Case Report

Cytodiagnosis of extranodal natural killer/T-cell lymphoma, nasal type: Report of two cases

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ABSTRACT

Extranodal natural killer (NK)/T-cell lymphoma, nasal type (NK/T) is relatively rare, associated with aggressive behavior and poor prognosis. Histopathological findings, immunohistochemical study, and Epstein-Barr virus-encoded ribonucleic acid *in situ* hybridization are essential for the diagnosis. There are a few case reports in the literature describing the cytological findings of these uncommon lymphomas. We herein describe cytological findings in two cases of extranodal NK/T-cell lymphoma, nasal type presenting as lacrimal gland and/or nasal masses. Fine-needle aspiration smears revealed small to medium-sized lymphoid cells showing irregular nuclear outline, moderate amounts of light basophilic cytoplasm containing fine azurophilic granules in most of the cells. Some of these atypical lymphoid cells showed tongue-like projections of cytoplasm from one or both sides of the cells. Histopathological examination revealed typical angoicentric, angiodestructive growth pattern of these lymphomas.

Key words: Extranodal natural killer/T-cell lymphoma, fine-needle aspiration cytology, lacrimal gland, nasal type

INTRODUCTION

Nasal extranodal natural killer (NK)/T-cell lymphoma is a rare aggressive lesion, characterized by a destructive process of the upper respiratory tract that has an unusual and rapid evolution.[1] Diagnosis is often difficult and requires expert clinical examination and analysis of biopsies using immunohistochemistry. We describe fine-needle aspiration (FNA) findings in two unusual cases of nasal extranodal NK/T-cell lymphoma and discuss the utility of FNA in the diagnosis of these aggressive lymphomas.

CASE REPORTS

Case 1

A 55-year-old female patient presented with swelling below medial canthus of left eye since 1 year. She also complained of the left side nasal obstruction, watering, bleeding and pus discharge from the left eye since 3 months. On examination, firm, nontender swelling of size 2 × 1 cm was present medially and below the left medial canthus. Skin overlying the swelling was erythematous. Lower eyelid was pushed upwards. However, there was no discharge from the swelling. Regurgitation test was negative. On examination of the nasal cavity, there was a mass in the left side, which was firm in consistency and was bleeding on touch. On contrast enhanced computerized tomography (CT), there was a heterogeneously enhancing soft tissue mass 2 × 1.9 × 1.8 cm involving left lacrimal sac and extending into medial part of the orbit. The growth was extending inferiorly along the nasolacrimal duct. In addition, the growth was extending into left maxillary antrum, frontal sinus and right maxillary sinus. FNA was done from the left medial canthus mass and stained with Giemsa stain.

Case 2

A 70-year-old male presented with mass in bilateral nasal cavity since 3 months. He also complained of swelling in the hard palate since 20 days. There was a history of bloody/purulent nasal discharge and nasal obstruction. Anterior rhinoscopy revealed a growth in bilateral nasal

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cavities eroding the nasal septum. On examination of the oral cavity, there was a 4 × 3 cm, firm growth in the palate along the midline extending to either side. CT scan revealed heterogeneously enhancing mass in bilateral nasal cavity with erosion of the nasal septum and extending into nasopharynx, ethmoid sinus, and medial wall of maxillary sinus. FNA of nasal mass was done and stained with Giemsa stain.

On microscopic examination of FNA smears of both cases, findings were similar and consisted of cellular smears showing a heterogeneous population of small to medium-sized lymphoid cells, along with occasional follicular center cells, plasma cells, eosinophils and some histiocytes. The medium-sized lymphoid cells showed readily discernible nuclear atypia with an irregular nuclear outline, moderate amounts of light basophilic cytoplasm [Figure 1] containing fine azurophilic granules in most of the cells [Figure 1, inset]. Some of these atypical lymphoid cells were showing tongue like protrusions from the cytoplasm. Keeping in view these cytomorphological features possibility of extranodal NK/T-cell lymphoma, nasal type was suggested in both cases.

Histological evaluation of biopsies from both cases revealed atypical angioinvasive and angiodestructive lymphoid aspirate comprising of small to medium sized cells with irregular nuclei, inconspicuous nucleoli and moderate pale to eosinophilic cytoplasm [Figure 2]. The infiltrate was present in a background of acute and chronic inflammatory cells with prominent areas of necrosis and ulceration. Immunohistochemical study showed neoplastic cells expressing CD3 and CD56. Blood and bone marrow were negative for involvement.

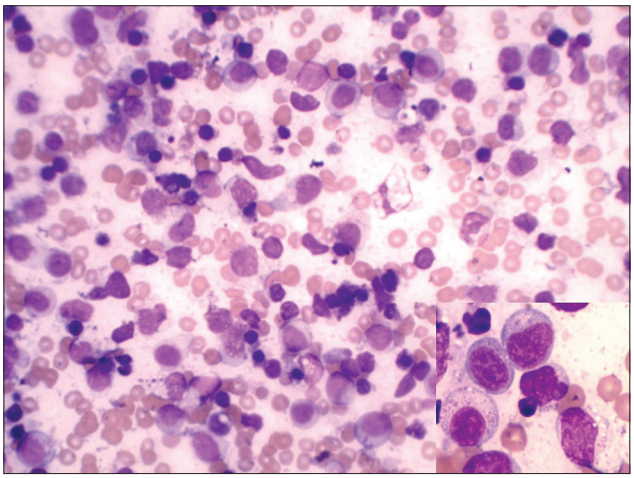

Figure 1: Fine-needle aspiration smears showing small to medium sized cells with irregular nuclei, inconspicuous nucleoli, and moderate amounts of basophilic cytoplasm (Giemsa stain, ×20). Inset shows azurophilic granules in the cytoplasm of these cells (Giemsa stain, ×100)

