case of a 16-year-old-male with primary histiocytic sarcoma of the nasal cavity. The diagnosis was based on classical histopathology and immunohistochemical findings. This malignancy has not shown consistent satisfactory responses to chemotherapy regimens.

Acta Med Iran 2018;56(11):726-728.

Keywords: Nasal cavity; Immunohistochemistry; Chemotherapy; Histiocytic sarcoma

Introduction

Histiocytic sarcoma (HS) is a very rare and aggressive hematopoietic malignant tumor, constituted by cells with morphology and immunohistochemical features of the mature tissue histiocytes (1-6). HS was formerly considered as T-cell or B-cell non-Hodgkin lymphomas or a proliferative reaction of histiocytes associated with lymphoma (1,2,4-6). This condition represents less than 1% of the hematolymphoid neoplasms (1-4), with a bimodal age prevalence (0-26 and 50-59 years), predominantly in adults (3-5), often occurring in lymph nodes, skin, and gastrointestinal tract (1,2,4,5). Other sites include central nervous system, neck, salivary gland, breast, lung, mediastinum, spleen, liver, pancreas, kidney, testis, uterus, bone marrow, and skeleton; this malignancy may be disseminated (1,4-6). Classical morphology of HS includes round to oval cells with abundant and eosinophilic cytoplasm, eccentric large round to oval multilobated and binucleated nuclei with variable degree of atypia (1,4). Immunohistochemical markers of histiocytes as CD68, CD163, and lysozyme, constitute diagnostic criteria of disease (1,3-6), and the outcome is poor due to the usually limited response to chemotherapy (1,3-6). Due to the rarity of HS, there is no consensual schedule of therapy, and lymphoma-based protocols are used (3.4). The objective of this case report is to describe a case of this very rare histiocytic malignancy, which primarily developed in the nasal cavity of a young male.

Case Report

A 16-year-old male claimed of nasal voice for 10 months, associated with night snoring; in addition to a lump in the left nasal cavity with a gradual growth. In the last three months, the lump grew rapidly, causing facial deformity, epistaxis, and ipsilateral cervical lymphadenopathy. There was no pain, fever, weight loss and other systemic manifestations. His personal and family medical antecedents were of no relevance. On physical examination He was eutrophic and afebrile; there was a tumor measuring 7x8 cm, occupying the left nasal cavity causing septal deviation and contralateral obstruction of the nasal vestibule. A group of left bilateral cervical lymph nodes, measuring 4x4 cm, was palpable. The remainder data of physical examination were unremarkable. Laboratory evaluations revealed C-reactive protein 4.3 mg/dl and ESR 36 mm/h; hemogram, electrolytes, liver enzymes, coagulation profile, renal function, and myelogram were all normal. Images of computerized tomography (Figure 1) revealed a large and moderately aggressive tumor, involving the left nasal cavity, the nasopharynx, the left maxillary sinus and

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adjacent soft tissues. Studies of tumor sample showed cells of histiocytic lineage with discrete to moderate atypias, oval nuclei of irregular contours, with small eosinophilic nucleoli and mildly eosinophilic cytoplasm, either scarce or abundant (Figure 2) Immunohistochemistry study showed diffuse positive CD 1a-Langerhans cell antigen and S-100 polyclonal protein; and weakly positive CD 68-lysosomal KP1 protein and addition to LCA, suggesting the diagnosis of Langerhans cell histiocytosis. However, a second biopsy revealed the following data: CD-20-antigen of B lymphocytes focal weakly positive; CD3-receptor of T lymphocytes (epsilon chain) focal weakly positive; CD 68-lysosomal KP1 protein strongly positive; and S-100 polyclonal protein (histiocytic lineage) focal weakly positive.

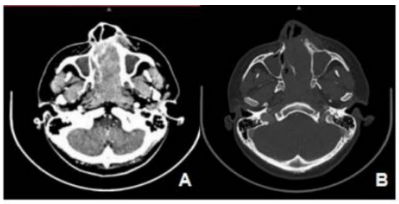

Figure 1. CT of upper airways revealing a large and moderately aggressive tumor, which involves the left nasal cavity, the nasopharynx, the left maxillary sinus and adjacent soft tissues

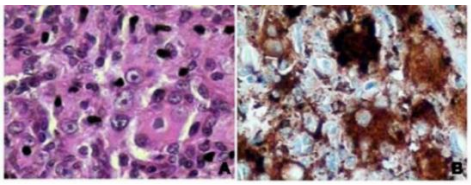

Figure 2. A: Light microscopy study showing abundant and eosinophilic cytoplasm of tumor cells. The nuclei are large, with vesicular chromatin and large nucleoli (HE x400); B: Immunohistochemistry study of tumor cells strongly positive for CD 68, showing granular cytoplasmic staining (x400)

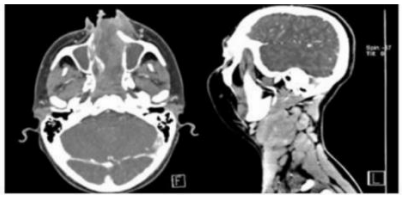

Figure 3. CT images of control on the week 22 of chemotherapy, showing the extensive progression of malignancy

