ISSN 2250-3153

Midline Lethal Granuloma Extra Nodal Natural Killer Cell / T Cell Lymphoma, Nasal Type- A Rare Presentation In Young Adult South Indian Female

Ramakrishnan R, Purushothaman P K, Vikram P S J

Department of ENT, Head and Neck Surgery, SRM Medical College Hospital and Research Centre, SRM nagar, Potheri-603203, Kancheepuram District, Tamil Nadu, India.

***Abstract*-** Extranodal natural killer/T cell lymphoma, nasal type, is a Non-Hodgkins lymphoma, most commonly affecting the nasal cavity, paranasal sinuses and nasopharynx. Clinically it is characterised by destruction of facial tissues, commencing in the midline. In most cases it either arises from malignant transformation of natural killer cells (NK) or cytotoxic T cells. Extranodal NK/T cell lymphoma, nasal type, is rare, but even rarer in females. The purpose of this article is to report a severe case of extranodal NK/T cell lymphoma, nasal type, in young south Indian female and improvement of midfacial swelling after radiotherapy.

***Index Terms*-** Midline lethal granuloma, Extranodal NK/T cell lymphoma

I. INTRODUCTION

Extranodal natural killer/T cell (NK/T cell) lymphoma, nasal type, is a rare non-Hodgkin lymphoma originating in the nasal cavity or paranasal sinuses. It is strongly associated with Epstein-Barr virus (EBV) infection. Its prevalence is higher in countries in South-East Asia and in Central and South America than in Europe and North America. It occurs in middle-aged persons and affects males more frequently than females [1-5]. Most cases arise from natural killer cells, only a few from cytotoxic T-cells [6, 7]. Clinically, extranodal NK/T cell lymphoma, nasal type, is characterized by progressive midline facial destruction.

We report a rare presentation of extranodal NK/T cell lymphoma, nasal type, in a young adult south Indian female, that had caused extreme deformity of the midface with improvement after radiotherapy.

II. CASE REPORT

A 20yr old female presented to ENT OPD of our hospital with midline facial swelling (Figure 1). The patient stated that about 6 months before, a small growth had appeared in her nose, became ulcerated and then enlarged progressively. As the lesion enlarged, her nose became blocked with a discharge. She frequently complained of headaches. She does not have any adverse habits and had been in good health until the facial condition started. On admission to hospital she had a fever, headache, left conjunctivitis. She had marked swelling of the left eyelids, lower part of the nose, and the entire midface. On anterior rhinoscopy, she had multiple ulcerations in the left inferior turbinate. (Figure 1) There were no intraoral or extra-facial cutaneous lesions. The regional lymph nodes were not enlarged and clinically and radiologically the chest was normal. Intravenous fluids and antibiotics were given. The patient was anaemic, was HIV-seronegative and was negative for syphilis. There was leucocytosis but not lymphocytosis, and the erythrocyte sedimentation rate, C-reactive protein and lactate dehydrogenase were elevated. Computed tomographic (CT) scans showed left frontal, ethmoid and maxillary sinus opacification, mild fullness of left fossa of rosenmuller due to pharyngeal involvement. (Figures 2).

Biopsy from left inferior turbinate showed necrosis, polymorphous proliferation of cells and vascular proliferation. No lining epithelium was seen and detached fragments of fibrinous exudates were also present. Many of the cells showed cleaved nuclei with some scattered mitosis and severe apoptosis. Fungal stain was negative. Immunophenotypically, the tumour cells were positive for CD3 and CD56 but negative for CD20. Some of the large atypical lymphocytes were positive for CD3. As facilities were not available for in situ hybridization analysis to demonstrate whether the malignant cells harboured EBV small-encoded RNA, it was not done.

As the clinical and histological features were consistent with a diagnosis of extranodal NK/T cell lymphoma, nasal type, the patient was referred to the Radiation oncology department for Radiotherapy. Radical dose wide field radiotherapy of 55Gy given for 5 days a week for 6 weeks. Patient had improvement of midfacial swelling after same. Post RT PET CT was taken which revealed minimal soft tissue thickening in the left neck involving the level II upper and mid jugular group encircling the ipsilateral carotid and IJV. It also showed few enhancing nodes in the level IIA jugular group, neck nodes involving the right IIA & IIB levels, mediastinal node involving the aortopulmonary regions. The patient is on regular 2 weekly follow up.

