Case Report

Plasmablastic lymphoma in the paranasal sinus in a HIV positive patient: A rare entity

Deepthi Shetty, Prashanth Shetty, Chethana Dinkar

Abstract

Non-Hodgkin's lymphoma (NHL) ranks second after Kaposi sarcoma in individuals who are infected with Human Immunodeficiency virus (HIV). Plasmablastic lymphoma (PBL) is a diffuse large B cell lymphoma (DLBCL), becoming increasingly more common in oral cavity of HIV patients. PBL has been a investigative and therapeutic challenge because of its atypical morphology, immunohistochemical profile and a clinical course which results in high rate of recurrence and demise. We have described a atypical case of PBL affecting the maxillary sinus extending to involve the ethmoid sinuses and nasal cavity in a HIV infected patient and a brief review of literature regarding PBL.

Keywords

Plasmablastic lymphoma, paranasal sinus, HIV infection

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Introduction

Non-Hodgkin's lymphoma (NHL) constitutes a collection of malignant neoplasm of lymphoreticular cells and repeatedly spreads into extra-nodal sites (33%). [1-2] "REAL (Revised European-American Lymphoma) classifies NHL as a heterogeneous group of diseases with peculiar morphological, phenotypic and molecular features". [3] It ranks the second most common HIV associated malignancy, providing clue for undiagnosed HIV infection, because these individuals are 60 times more at risk than the general population. [4-5] The most common area of presentation of extra-nodal NHL is the gastrointestinal tract and the rarest area is the head and neck region which accounts to 4% of all head and neck tumours.The most common site in the head and neck region is the Waldeyer's ring. [1]

Oral non hodgkins lymphomas are extremely rare and accounts for 0.1 to 5% of the cases with palate being the predominant site. [1-5] The sites which are rarely affected by primary NHL are the nasal cavities and the paranasal sinuses.[3] "Stein and coworkers in 1997 reported a series of aggressive non-Hodgkin's lymphomas (NHL) arising in the oral cavity of humanimmunodeficiency virus (HIV)-positive patients which consisted of large cells with plasma celldifferentiation, and were called plasmablastic lymphoma (PBL)".[6] Middle-aged and the elderly people are more commonly affected with a slight male predilection. [5] PBL has been a investigative and therapeutic challenge because of its atypical morphology, immunohistochemical profile and a clinical course which results in high rate of recurrence and demise. [7] We have described a atypical case of plasmablastic lymphoma in the maxillary sinus extending to the ethmoid sinus and nasal cavity in a HIV positive patient.

Case report

A 43 year old Indian lady presented to us with the chief complaint of painless swelling in the left cheek region since 2 months. She also complaints of nasal obstruction in relation to the left nostril and watering of the left eye with no visual disturbances. Her medical history revealed that she was diagnosed with HIV (Human immunodeficiency virus) infection 6 months back and is on ART (Anti retroviral therapy). Her family history revealed that she had lost her husband who also suffered from AIDS. Extraoral examination revealed a diffuse swelling over the left middle third of the face extending superiorly from the infraorbital rim and inferiorly till a line joining the alae of the nose and tragus of the ear, anteriorly from the alae of the nose and posteriorly till the tragus of the ear. On palpation swelling was firm, non tender with the lesion seen through the left nostril [Figuer 1]. She also had skin lesions on her hand which was clinically diagnosed to be molluscum contagiosum commonly found in immunodeficient individuals.

