

A Rare and Challenging Entity: Sino-Nasal Nk/T-Cell Lymphoma

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Submitted: 2024, Jan 17; Accepted: 2024, Jan 23; Published: 2024, Feb 15

Citation: Romdhane, N., Nefzaoui, S., Jouini, S., Kharrat O., Rejeb, E., et al. (2024). A Rare and Challenging Entity: Sino-Nasal Nk/T-Cell Lymphoma. *J Clin Rev Case Rep*, 9(2), 01-03.

Abstract

Extranodal NK/T-cell lymphomas are a rare subtype of non-Hodgkin's lymphomas. They represent a diagnostic challenge due to their clinical presentation polymorphism and to the abundance of the necrotic tissues on biopsies.

We report the case of a male patient that initially presented with chronic facial and palatine pain, associated to a palatine substance loss and a jugal edema on physical examination. Facial CT scan showed the lesion and its extension to the nasopharynx and association to multiple cervical lymph nodes. Initial biopsies have erred the diagnosis showing signs of a mycotic infection with no malignant cells. Considering the bad response to anti-fungal treatment, biopsies and radiological explorations were redone and were in favor of a NK/T-cell lymphoma. Locoregional and distant extensions of the disease were studied, showing an hepatic suspicious nodule and mediastinal lymph nodes. Then, the patient underwent sequential chemo and radiotherapy with a good response to treatment.

Keywords: NK/T-cell lymphomas, Muco-fungal infection, Nasopharynx, Non-Hodgkin's lymphomas

1. Introduction

Extranodal NK/T-cell lymphomas are rare extranodal non-Hodgkin's lymphomas, accounting for only 0,2 % of them [1]. They are divided into nasal, non-nasal and disseminated subtypes. Nasal NK/T-cell lymphomas represent 1 to 2 % of all NK/T lymphomas [1]. They can spread through the nose, the nasopharynx and the upper aerodigestive tract. They are characterized by their aggressivity, angiotropism, necrosis and poor prognosis.

The aim of our study is to report a case of this rare entity, to investigate through it the clinicopathological, radiological and histological characteristics of nasal T/NK cell lymphomas and to analyze their management and prognosis particularities.

2. Observation

We report the case of a 41-year-old male patient with no significant medical history, who presented with facial and palatine pain evolving in the last 7 months. He was a smoker and presented habits of snuffing and regular alcohol consumption. Physical examination revealed the presence of a median soft palatine substance loss with bony destruction and communication with the rhinopharynx (Figure 1) associated with a left jugal edema (Figure 2).

No facial nerve palsy nor decrease in the facial sensitivity were noted.

A 2 cm firm and mobile adenopathy of the left second sector was found.

The facial CT scan objectified the soft palate substance loss causing a bucco-nasal communication in addition to a suspicious bilateral soft tissue thickening of the posterolateral nasopharyngeal wall. Multiple cervical lymph nodes were found bilaterally on sectors IIA, IIB and III.

Initially, the patient was explored abroad. Multiple biopsies of the palatine lesion were realized showing no signs of malignancy but signs of a mycotic infection. One anatomopathological study concluded to a traumatic ulcerative granuloma with stromal eosinophilia (TUGSE) associated to a mycotic infection.

Based on these explorations, the retained diagnosis was a muco-fungal infection of the palatine bone and the patient underwent a two-month treatment based on Itraconazole with no significant improvement. Mucormucosis was then suspected and the patient was addressed to our department for further investigations.

Immunodepression was eliminated after biologic screening: HIV and hepatitis B and C serologies were negative and no lymphopenia was noted. Granulomatosis with polyangiitis was suspected and eliminated through a normal chest x-ray, absence of renal or cardiac symptoms, absence of hyper eosinophilia and

negative immunologic blood tests (ANCA).

Deep biopsies including soft tissue and bone were redone revealing the aspect of a NK/T-cell lymphoma. Histological examination found a neoplasm infiltrated by a polymorphic population of altered polynuclear neutrophils, histiocytes and lymphocytes. Focally, it was made of apoptotic bodies and inflammatory cells. Multiples necrotic tissues were associated. Additionally, images of angiocentrism and angioinvasion were found.

Immunohistochemistry of the tumoral cells showed CD56 and CD2 positivity and CD3, anti-CD1a and anti-PS100 negativity. An intense and focal nuclear marking of EBER was also described.

Spread assessment was performed using a cervical-thoracic-abdominal-pelvic CT scan. A local extension to the parapharyngeal space and to the left tonsil were noted. A complete lysis of the soft palatine, a partial lysis of the hard palatine and an extension to the left maxillary sinus floor were described (Figure 3). CT scan also discovered a hepatomegaly with multiple suspicious hepatic nodules and mediastinal lymph nodes.