The studies for CD30-Ki-1 BerH2 antigen and CD 1a-Langerhans cell O10 antigen were negative. CD 163 was not studied. Immunohistochemistry was considered positive if 10 or more tumor cells expressed strong reactivity, and focal weakly positive tests showed reactivity in less than 10 cells (5). The diagnosis of HS was established, and chemotherapy was initiated. There was the initial response to the LCH III protocol-group I (risky group) and maintenance with vinblastine (VBL) and prednisone (PDN), which resulted in reduction of tumor size. On the week 12 of treatment, the first schedule was changed by methotrexate (MTX) and 6-mercaptopurine (6 MP) due to the disease progress, and alternate changes in tumor size were observed. The searches for fungi and for AAFB and the PPD test were all negative. The CT of control done in the week 22 detected a clear progression of disease (Figure 3). The ICE protocol (ifosfamide, carboplatine, and etoposide) was utilized, with a good initial response; nevertheless, the tumor starts growing after the third cycle, probably because of delays between cycles due to severe neutropenia and sinusitis. Therefore, the second schedule of induction was employed in March 2014 with vincristine, ifosfamide, doxorubicin, and etoposide (VIDE); after the third cycle, It was achieved just stable disease. Another induction schedule was tried; a cycle with high-dose of cytarabine (HD Ara-C) plus idarubicin and cladribine (2-CdA), a myeloid-like treatment. The patient developed overt disease progression during the first 15 days of chemotherapy, with subsequent complete airway obstruction requiring palliative tracheostomy and gastrostomy; furthermore, bilateral ocular proptosis, invasion of the CNS and multiple subcutaneous nodules, dying 64 days later.

Discussion

This young male presented with primary HS of the nasal cavity, and lymph node involvement. The tumor was detected in a locally advanced stage and has shown an aggressive course, which has not been well controlled by chemotherapy. The diagnosis was promptly established by histopathology features with positive immunohistochemistry expression of LCA and CD 68 (lysosomal protein KP1), weakly B and T-cell markers and absence of Langerhans cell marker CD1a (4-6). These findings ruled out main differential diagnoses such as lymphoma, carcinoma, and melanoma (1,4-6). Malignancies with origin from histiocytes, macrophages, or dendritic cells were also ruled out, as an example of Langerhans cell HS, interdigitating dendritic cell sarcoma, follicular dendritic cell sarcoma, and another kind of dendritic cell sarcoma (4-6). Primary HS arising from extranodal sites constitutes an exceedingly rare condition (2,4,7). Hornick *et al*., (2), reviewed 14 cases of extranodal HS and described a unique tumor localized in the nasal cavity; the other sites were soft tissue of the

extremities (7:50%), gastrointestinal tract (5:35%), and lung. All tumors expressed reactivity for LCA, CD45RO, and CD68 (KP1 and PG-M1); 93% for CD4, 86% for lysozyme, 80% for CD31, and 50% for S-100 protein; worthy of note, 36% of the HS expressed focal weak CD1a reactivity similar to the first specimen of the tumor herein described (2). HS is aggressive, with disease dissemination at diagnosis, and shows poor response to therapy, besides multimodal therapy with surgery and chemo-radiotherapy. Chemotherapy is usually focused on non-Hodgkin lymphoma protocols, but there are some experiences with sarcoma and myeloid based schedules. Mainardi *et al*., (8), reported a case of a 9-year-old male with HS in the rhinopharynx successfully treated using a chemotherapy protocol for aggressive B-cell non-Hodgkin lymphoma, consolidation with autologous peripheral blood stem cell transplant and posterior radiotherapy in the primary site. Buonocore *et al*., (9), described a pediatric patient with HS treated with myeloid based protocol, with idarubicin and 2-chlorodeoxyadenosine (2CdA) and radiotherapy, with good result. Agarwal *et al*., (7), studied seven patients with sinus histiocytosis and massive lymphadenopathy; and, in one of these individuals, a classic case of nasal HS developed after the evaluative period of four years. The tumor size (≥ 3.5 cm) at diagnosis is inversely proportional to the rate of favorable responses of HS to chemotherapy (2,3,5); and, in the major number of patients, the outcome is poor (4-6). Notwithstanding, Narita *et al*., (3), reported the successful result to the treatment of this malignancy utilizing a schedule with cyclophosphamide plus vincristine, doxorubicin, and prednisone in a 61-year-old man affected by concurrent HIV infection treated with routine antiretroviral therapy. Moreover, Yoshida and Takeuchi (6) also described a 56-year-old male with HS successfully controlled with a combination of cyclophosphamide plus vincristine, doxorubicin, etoposide, and prednisone, followed by utilization of recombinant human granulocyte–colony-stimulating factor (rhG-CSF). Possible concerns in the present case study might be about the lack of microdissection of individual tumor cells for PCR amplification and sequence analysis; as well as of molecular genetic study (5). Nevertheless, these more sophisticated complementary tools of high-costs are not mandatory for the diagnostic criteria of HS, and also may be not available in developing countries. Although with the inherent weaknesses of single reports, this case study of an exceedingly rare malignancy could contribute to enhancing the suspicion index of general physicians about this tumor.

Histiocytic sarcoma is a very uncommon malignancy, which constitutes a diagnosis of exclusion. Moreover, the primary involvement of the nasal cavity represents an exceedingly unusual condition. The worth of note is the poor outcome of this disease, with an average survival time of only two years. Data obtained from a major number of reports might increase the knowledge about etiopathogenesis and could propitiate the further establishment of consensual and more effective therapeutic options.

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