Fig 1 showing before and after radiotherapy in a case of “Midline lethal granuloma” Fig .2 showing CT scan – showing soft tissue encroachment in midline lethal granuloma

Fig 1

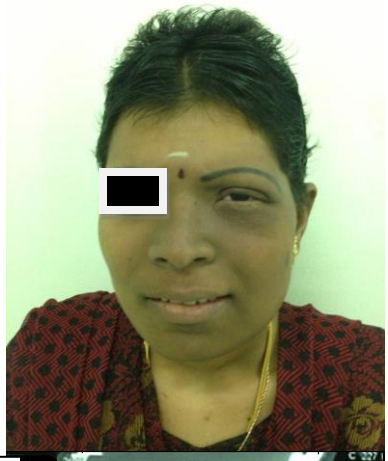
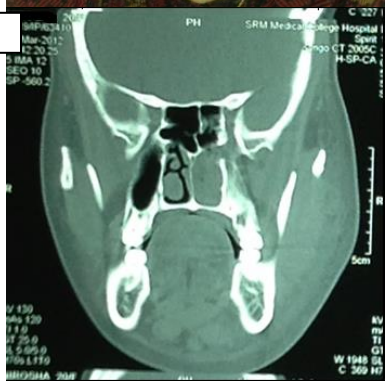


Fig 2



III. DISCUSSION

Progressive destructive necrotic lesions involving the midface, nose, paranasal sinuses and mouth were referred to by the generic name 'Midline Lethal granulomata'. However, with the advent of immuno-histochemical phenotyping methods it has become evident that 'midline lethal granuloma' comprises a heterogeneous group of disorders including non-Hodgkin lymphoma, Wegener granulomatosis and various granulomatous infections [2].

Extranodal NK/T cell lymphoma, nasal type, accounts for 7-10% of all non-Hodgkin lymphomas in Asia and Latin America, but for only 1% in Europe and North America [8]. In Korea, it accounts for about 75% of lymphomas arising within the nasal cavity and the paranasal sinuses. To the knowledge of the authors based on published reports, the prevalence of the disease in Indians, especially in south Indian female population is rare. Extranodal NK/T cell lymphoma, nasal type, is characterized histopathologically by angiocentric and angiodestructive growth, by tumour cells that vary in size and may harbour EBV in a clonal episomal form, and by an inflammatory cell infiltrate of plasma cells, histiocytes and eosinophils [1].

Initial signs and symptoms include nasal stuffiness, epistaxis and pain, owing to progressive tumour growth in the nose. As the tumour mass enlarges, invading and destroying structures in the upper anterior aerodigestive tract, it becomes progressively necrotic with a purulent discharge. Signs and symptoms are related to the sites involved. Secondary infection and haemorrhage are not infrequent [5, 6]. Metastasis is uncommon [8]. As extranodal NK/T cell lymphoma, nasal type, may clinically mimic other destructive disease entities affecting mid-facial structures including other lymphomas, nasopharyngeal squamous cell carcinoma, tertiary syphilis, Wegener granulomatosis and fungal infections, the definitive diagnosis must be based on histopathological, immunological and molecular studies [5].

Localised extranodal NK/T cell lymphoma, nasal type usually responds favourably to radiotherapy. As in any neoplasm the best clinical outcome is achieved when treatment is started early in the course of the disease. When the tumour has invaded or with bony erosion, radiotherapy must be supplemented with chemotherapy. Nevertheless, local recurrence occurs in about 50% of cases. Extensive local invasion, regional lymph node involvement, elevated serum lactate dehydrogenase, raised EBV DNA titres and systemic signs (fever, night sweats, weight loss) are associated with a poor prognosis [3,4,6,9], and overall, the prognosis is poor. The five year survival rate is reportedly between 38% and 85%. About 25% of lymphomas that fulfil the histological, immunological and molecular criteria of diagnosis for extranodal NK/T cell lymphoma, nasal type, may arise in other sites of the upper aerodigestive tract (e.g. nasopharynx, palate), and in sites outside the upper aerodigestive tract including the skin, the gastrointestinal tract and the testis. It appears that no matter where it arises in the upper aerodigestive tract, the course of the disease is similar; but when it arises at other sites it runs a more aggressive clinical course, frequently disseminating to the spleen, skin or to bone marrow [1].

