

Extranodal NK/T cell lymphoma, nasal type: CT imaging findings

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Abstract: Extranodal NK/T cell lymphoma (ENKTL), nasal type is a rare, aggressive disease affecting the midfacial and nasopalatal region in the head. The pathogenesis of the disease is unknown, but the disease has been linked to Epstein - Barr virus (EBV) infection. Early diagnosis of the disease is the best way to increase the prognosis and quality of life in the patients. However, it is still a challenge to diagnose this disease earlier. Early sign and symptoms like nasal blockage and rhinorrhea of this disease mimic that of the benign nasal diseases and in the later stage, it is confused with other destructive nasal diseases. This disease is diagnosed histopathologically. Cytoplasmic CD3 (Epsilon), CD2 and CD56 antigens of NK and T cells are expressed by the diseased tissue. Pathologically, tumor cells surround the vessel in a circular manner sometime infiltrating the vessel itself and destroying it. CT and MRI scans are helpful in staging the disease and finding out the extent of destruction. Radiotherapy is used in the early stage of the disease with or without chemotherapy, but the later stage and relapse cases are treated with chemotherapy. Relapse rate is high in this disease.

Keywords: Extranodal NK/T cell lymphoma (ENKTL), nasal type; Epstein Barr virus; radiotherapy; chemotherapy

I. Introduction

Extranodal Natural Killer (NK)/T-cell lymphoma (ENKTL), nasal type is an entity of non-Hodgkin's lymphoma, which was previously called by various names, such as lethal midline granuloma, midline malignant reticulosis or pleomorphic reticulosis [1]. It is a rare aggressive tumor. It affects midface, nasopalatine and orbital wall leading to total destruction if untreated early [2]. Besides nasopharyngeal region, it can also affect extra nasal areas as skin, soft tissue, testes, gastrointestinal and upper respiratory tracts [2]. It is now definitively categorized in the World Health Organization lymphoma classification system as Extranodal NK/T cell lymphoma, nasal type [1, 2, 3]. This disease is more prevalent in the descendants of Southeast Asian, south and Central American while less common in African and European descents [1, 2]. This disease accounts to about 7-10% of every non-Hodgkin's lymphoma in Southeast Asia [8, 16]. It affects male more than the female in the ratio of 2-3.6:1 according to various literatures [2].

The clinical history of this disease is nonspecific. Majority of the patients present with symptoms such as nasal blockage, rhinorrhea initially, which mimic benign nasal diseases [3, 6, 8]. In the later stage of the disease progression, necrotic purulent discharges with blood are found due to destruction of the aerodigestive tract, thus resembling destructive nasal diseases such as tertiary syphilis, Wegener's granulomatosis, pharyngeal squamous-cell carcinoma and lymphoma [3,4]. Prognosis depends on early diagnosis and treatment for increasing the overall quality and survival of the patients in this disease [6]. Multiple biopsies of the lesion for histologic and immunophenotyping examination provide a definitive diagnosis [1]. Imaging like CT, MRI and PET/CT is best helpful in finding the extent of disease progression and staging of the disease after the histopathological diagnosis has been made [3,8].

The pathogenesis of the disease is unknown but has been linked to EBV infection, which is associated with poor prognosis [1, 2, 5]. Pathologically, the disease presents with angiocentric and angiodestruction of the vessel [5]. Histologically, it expresses cytoplasmic CD3 Epsilon and CD56 with the evidence of EBV infection in the past or concurrent [8]. Cytoplasmic granules like TIA-1, granzyme B and perforin are also expressed [8]. While the disease is known to spread and destruct the surrounding structures, metastasis of this disease is uncommon [7]. Five-year overall survival of this disease is 42% [8].

II. Material and methods

Scan of 10 cases of Extranodal NK/T cell lymphoma, nasal types were collected and retrospectively reviewed between 2001 and 2011 from our hospital. The ages of the patients range from 33 years to 71 years (mean 53 years); of them 7 were male and 3 female. Cases were all histopathologically diagnose using immunohistochemical methods and conformed to be ENKTL nasal type.

All the patients went through standard CT scan examination of the head and sinonasal region in the axial and coronal planes. The scan was taken from the hard palate to the end of the frontal sinus on either one of the two scanner machines available in the hospital; Siemens Somatom sensation 64 (Siemens, Germany) and Brilliance Ict 256 slice (Philips Medical Systems, USA) machines with the following parameters: 120 kvp, 150-

200 mAs, collimation of 64*0.6mm, pitch of 0.8mm and primary reconstruction of 0.4 mm, 100-120 ml Of intravenous contrast medium, flow rate of 2.0 ml/s. 3mm thick axial reconstruction And 3 mm coronal multiplanar reconstruction (MRP) were obtained with bone and soft tissue algorithms. CT images were retrospectively reviewed by two Radiologists who knew about the histological diagnosis. Tumors were investigated for signal characteristics, size, distribution, appearance, local invasion and bone destruction and were staged according to Ann Arbor classification system. Our institution (Zhenjiang City No. 1 Hospital affiliated to Jiangsu University) review board approved this retrospective study.

