Case Report

Primary isolated extranodal NK/T-cell lymphoma of the orbit: A case report and diagnostic dilemma

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ABSTRACT

Natural killer T-cell lymphoma (NKTL) is associated with Epstein-Barr virus, a highly malignant tumor that typically arises in the nose and/or paranasal sinuses isolated orbital involvement by NKTL is extremely rare. Herein, we report a case of primary orbital NKTL in a young female patient. A 32-year-old female presented with gradually increasing painful swelling of the right eye. On examination, abaxial proptosis, inferolateral displacement of the eyeball, restricted extraocular muscle movement, and solid mass in the subconjunctival fornix and superior quadrant. The rest of the ocular and systemic examination was unremarkable. Magnetic resonance imaging with contrast of the orbit shows a lobulated mass lesion 35×30×18 mm involving the medial aspect of the right orbit extraconal and superior intraconal space extending up to the preseptal region. Informed consent and biopsy were done and sent for histopathology examination. Histopathological examination shows the spectrum of atypical lymphoid cells, indented or cleaved nuclei and pale to clear cytoplasm, few histiocytes, giant cells, and apoptotic body. To rule out lymphoma, immunohistochemistry (IHC) was advised. On IHC, tumor cells were positive for CD3, D56, CD4 focally, CD7, Ki-67–90% and negative for CD20, CD2, Tdt, PAX5, CD34, CD5, Cd8 leading to a diagnosis of extranodal NKTL of the orbit. To the best of our knowledge, around 20 cases of isolated orbital extranodal NKTL were reported in the literature review. Polymorphic lymphoid cell in a young patient often mimics the inflammatory conditions of orbit. The rarity of this tumor and inflammatory signs make it challenging to identify these tumors early.

Key words: Extranodal natural killer T-cell lymphoma, Non-Hodgkin lymphoma, Orbit

Extranodal natural killer/T-cell lymphoma (ENKTCL) is an aggressive nonHodgkin lymphoma (NHL) that has a strong association with EpsteinBarr virus (EBV) infection. There is a characteristic geographic variation in the prevalence of ENKTCL, more common in Asia and South America than in the United States and Europe and is commonly seen in adult patients [1]. The most common affected site is the upper aerodigestive tract, with the nasal cavity, amounting to >75% of cases [1].

Isolated orbital involvement of ENKTCL is very rare and limited to a few case reports. Here, we discuss the case of a primary isolated ENKTCL of orbit associated with diagnostic pitfalls and a brief review of the literature.

CASE REPORT

A 32-year-old female presented with gradually increasing painful swelling of the right eye, on examination abaxial proptosis, inferior-lateral displacement of the eyeball, restricted extraocular muscle movement, and solid mass measured 30×25×20 mm in the subconjunctival fornix and superior quadrant (Fig. 1a). The rest of the ocular and systemic examination was unremarkable.

On examination, visual acuity was 20/20 in both eyes. Magnetic resonance imaging with contrast of orbit shows a lobulated mass lesion 35×30×18 mm involving the medial aspect of the right orbit extraconal and superior intraconal space extending up to the preseptal region. The lesion appears isointense on T1wt and hyperintense on T2wt images and shows mild heterogeneous post-contrast enhancement (Fig. 1b). The lesion was encasing the right superior rectus muscle and the mass effect shows anterior inferior displacement of the eyeball. The paranasal sinus and nasal bone appear normal. Informed consent and incisional biopsy was done and sent for histopathology examination.

Histopathological examination shows the spectrum of atypical lymphoid cells, indented, or cleaved nuclei and pale to clear cytoplasm, few histiocytes, giant cells, and apoptotic body (Fig. 2a-d). To rule out lymphoma, immunohistochemistry (IHC)

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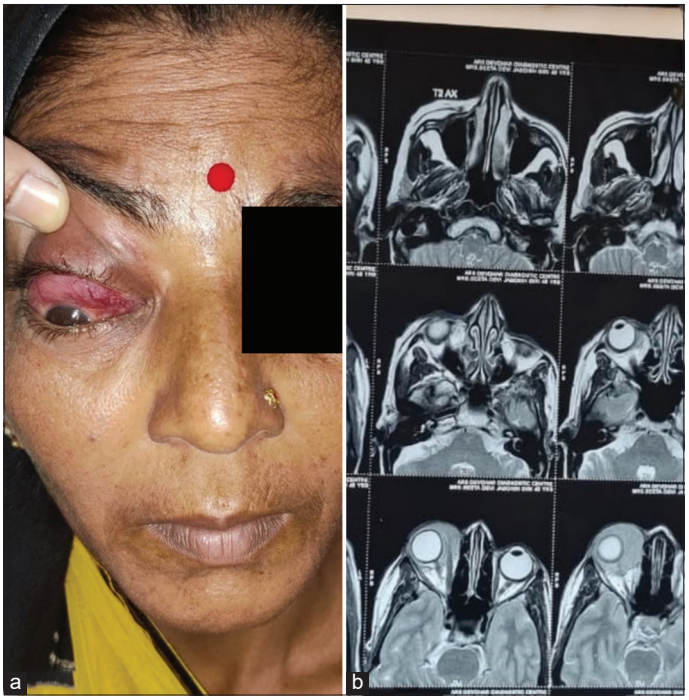