Consequently, the patient was classified stage IV on the CSWOG staging. He underwent 3 chemotherapy sessions followed by radiotherapy with a good clinical response to treatment.

3. Discussion

The case reported here is a nasal-type natural killer T-Cell lymphoma, a rare clinicopathological entity with destructive characteristics. Its fatal outcome makes of this disease a diagnostic and therapeutic emergency. This disease occurs mainly in males at middle-age [2].

Although the pathogenesis remains unknown, an association with EBV infection [3] as well as a genetic predisposition have been reported (p53 and c-kit gene mutations) [4]. The symptoms are unspecific [5], making a malignant diagnosis difficult to suspect.

The nose is the most common initial involved site with obstructive symptoms, bleeding and purulent nasal discharge [6]. This type of lymphoma can easily be mistaken for chronic sinusitis [7].

Associated cervical lymphadenopathy is reported in 15% to 25% of cases [8], like in our patient. Hemifacial pain, facial edema or dysphagia can be reported [9].

This disease tends to be very localized initially, although dissemination is common [10]. The primary site where the lymphoma spreads is the skin, with multiple and dark purple subcutaneous nodules being the most frequent cutaneous finding [11]. Eyes, gastrointestinal duct, lungs and nerves may be involved [12]. It is probably due to its angiocentric and angioinvasive nature, which is responsible for the blood vessel wall destruction. Our patient had destructive lesions of the nasopharynx, the oropharynx and the palate mucosa. He didn't have any invasion of the adjacent tissues.

The laboratory evaluation may show an elevated C-reactive

protein or erythrocyte sedimentation rate, lymphocytosis or lymphopenia [13,14].

The radiological findings have been investigated by some studies. Computed tomography allows to visualize the tumor, its extension to adjacent structures and the bone destruction. The magnetic resonance imaging can distinguish between neoplastic disease and inflammatory or infectious disease. These radiological findings are also useful for pretreatment and post-treatment evaluation. Currently, the standard imaging modality for NK/T-cell lymphoma is the PET/CT scan [15]. For newly diagnosed patients, it is interesting to undergo PET/CT scan for accurate staging, and predicting the prognosis [16].

In the case of our patient, the diagnosis was delayed by the clinical presentation which led to the suspicion of oral mycosis. Histological diagnosis is difficult and multiple biopsies might be required to confirm the diagnosis [17]. The samples of the patient were analyzed by several pathologists to confirm the diagnosis.

Immunophenotyping reveals expression of T lymphocyte and NK lymphocyte cell markers. The regular immunophenotype of extranodal NK/T-cell lymphoma, especially nasal type, is: CD2+, CD56+ (the specific markers of NK) with intracytoplasmic expression of anti-CD3 antibody and negative expression of CD3 on the cell surface [18].

The staging of centro-facial T/NK lymphoma is still an area of research in order to predict the survival. Lin [19] proposed the new staging system (CSWOG Staging) in 2014. Our patient was classified as stage IV due to the presence of hepatic metastasis. The standard therapies have not been defined, because of the rarity of this disease. As these tumors are generally sensitive to chemotherapy and radiation therapy, surgery isn't mandatory [20]. Treatment is mainly based on systemic chemotherapy [21]. Radiotherapy may be effective in localized disease [22], but when used exclusively, it is associated with high systemic relapse rates [23]. Besides, it cannot prevent recurrence outside of the radiation field [24]. Chemotherapy protocols are based on-anthracycline-containing regimens particularly with L-asparaginase [25]. Allogenic hematopoietic stem cell transplantation may be useful in patients with stage III/IV and relapsed diseases. Immunotherapy with antibodies against CD30, programmed cell death protein 1 and CD38 is currently being studied and looks promising [26]. Our patient received 3 cycles of chemotherapy followed by radiotherapy.

The prognosis of NK/T-cell lymphoma depends on presentation, middle and end-of-treatment parameters. Therefore, patients should be carefully evaluated throughout the treatment, in order to enable timely therapeutic modifications to be adopted [22]. These tumors have a relatively poor prognosis [27], with 5-year survival rate between 38% and 64% [28].

Conclusion

This case report highlights the difficulty of making the diagnosis of this rare entity due to the misleading initial symptomatology. Nasosinusal lymphoma has to be bared in mind in front of any

centro-facial necrotic lesion. Radiology is non-specific, and the diagnosis remains histological.

Funding

The authors declare that no funds, grants, or other support were received during the preparation of this manuscript.

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