Case Report

Extranodal natural killer/T-cell lymphoma, nasal type with central nervous system and bone marrow involvement: Report of a rare case with review of literature

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ABSTRACT

Extranodal natural killer (NK)/T-cell lymphoma is the predominant type of primary nasal lymphoma, especially in the Asian population. Only a few studies have specifically reported on the incidence of cerebrospinal fluid (CSF) and bone marrow involvement in peripheral T-cell lymphomas. We report a case of extranodal NK/T-cell lymphoma with CSF and bone marrow involvement which is a rare occurrence.

Key words: Bone marrow, cerebrospinal fliud, extranodal NK/ T -cell lymphoma, nasal type

INTRODUCTION

Natural killer (NK) cells are distinctive cells of the innate immune system, which play an important role in mucosal and cutaneous immunity. They represent the first line of defense and do not require antigen sensitization to initiate an immune response.[1] Aggressive NK-cell leukemia and extranodal NK/T-cell lymphomas are the two main categories of NK-cell-derived neoplasm in the latest World Health Organization classification. Extranodal NK/T-cell lymphoma is a localized disease usually in the midline facial area although other extranodal sites can also be involved without nasal involvement.[2] It accounts for around 7% of peripheral T-cell lymphomas in South India, and its frequency is slightly higher than that reported for Western countries.[3,4] Cerebrospinal fluid (CSF) dissemination is reported in only a minority of cases.[2,3] Peripheral blood and bone marrow can be minimally involved although disseminated involvement is uncommon.[2] We report an unusual case of extranodal NK/T-cell lymphoma with leptomeningeal and bone marrow involvement.

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CASE REPORT

A 46-year-old male patient presented with bilateral nasal obstruction of 1-year duration. He was treated with a clinical diagnosis of rhinosporidiosis. He developed symptoms of increasing nasal obstruction and nasal bleeding of 8 months duration and was evaluated in a local hospital. General examination was unremarkable. Local examination revealed edema in the left periorbital area and left side of root of nose. Computed tomography scan of the neck, chest, and pelvis revealed homogenous soft-tissue dense lesion in bilateral nasal cavities and ethmoid air cells external to the left orbit with homogenous thickening of nasopharyngeal structures. No significantly

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enlarged cervical, mediastinal, intra-abdominal, or inguinal lymph nodes were present. No hepatosplenomegaly was present. His blood counts and peripheral smear were within normal limits. Lactate dehydrogenase (LDH) level was 1149 u/L. Histopathology revealed fragments of tissue lined partly by respiratory epithelium, with an underlying neoplasm composed of cells arranged in diffuse sheets. Individual cells were large with moderate-vacuolated cytoplasm and round to oval nucleus with irregular nuclear membranes and prominent nucleoli. Tumor cells were seen destroying the adjacent mucous glands. Angiocentricity, angioinvasion, and perineural invasion were present [Figure 1a and b]. Immunohistochemistry showed that the tumor cells were positive for CD3, CD56, perforin, granzyme, and Epstein-Barr virus-encoded RNA [Figures 1c, d and 2a-d] with loss of CD5 and negative for CD20, CD8, CD4, bcl6, Tdt, CD34, PAX5, and myeloperoxidase. CSF examination also revealed similar tumor cells [Figure 2e]. Bone marrow biopsy showed focal infiltration by the tumor cells [Figure 2f]. Thus, diagnosis of extranodal NK/T-cell lymphoma nasal type with CSF and bone marrow infiltration was given.