Figure 1: (a) Solid mass in subconjunctival fornix of the right eye and (b) magnetic resonance imaging shows post-contrast enhancement, lobulated extraconal mass medial aspect of the right orbit measures 35×30×18 mm

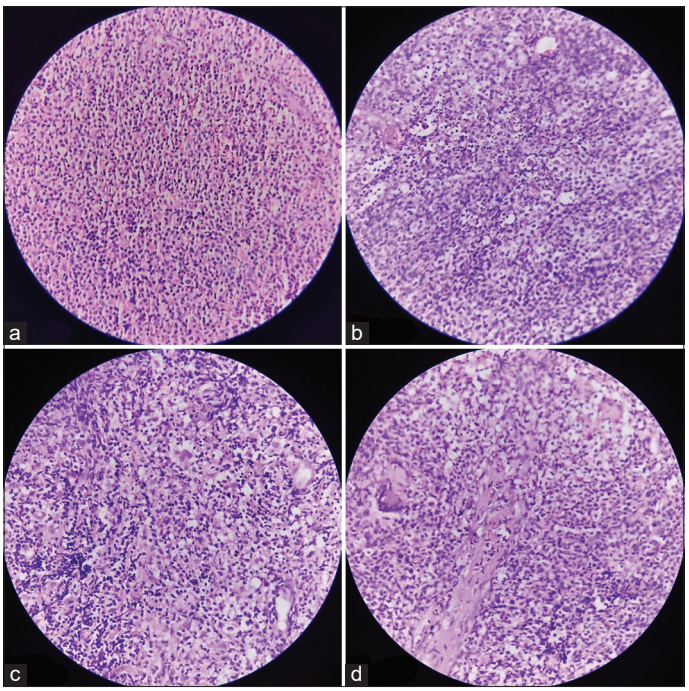

Figure 2: (a-d) Hematoxylin and eosin stain (H&E, ×400) shows spectrum of atypical lymphoid cells, histiocytes, apoptotic debris, and foreign body giant cells forming ill-defined granuloma

was advised. On IHC, tumor cells were positive for CD3, D56, CD4 focally, CD7, Ki-67–90%, and negative for CD20, CD2, Tdt, PAX5, CD34, CD5, and Cd8, leading to the diagnosis of ENKTCL of the orbit. Metastatic workup including a whole-body positron emission tomography-computed tomography scan and bone marrow biopsy did not reveal any metastasis.

DISCUSSION

The World Health Organization defines ENKTCL as "an extranodal lymphoma of NKcell or Tcell lineage, with characteristic angiodestruction, prominent necrosis, cytotoxic phenotype, and an association with EBV" [2]. In India, it accounts for approximately 2% of NHL [3]. NKTCL is very infrequent in the orbit [4]. The mean age at diagnosis is around 50 years and the male/female ratio is around 2:1 [5].

Akbar *et al*. studied, 82 reported cases of primary extranasal ENKTCL, out of that, 83% and 17% were presented with localized and disseminated disease, respectively. The most frequent locations in patients with localized disease were the lung (25%), while orbit and intraocular tissue represent only 6% of cases. They found a median age of 65 years in a patient with orbital involvement of ENKTCL. The prognosis of patients with both localized and disseminated extranasal NKTCL was very poor [6].

The ratio of extranasal to nasal cases of ENKTCL is reported to be between 1 and 6, with lower ratios in the USA and higher ratios in Asia [7]. EBV strain, genetic background, and environmental factors can be attributed to this geographical variation. The EBV demonstrates a type II latency pattern. Demonstration of EBVencoded small RNA by *in situ* hybridization is the gold standard for EBV detection. There is no association between EBV status and ENKTCL prognosis [8]. Wang *et al*. reported seven cases of EBV-negative ENKTCL and also reviewed 22 published articles on EBV-negative ENKTCL [5].

The most common clinical presentations of primary orbital NKTCL that are reported include proptosis, extraocular movement limitation, decreased vision, and signs of ocular/orbital inflammation. They are histologically characterized by angiodestruction and coagulative necrosis and are associated with EBV infection. Orbital NKTL commonly occurs in the fifth decade of life [9]. A younger age at presentation as in the current case can, therefore, confuse the treating ophthalmologist. Two previously reported cases of orbital NKTCL in young adults were misdiagnosed as acute orbital cellulitis [10]. Similar to this study, our case displays a spectrum of lymphoid cells, aggregates of histiocytes, and foreign body giant cells that closely mimic to inflammatory/granulomatous pathology of orbit. IHC will be helpful for the early diagnosis of these cases.

Extranasal NKTCL is aggressive and behaves similarly to stage III/IV nasal disease, with worse median survival, reported to be only 4 months. Combined chemoradiotherapy protocols are advocated for the treatment of ENKTCL. Optimal chemotherapy regimens varied among institutions. SMILE regimens (dexamethasone, methotrexate, ifosfamide, lasparaginase, and etoposide), a relatively new induction therapy along with radiotherapy are used by most of the centers. It shows an overall response rate of 81% in NKTCL patients [2]. In a follow-up of 3 months, our patient is alive after initial chemotherapy.

CONCLUSION

The case presented here is the young age female patient who presented with proptosis and painful swelling of the right eye, creating confusion for treating general ophthalmologist. The rarity of this tumor and histopathology closely mimics inflammatory/ granulomatous pathology making it challenging to identify these tumors early. Even though our case is localized to the orbit, prognosis remains poor.

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