III. Results

The presenting symptoms of the patient were nasal blockage (n = 6), anosmia (n = 5), nasal discharge (n = 2), swelling of the nose (n = 2), facial swelling with blood in the tears (n = 1) and fever (n = 1). More than one symptom was present in many individuals.

On the non-contrast CT scan, 8 cases (80%) had mucosal thickening and infiltrative lesion in the nasal septum. The lesion was homogenous to the surrounding tissues (Fig.1). On contrast CT, infiltrative lesions were heterogeneously enhanced compare to the surrounding tissues (Fig.2, Fig. 4, and Fig.5). 5 cases (50%) had nasal ala thickening and infiltrated by the lymphoma (Fig.5, Fig.6). Meanwhile, 4 cases (40%) had bony erosion of the nasal septum and maxillary sinus wall destruction (Fig. 1, Fig. 3, and Fig. 4). 4 cases (40%) had a thickened posterior nasopharyngeal wall mucosa with enhancement (Fig.5, Fig. 6, Fig. 7, and Fig.8). Finally, according to the Ann Arbor staging, 6 patients were categorized as stage IE and remaining 4 patients were categorized as stage IIE Extranodal NK/T cell lymphoma, nasal type.

Biopsy was taken on all patients. Under the microscope, the biopsied specimen shows necrosis and exudates infiltration. Atypical lymphoid cell, histiocytes and eosinophils were present diffusely. The size of the cells was variable between different specimens. These cells have an irregular nucleus with various amounts of cytoplasm. The cells were arranged around the vessel angiocentrically with perivascular cuffing and destroying the vessel by infiltrating the vessel wall. The immunohistochemical reports were positive for expression of cytoplasmic CD3 (Epsilon), CD56, TIA-1, granzyme B, perforin (+), while negative for CD20, CD21, CK, CD30, CD5, CD4, CD8 (-). The disease was diagnosed as Extranodal NK/T cell lymphoma, nasal type.

6 patients with stage I E ENKTL nasal type were treated with radiotherapy alone. Remaining 4 patients with stage II E ENKTL nasal type received a combination of radiotherapy and chemotherapy. Standard chemotherapy regimen of CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) was initiated before radiotherapy.

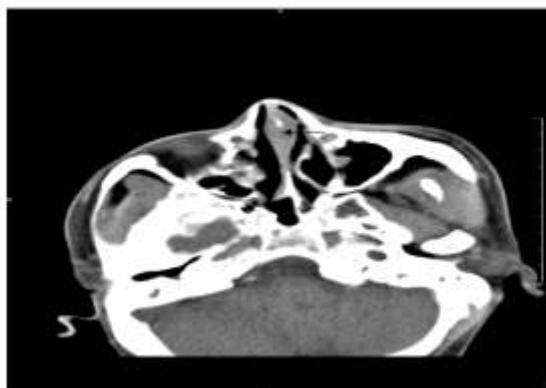


Fig.1

Fig.1 Axial CT of a 47 years old man shows a thickening of the nasal septum(black arrow) with bone erosion noted in the nasal septum.



Fig.2

Fig. 2 Axial CT of a 38 years old man shows a left nasal cavity mass and blockage, with nasal septum deviated to the left side.



Fig.3

Fig.3 An axial CT scan of a 33 years old man shows a large mass occupying right maxillary sinus, and the ostiomeatal complex is totally obstructed and enlarged by the mass (black arrow). Bone destruction noted at the right maxillary medial wall.



Fig.4

Fig.4 A CT scan of a 64 years old man with a mass noted at the left nasal cavity and obstruction of the left nasal cavity (black arrow). Bony destruction noted on the nasal septum and left maxillary sinus wall.