Immunophenotypically, the malignant tumour cells, like the natural killer cells from which they originate express CD2, cytoplasmic CD3 and CD56. In some cases they may also express cytotoxic granular-associated proteins, granzyme B, perforin, and T cell-restricted intracellular antigen (TIA-1). Genotypically, the malignant tumour cell expresses the T cell receptor gene in its germline configuration, but there is no monoclonal rearrangement of the T cell receptor [1]. However, there are cases in which the malignant cells lack CD56 and thus do not express the classic phenotype of NK cells or they express an aberrant profile of CD8+ T cell antigens. Nevertheless these are well-recognised subsets of extranodal NK/T cell lymphoma, nasal type, because the clinical and histological features are characteristic [1]. As NK cells and T cells may arise from common progenitor cells, NK cells may express some T cell

antigens, and T cells may express some NK cell antigens, so that cells of extranodal NK/T cell lymphoma, nasal type, may express both NK cell and T cell antigens [8].

Our patient's tumour showed an angiocentric pattern of growth, and immunophenotypically, the tumour cells were CD56 positive, confirming the histological diagnosis of extranodal NK/T cell lymphoma, nasal type. Some extranodal NK/T cell lymphomas, nasal type consist of large cells expressing CD3[1]. The large atypical cells in our patient was also positive for CD3 apart from CD56, it was confirmed that she was suffering from extranodal NK/T cell lymphoma, nasal type. In the nose and paranasal sinuses, extranodal NK/T cell lymphoma, nasal type, is characterized by extensive local destruction of soft tissue, cartilage and bone, brought about by the aggressive angiocentric and angioinvasive nature of the tumour that results in functional incompetence of the vasculature with consequent ischaemia. [4, 6].

Typically, as seen on CT scans, the established soft tissue tumour obliterates the nasal passages and frequently invades and obliterates the maxillary sinuses. Our patient presented with extensive mid facial swelling, and her disease was diagnosed only late in the course of the disease, about six months after the initial symptoms. By then the tumour had already largely destroyed the structure of the nose and had invaded the maxillary, ethmoidal, frontal, sphenoidal sinuses and the nasopharynx.

Our patient was diagnosed as T3 stage of the tumour based on the TNM staging. The extent of invasion by the tumour is classified by TNM staging: T1 refers to a tumour confined to the nose; T2 to additional tumour invasion of the maxillary and anterior ethmoidal sinuses and/or the hard palate; T3 to further tumour invasion involving the posterior ethmoidal sinuses, sphenoidal sinuses, orbit, maxillary alveolar process of bone, and buccal tissues; and T4 to tumour invasion extending to the mandibular alveolar process of bone, to the infratemporal fossa, to the nasopharynx and to the cranial fossa [1, 5].

The almost invariable presence of EBV in a latent clonal episomal form in the cells of the extranodal NK/T cell lymphoma, nasal type, strongly suggests a direct role of the virus in the pathogenesis of the tumour [1, 6]. EBV infects the NK/T cells and establishes latent infection before initial transformation of NK/T cells has occurred, prior to the clonal divergence and clonal expansion of the cancerous cells. The presence of this clonotypic EBV genome in a latent form in the tumour cells strongly supports, but does not prove the pathogenic role of EBV in NK/T lymphomagenesis [7]. The active involvement of EBV in the pathogenesis of extranodal NK/T cell lymphoma, nasal type, is further supported by the direct positive correlation between EBV load in the tumour and the extent of the disease, and by the high titres of IgG antibodies to EBV in persons with the disease. Plasma titre of EBV DNA serves as a marker of tumour viral burden and fluctuates with the status of the disease and the response to treatment because EBV DNA fragments are released from apoptotic tumour cells and escape into the circulation [4, 6, and 8]. In our hospital, as there were no facilities for in-situ hybridization studies, we were not able to determine whether or not the cells of the extranodal NK/T cell lymphoma, nasal type, of our patient carried EBV encoded early RNA.

