A nasal type extranodal NK/T-cell lymphoma (ENKL) is very rare in children. A pediatric nasal type ENKL is generally localized and is likely to have sensitivity to radiotherapy. The most common site is the upper airway tract, such as nasal region, Waldeyer’s ring, paranasal sinuses and palates. It usually presents with nasal symptoms, such as obstruction or epistaxis. We describe our experience of concurrent chemoradiotherapy in a 13-year old boy having incidentally detected nasal type ENKL on laryngoscopic examination who did not have nasal symptoms. He received three cycles of dexamethasone (40 mg/day for 3 days), ifosfamide (1,000 mg/m²/day for 3 days), VP-16 (67 mg/m²/day for 3 days) and carboplatin (200 mg/m² for 1 day) at 3-week intervals and 45 Gy intensity-modulated radiation therapy. He has been disease-free for 18 months after cessation of therapy.

Key Words: Extranodal NK/T-cell lymphoma, Nasal type; Laryngoscopic examination

Introduction

A nasal type, extranodal NK/T-cell lymphoma (ENKL) is extremely rare in children [1]. Nasal type ENKL is mostly seen in male adults in their 4th to 5th decade of life, and the prognosis is variable [1,2]. In the largest study from Peking Union Medical Center between 1988 and 2008, only 8 cases less than 15 years of age were diagnosed to have nasal type EKTL [1]. Only 4 (3.3%) among 121 non-Hodgkin lymphoma patients less than 18 years of age were having nasal type ENKL from the report of Korean pediatric/adolescent lymphoma [3]. Most patients present with nasal symptoms, such as, nasal congestion, sore throat, dysphagia and epistaxis due to a destructive mass involving the midline facial tissues [1,2,4].

We describe our rare experience of incidentally detected nasal type ENKL on laryngoscopic examination who did not have nasal symptoms in a 13-year-old boy.
Case Report

A 13-year-old boy presented with a 1 cm-sized palpable cervical lymph node (LN). He was healthy, and did not have any remarkable symptoms such as fever, weight loss, and sweating.

Liver, spleen and other lymph nodes were not palpable. A complete blood count and biochemical tests including serum lactate dehydrogenase level were within normal ranges. An ultrasonography of the neck revealed a 3.5 cm LN in the neck. He was referred to an otolaryngologist for biopsy. An ulcerative, necrotic mass was incidentally detected in the nasopharynx on routine laryngoscopic examination (Fig. 1A). At the time, the patient did not have nasal symptoms, such as congestion, sore throat, dysphagia or epistaxis. A facial computed tomography (CT) revealed a 1 cm extent of irregular mass-like lesion in posterior nasopharynx which was suggestive of lymphomatous involvement (Fig. 1B). The patient underwent a laryngoscopic biopsy. Histologically, the nasal tumor was composed predominantly of polymorphous cells with irregular nuclei and was positive for CD3, CD16, granzyme B, TIA but negative for CD56 by immunohistochemical stains (Fig. 2A-C). Epstein-Barr virus (EBV) was positive by in situ hybridization (Fig. 2D). These pathologic findings were compatible with ENKL. An excision biopsy of the node showed findings of reactive lymphadenitis. There was no evidence of involvement in other organs or metastasis on positron emission tomography-CT, bone marrow biopsy and cerebral spinal fluid exam. Polymerase chain reaction for EBV DNA was negative in peripheral blood. The patient was diagnosed with nasal type ENKL, stage IE. He received concurrent chemoradiotherapy (CCRT), consisting of three cycles of 2/3 DeVIC chemotherapy at 3-week intervals and 45 Gy intensity-modulated radiation therapy (IMRT) using simultaneous integrated boost approach to the involved field [5]. The 2/3 DeVIC chemotherapy consisted of dexamethasone (40 mg/day for 3 days), ifosfamide (1,000 mg/m²/day for 3 days), VP-16 (67 mg/m²/day for 3 days) and carboplatin (200 mg/m² for 1 day). Seven days after the beginning of chemotherapy, a total of 45 Gy in 25 fractions was given to the gross tumor volume with 37.5 Gy in 25 fractions to the clinical target volume, which included gross tumor volume with at least 1 cm margin.