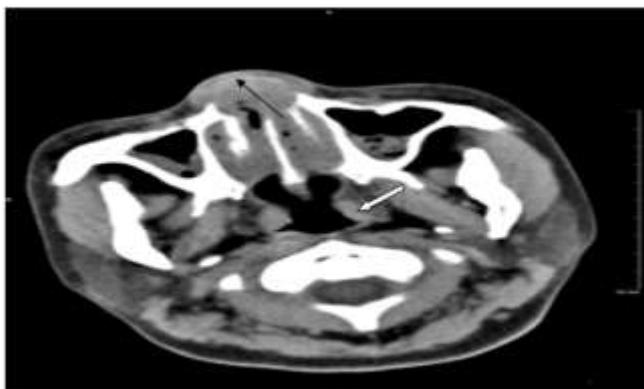


Fig.5

Fig.5 An axial CECT scan of a 38 years old man shows enhancement of mucosal mass in the nasal cavity bilateral and mild thickening of peripheral wall of maxillary sinus bilaterally. Bilateral nasal ala thickened and infiltrated (black arrow) and the posterior nasopharyngeal mucosal wall thickened and enhanced (white solid arrow).

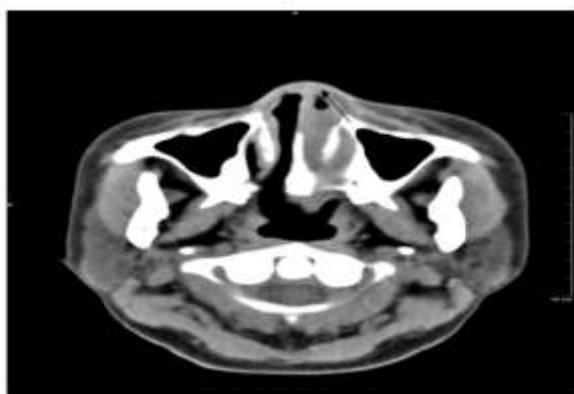


Fig.6

Fig.6 An axial CT of 45 years old man shows nasal ala enhancement and infiltration (black arrow) with presence of mucosal mass in the left nasal cavity.

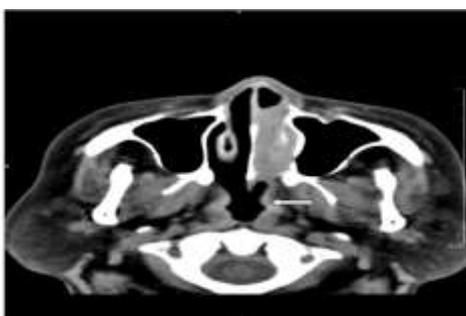


Fig.7

Fig.7 An axial CT scan of a 60 years old woman shows left nasal cavity mass with obstruction. Posterior nasopharynx wall thickening and enhanced compare to the surrounding tissue (white solid arrow).

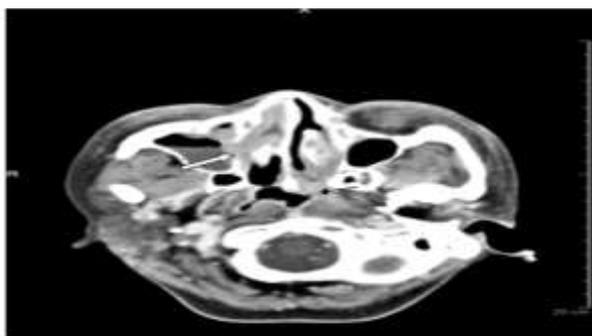


Fig.8

Fig.8 An axial CT scan of a 61 years old man shows right nasal cavity mass extended to right maxillary sinus and bony destruction is noted at the maxillary sinus wall (white solid arrow). Posterior wall of the nasopharynx thickened and enhanced with obliteration of the left pharyngeal recess (black arrow).

IV. Discussion

ENKTL lymphoma nasal type is a rare disease common in the Southeast Asian, Mesoamericans and the South American heritage [7, 8]. However, the disease is less common in the European and the African population [7, 8, 16]. ENKTL lymphoma nasal type accounts about 7-10% of all non-Hodgkin's lymphoma present in the Southeast Asian population [8, 16]. Typically, patients present with this disease in the fourth and fifth decade of life, but it can occur at any age [8]. Mean age of the patients in our studies was 53 years. Male has a higher predilection than the women in the ratio of 2-3.6: 1, in our case 2.3-1 [2, 4].

It is one of the most aggressive diseases, and the prognosis depends on early diagnosis of the disease [8]. However, many benign diseases mimic the sign and symptoms of this disease. Symptoms such as nasal blockage and rhinorrhea are common to many nasal diseases like rhinitis, sinusitis and nasal polyps [3, 6, 8]. Early diagnosis is a challenge to this disease [13]. That is why many patients arrive late in disease course.