DISCUSSION

Extranodal NK/T-cell lymphoma most commonly involves nasal cavity and upper aerodigestive tract. Presenting symptoms are usually nasal obstruction, nasal discharge, and epistaxis.[2] Tumor is locally destructive with frequent erosion of bones. Incidence of central nervous system (CNS) and bone marrow involvement in extranodal NK/T-cell lymphomas is found to be rare accounting for <3% and 7%, respectively.[5] Minimal involvement of CNS and bone marrow can occur in extranodal NK/T-cell lymphoma, but extensive involvement is rare thus, contrasting with marrow-based aggressive NK-cell leukemia. Advanced disseminated extranodal NK/T-cell lymphoma and aggressive NK-cell leukemia have many overlapping features, thus making them hard to differentiate. Most accepted distinguishing features are that disseminated extranodal NK/T-cell lymphoma often presents at an older age with reported higher incidence of cutaneous involvement, absence of B symptoms, less frequency of liver spleen and bone marrow involvement, and less frequent expression of CD16.[2] Genetic studies have shown significant differences between the two where 6q− is typical of extranodal NK/T-cell lymphoma whereas $7p^-$, $17p^-$, 1q+ are more common in aggressive NK-cell leukemia.[6] The presence of several overlapping features advocates the need for further studies to clarify whether they represent different spectra of the same disease. Routine CNS prophylaxis has been recommended for aggressive lymphomas such as lymphoblastic and Burkitt lymphomas.[7] A few studies have specifically reported on the incidence of CNS involvement in peripheral T-cell lymphomas.[8] One of the studies had suggested elevated LDH and paranasal sinus involvement as risk factors for peripheral T-cell lymphomas for CNS involvement.[9] A high NK/T-cell lymphoma prognostic index score (NKPI) was suggested as a predictive factor for CNS involvement.[10] Risk factors for CNS involvement in extranodal NK/T-cell lymphoma include group ¾ NKPI, presence of B symptoms, advanced stage, elevated LDH levels, and regional lymph node involvement.[10] Our patient was treated with CHOP regimen with triple intrathecal therapy and radiotherapy and is doing well.

To conclude, several overlapping features in disseminated extranodal NK/T-cell lymphoma and aggressive NK-cell leukemia often make them hard to differentiate. Future studies are needed to evaluate whether they represent different clinical manifestations of the same disease.

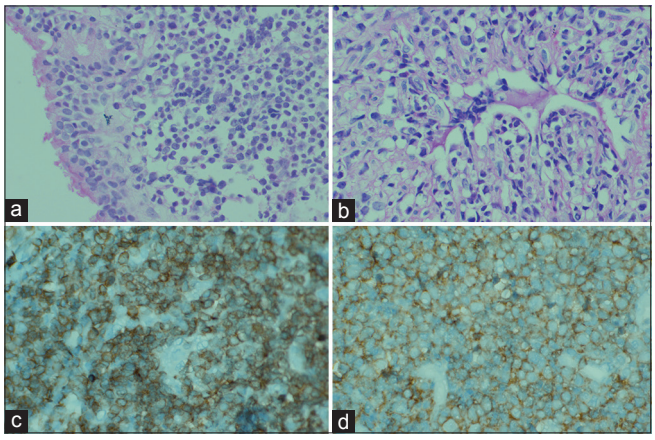

Figure 1: (a) Tissue lined by respiratory epithelium and subepithelium showing diffuse infiltration by the tumor cells (H and E, ×400). (b) Angioinvasion by the tumor cells (H and E, ×400). (c and d) Tumor cells are positive for CD3 and CD56, respectively (IHC, ×400)

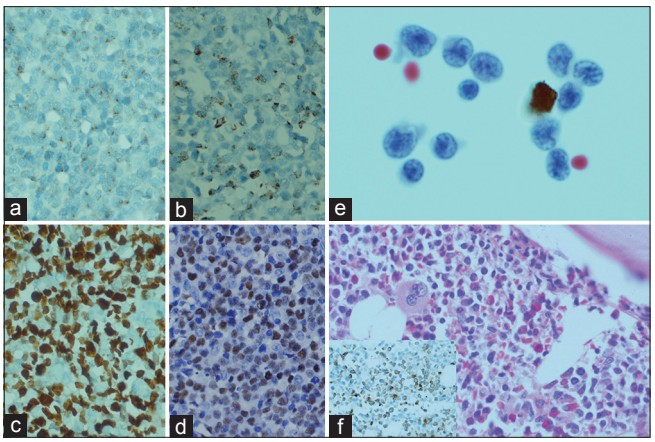

Figure 2: (a and b) Tumor cells are positive for perforin and granzyme (IHC, ×400). (c) Tumor cells show MIB1 labeling index of around 90% (H and E, ×400). (d) Tumor cells are Epstein-Barr virus encoded RNA positive (IHC, ×400). (e) Tumor cells in the cerebrospinal fluid (Pap, ×1000), (f) bone marrow infiltration by the tumor cells (H and E, ×400). Inset showing the CD3 positive tumor cells (H and E, ×400)

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Conflicts of interest
There are no conflicts of interest.

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