He tolerated the CCRT sessions without any grade 3-4 toxicity. Two months after completion of CCRT, the follow-up facial CT showed disappearance of the nasopharyngeal mass (Fig. 1C). He remains disease-free without significant side effects for 18 months after cessation of therapy.

Discussion

The main presenting symptoms of nasal type ENKL are

![Fig. 1.](image)

(A) A necrotic lesion in the nasopharynx was incidentally detected on laryngoscopic examination. (B) Facial CT reveals a 1 cm, irregular mass-like lesion in posterior nasopharynx suggestive of lymphomatous involvement (arrow). (C) Two months after therapy, facial CT shows disappearance of nasopharyngeal mass.
nasal obstruction or epistaxis due to the site of involvement of the disease. The most common site is the upper airway tract, such as nasal region, Waldeyer’s ring, paranasal sinuses and palates. Preferential sites of extranasal involvement include the skin, gastrointestinal tract, and testis [6]. A nasal type ENKL is characterized by vascular damage and destruction, causing geographic necrosis and ulceration, especially in mucosal sites [6]. This case is very unique because he did not have any nasal symptoms, but the diagnosis could be suspected by the necrotic lesions, incidentally detected by laryngoscopy.

Histologic spectrum of nasal type ENKL is very broad, with diffuse infiltration of variable sized lymphomatous cells and atypia [6]. The typical immunophenotype of nasal type ENKL is positive for CD2, cytoplasmic CD3 epsilon, CD56, and negative for surface CD3. Cytotoxic granules, such as granzyme B, perforin and TIA-1 are also positive [7]. EBV is closely associated with ENKL with regard to lymphomagenesis. Apoptosis of EBV-related lymphomatoid cells releases EBV DNA into the peripheral blood [7]. Thus, it is important to measure the plasma or whole blood EBV DNA level for predicting the prognosis before the treatment, monitoring of the response to treatment and follow-up after treatment [8]. The present case showed negativity for CD56, but positivity for CD16 as the marker of NK cells, and also for granzyme B and TIA as cytotoxic molecules. EBV in situ hybridization was positive, but whole blood EBV DNA was absent at diagnosis, which might portend a good prognosis.

Nasal type ENKL has a variable prognosis. In adults, it usually has aggressive clinical course and poor prognosis.

Fig. 2. (A) The pathologic finding shows necrotic change (H&E, ×40). (B) The tumor cells are polymorphous appearance with irregular nuclei (H&E, ×400). Tumor cells are positive for CD16 immunohistochemistry (C) and for EBV in situ hybridization (×400) (D).
with 45% of 1-year overall survival rate for stage IV disease [2,9]. However, nasal type ENKL in children was characterized by good performance, propensity of localized disease (stage I and II) and low-score (less than 2) in the age-adjusted international prognostic index [1,10]. The 5-year progression-free survival was 68% with primary radiotherapy and/or combined chemotherapy [1].

Given its rarity, no randomized or prospective studies have been performed on pediatric patients with nasal type ENKL, and current treatment strategies are based on treatments for adult ENKL. Radiotherapy is an important modality in pediatric ENKL, especially in localized disease [1]. However, although the complete remission rate of initial radiotherapy was much higher than that of chemotherapy (73.7% vs. 16.7%), most patients had to receive combined chemotherapy due to high relapse rate [1]. The present patient also underwent the CCRT and is disease-free for 18 months after the end of therapy. Even though this patient received IMRT in an attempt to reduce late complications induced by radiotherapy such as bony deformity, or functional changes, long-term follow-up is needed to address the issues.

In conclusion, although very rare, a nasal type ENKL should be considered in children and adolescents when any unusual necrotic lesion is seen on the nasopharynx. As there is no consensus in the management for ENKL in children and adolescents, the treatment plan has been extrapolated from adult experiences. Thus, a prospective, collaborative study including a larger number of cases is warranted.

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