CT scan is the first examination done on the PNS to rule out various pathologies. It can provide useful information about the size, morphology and extent of invasiveness of the tumor lesion as well as bone destruction of the surrounding structure [8]. CT scan is used in the staging of the disease, predicting the prognosis, overall survival and disease free state of the patient [10]. CT scan is also better in differentiating bone erosion and destruction compare to MRI. However, MRI is the first choice in detecting the extent of diseases' progression. MRI has a good resolution in differentiating various soft-tissue structures and also has a multiplanar scanning function [6, 16, 17]. These functions are helpful in differentiating normal tissue or inflammation from the tumor infiltrated tissue in the nasal cavity [6]. Moreover, CT and MRI findings are complimentary to one another in distinguishing ENKTL nasal type from various sinonasal destructive diseases [1, 12]. Thus CT/ MRI have been helpful in the staging of the disease and prognosis of the disease [3, 8]. Recent studies have demonstrated that 18F-FDG PET/CT scan are more sensitive in detecting both nodal and infiltrative ENKTL patterns [9]. In addition, 18F-FDG PET/CT scan are better and more accurate in staging ENKTL nasal type [9].

Definitive diagnosis should depend on the histopathological reports of the lesion biopsy and clinical finding [1, 7]. Presence of EBV titer can further aid in the diagnosis as well as predicting the prognosis. Recent advances in diagnosis and knowledge about the disease have led to better understanding of the disease and increase in the numbers of new cases around the world.

The pathogenesis of the disease is relatively unknown. However, it has been linked to Epstein Bar Virus infection, and the prognosis of the diseases is poor [1, 2, 5]. There are high recurrence rate and extension to other extranasal sites with EBV positive disease [7]. Under a microscope, ENKTL nasal type has very distinct pathologic findings. The tumor cells are present in a circular fashion around a vessel wall (angiocentric), sometime penetrating into the vessel itself causing destruction of the vessel and thrombosis (angiodestructive lesion) [5]. Hence angiocentric lymphoma as it had been called in the Revised European- American classification of lymphoid neoplasm (before revision), which has not always been the case [3, 16].

Immunophenotypically, tumor cells like NK and T lymphocytes express various markers, which are typical for the disease. NK cell expresses CD2+, CD56+ and cytoplasmic CD3 Epsilon but negative for CD3 and CD20 expression [8, 15]. These activated NK cells also express cytotoxic granules associated protein such as granzyme B, perforins and T cell-restricted intracellular antigen (TIA) [8, 15]. Expression of these cytotoxic granules together with EBV positivity is the requisite for the diagnosis of Extranodal NK/T cell lymphoma nasal type according to WHO classification [8, 13].

There are various treatments protocols for this disease. Treatment is planned according to the stage of the disease on presentation [8]. Radiotherapy is initiated for the patient with localized disease [8]. Complete remission of the disease occurs in about 70% of the cases with localized disease. However, there is high relapse rate about 50% among those treated with radiotherapy alone [8]. Concurrent use of chemotherapy followed by radiotherapy is the only way to decrease relapse rate [15]. Common anthracycline containing chemoagents like cyclophosphamide, doxorubicin, vincristine and prednisolone combination also called as CHOP regimen is used [8, 14]. For more advance diseases, chemotherapy is the treatment of choice [14]. Still the result is far from satisfactory. There is a significant relapse of the disease in the patient with this treatment; it may be due to the expression of multi-drug resistant 1 (MDR1) Gene, leading to over production of p-glycoprotein [15]. Therefore, non-anthracycline drugs are more suitable for this kind of patient. Recently, combination regimens of dexamethasone, methotrexate, ifosfamide, L- asparaginase and etoposide (SMILE) have been tried on different patients with relapse or refractory cases [8, 15]. The results were quite remarkable. However, it is too early to get a definitive long-term result [8, 15].

V. Conclusion

ENKTL nasal type is an aggressive form of lymphoma, which has a poor prognosis. It is a disease which needs early diagnosis to increase the overall survivability and quality of life. Immunohistochemistry is used in the diagnosis of the patients [8, 13]. Clinical signs and symptoms of this disease are not that specific. It mimics benign nasal disease so definite early diagnosis is a challenge [13]. Treatment is also a challenge to this disease [5]. In our studies, we found some radiologic signs that might be helpful in making a diagnosis of the ENKTL nasal type. Most cases (80%) present with mucosal thickening of the nasal septum. The lesions were infiltrative and homogeneous on the non-contrast CT scan. On the contrast scan, the lesion was heterogeneously enhanced compare to the surrounding tissues. Nasal septum, nasal ala, sinuses and nasopharynx have been invaded in our studies. Bony erosion was present in nasal septum and the maxillary sinus wall in 40% of the cases. Therefore, disease presenting with nasal mass that involves surrounding soft tissue, sinuses, nasopharynx with or without bony erosion; ENKTL nasal type should be included in the differential diagnosis. Earlier the diagnosis of the disease, better the survival and quality of life in the patient.

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