DISCUSSION

The extranodal NK/T-cell lymphoma is a rare type of non-Hodgkin lymphoma once known as lethal midline granuloma. The prevalence of nasal lymphoma is estimated at 0.17-1.5% for all non-Hodgkin's lymphomas (NHL), of which 45% originate from the NK/T-cell.[2] The most common site is the upper aerodigestive tract (nasal cavity, nasopharynx, paranasal sinus, and palate) in addition to skin, gastrointestinal tract, spleen, breasts, testis and kidney.[3]

Extranodal NK/T-cell lymphomas, "nasal type" belong to the broader heterogeneous group of generally aggressive peripheral T-cell lymphomas, which constitute less than 15% of NHL.[4] Its main characteristic feature is the destruction of mid-facial region and represent the most common cause of lethal midline granuloma. This entity has also been referred to as polymorphic reticulosis, angiocentric immunoproliferative lesion and angiocentric T-cell lymphoma.

There is male to female ratio 2:1 and it is encountered in all age groups (6-86 years). The common clinical features are nasal obstruction, purulent rhinorrhea, epistaxis, and sore throat; however, the systemic symptoms such as fever and weight loss are not typically noted. Nonspecific nasal symptoms often predate the appearance of mucosal ulceration and tissue necrosis by a year or more which can cause delay in diagnosis. Majority of patients have localized disease with a destructive mass involving the nasal septum, lateral nasal wall and palate. Nasal septal perforation was reported in 40% of cases. The lymphoma can extend to adjacent tissues including the orbit as in our cases. Bone marrow involvement is uncommon. Though, it may disseminate rapidly or be complicated by hemophagocytic syndrome.

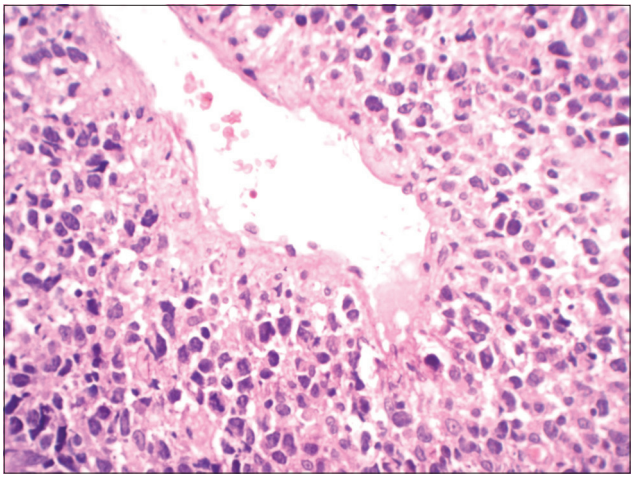

Figure 2: Histopatological examination revealing angiocentric growth pattern of lymphoid cells (H and E, ×20)

Cytologically, most cases involve cells or a mixture of small and intermediate cells. The nuclei are often folded but can be elongated, with granular chromatin and a moderate amount of pale to clear cytoplasm. Mitotic figures are easily found. Giemsa stained touch preparations commonly highlight the azurophilic granules within cytoplasm, which resemble those found in normal NK-cells.[5] According to Ng *et al*. recognition of the subtle but definite cytologic atypia of malignant lymphoid cells and presence of an appropriate background (including more eosinophils than usual), together with proper application of ancillary techniques, is crucial to arriving at a correct diagnosis.[6] Cho *et al*.[7] in their study on FNA findings of extranodal NK/T-cell lymphomas concluded that the presence of malignant lymphoid cells in a necrotic background with an abundance of apoptotic bodies is a highly characteristic and consistent finding in FNA of NK/T-cell lymphoma involving soft tissue. Kishimoto *et al*.[8] studied nasal brush cytological findings in three cases and found that lymphoma cells were medium to large lymphoid cells possessing light blue and abundant cytoplasm. A characteristic feature of these cells was the presence of the tongue-like projections of cytoplasm from one or both sides of the cells. We believe these intriguing cytologic findings are indicators of NK/T-cell lymphoma of the nasal type. Azurophilic granules were observed in all cases, ranging from extremely fine granules to large granular lymphocyte-like granules. Tongue like projections of cytoplasm's were noted in some of the cells in our cases, whereas cytoplasmic azurophilic granules were noted in the majority of the lymphoid cells.

Due to extensive necrosis and reactive inflammatory changes, superficial biopsies are often inconclusive. Coagulative necrosis with angioinvasion and angiocentricity are highly indicative of NK/T-cell lymphoma. The typical immunophenotype is CD2+, CD56+, surface CD3-with cytoplasmic CD3+. Cytotoxic molecules (granzyme B, TIA-1 and perforin) are also positive. Other T- and NK-cell-associated antigens are usually negative. Epstein-Barr virus (EBV)-encoded ribonucleic acid *in situ* hybridization demonstrates virtually all lymphoma cells are positive.[9]

These lymphomas have variable prognosis. Historically, the 5 years survival rate has been poor at 30-40%, but it has been recently improved to 71% with intensive therapy including upfront radiotherapy.[3,10] Significant unfavorable factors include advanced stage disease, unfavorable international prognostic index score, invasion of bone or skin, high circulating DNA levels, and the presence of EBV-positive cells in the bone marrow.

CONCLUSION

Extranodal NK/T-cell lymphomas, "nasal type" are aggressive neoplasms and their cytological features are characteristic enough to allow their early diagnosis by FNA when interpreted in correlation with the clinical and radiological features.

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