Chemotherapy is the mainstay of treatment for advanced stage NK cell lymphomas. Conventional CHOP or CHOP like regimens give poor outcome.

When the clinical and histological features were consistent with a diagnosis of extranodal NK/T cell lymphoma, nasal type the management of choice is a radical dose, wide field radiotherapy of 55Gy and chemotherapy. Initial biopsy can prove to be negative; hence multiple site biopsies with high degree of suspicion are important

IV. CONCLUSION

We present a case of extranodal NK/T cell lymphoma, nasal type in a young adult south Indian female, and a tumour which appears to be rare in south Indian females. We could find few cases so far reported in the literature of this rare presentation in south Indian female population.

The purpose of this article is to add to the information available with regard to extranodal NK/T cell lymphoma, nasal type about its clinical features, pathology, investigations and management of the disease. A high degree of suspicion regarding same will help in early diagnosis and early appropriate intervention. Immunohistochemistry is mandatory to identify lesion for its appropriate management.

REFERENCES

[1] Hasserjian RP, Harris NL: NK-cell lymphomas and leukemias: a spectrum of tumors with variable manifestations and immunophenotype. Am J Clin Pathol 2007, 127:860–868.

[2] Rodrigo JP, Suarez C, Rinaldo A, Devaney KO, Carbone A, Barnes L, Heffner DK, Ferlito A: Idiopathic midline destructive disease: fact or fiction. Oral Oncol 2005, 41:340–348.

[3] Isobe K, Uno T, Tamaru J, Kawakami H, Ueno N, Wakita H, Okada J, Itami J, Ito H: Extranodal natural killer/T-cell lymphoma, nasal type: the significance of radiotherapeutic parameters. Cancer 2006, 106:609–615.

[4] Al-Hakeem DA, Fedele S, Carlos R, Porter S: Extranodal NK/T-cell lymphoma, nasal type. Oral Oncol 2007, 43:4–14.

[5] Neville B, Damm D, Allen C, Bouquot J, Neville B: Hematologic Disorders. In Oral and Maxillofacial Pathology. 3rd edition. Edited by Neville B, Damm D, Allen C, Bouquot J, Neville B. Missouri: Saunders Elsevier; 2009.

[6] Liang R: Advances in the management and monitoring of extranodal NK/T-cell lymphoma, nasal type. Br J Haematol 2009, 147:13–21.

[7] Chiang AK, Tao Q, Srivastava G, Ho FC: Nasal NK- and T-cell lymphomas share the same type of Epstein-Barr virus latency as nasopharyngeal carcinoma and Hodgkin's disease. Int J Cancer 1996, 68:285–290.

[8] Gill H, Liang RH, Tse E: Extranodal natural-killer/t-cell lymphoma, nasal type. Adv hematol 2010, 2010:627401.

[9] Kim TM, Park YH, Lee SY, Kim JH, Kim DW, Im SA, Kim TY, Kim CW, Heo DS, Bang YJ, et al: Local tumor invasiveness is more predictive of survival than International Prognostic Index in stage I(E)/II(E) extranodal NK/T-cell lymphoma, nasal type. Blood 2005, 106:3785–3790.

[10] Yamaguchi M, Oqawa S, Nomoto Y, Oka K, Taniguchi M, Nakase K, Kobayashi T, Shiku H: Treatment outcome of nasal NK-cell lymphoma: a report of 12consecutively-diagnosed cases and a review of theliterature. J Clin Exp Hematopathol 2001, 41:93–99.

AUTHORS

First Author – Ramakrishnan R, MS (ENT), DNB (ENT), Assistant professor, SRM medical college hospital and research centre, openupramki@gmail.com
Second Author – Purushothaman P.K, MS (ENT), Associate professor, SRM medical college hospital and research centre, entpurush@gmail.com

Third Author – Vikram P.S.J, MBBS, Postgraduate resident, SRM medical college hospital and research centre, vikrampsj@yahoo.com.

Correspondence Author – Ramakrishnan R, MS (ENT), DNB (ENT), Assistant professor, SRM medical college hospital and research centre, openupramki@gmail.com,contact no: +919840705466, 044 22232258.