PNS radiograph was taken which revealed radiopacity in the left maxillary sinus. Contrast enhanced computed tomography (CECT) scan of the maxillary region with coronal [Figure 2] and axial sections were taken which revealed a irregular heterogeneously enhancing soft tissue density lesion in the left maxillary sinus with erosion of anterior and medial walls and central area of hypodensity suggestive of necrosis. There is extension of the soft tissue into anterior aspect of maxilla, medially extending into ethmoid sinus and nasal meatuses. Differential diagnosis of lymphomas, squamous cell carcinoma and fungal lesions were arrived at. An incisional biopsy was carried out after doing routine blood investigations. The biopsy sections showed skeletal muscle fibres, fatty tissue and fibrocollagenous tissue infiltrated by lymphoplasma cells and individual tumor cells with destruction of muscle fibres and fat necrosis leading to giant cell formation and granulomatous response.The tumor cells had scanty to moderate amphophilic cytoplasm with indistinct cell margin and large uniform round nuclei with prominent nucleoli suggestive of non hodgkins lymphoma, probably a plasmablastic lymphoma(PBL), a atypical variant of diffuse large B cell lymphoma (DLBCL) [Figure 3]. A confirmed diagnosis of PBL was arrived after an immunohistochemical study was done which showed malignant cells which were strongly positive for CD 138 with lambda chain restriction and negativity for CD 20, CK and CD 30 [Figure 4]. Patient was planned for chemotherapy and started on a standard CHOP regime. Day 1: cyclophosphomide 750 mg/m2, doxorubicin/adriamycin 50 mg/m2 and vincristine 1.4 mg/m2. Day 1 to Day 5: prednisolone (oral) 100 mg. Patient was lost for further follow up.

Figure 1*: Lesion seen in the left nostril*

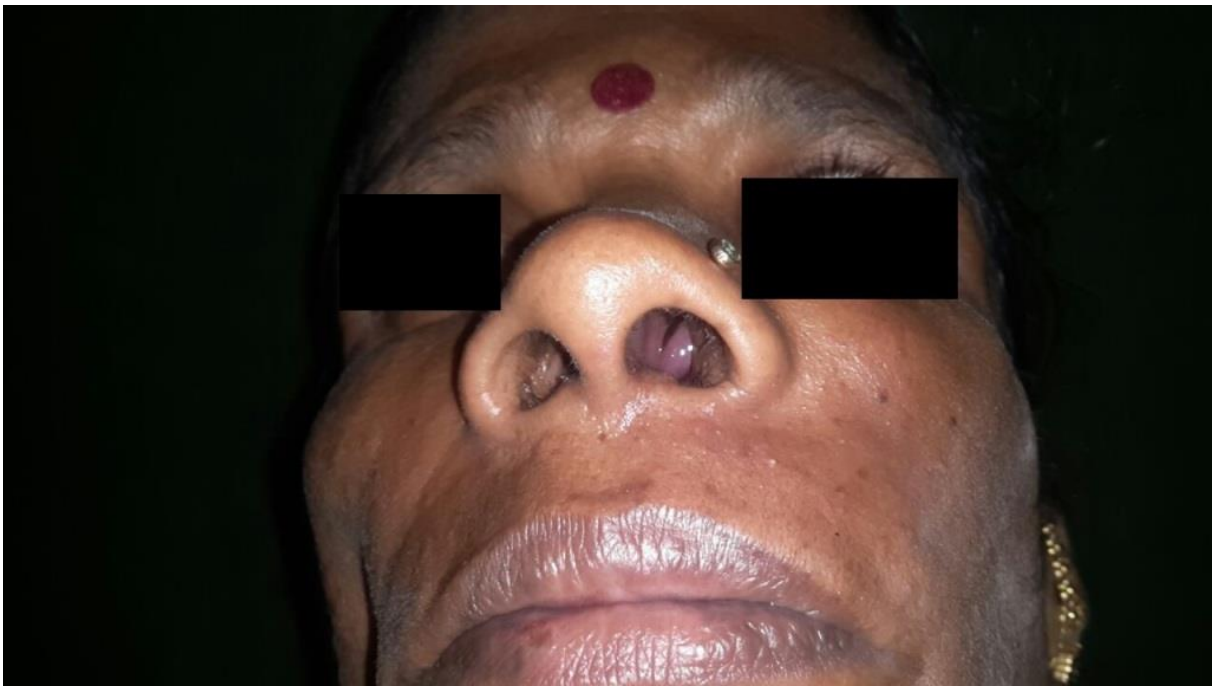


***Figure 2**: Coronal CT*

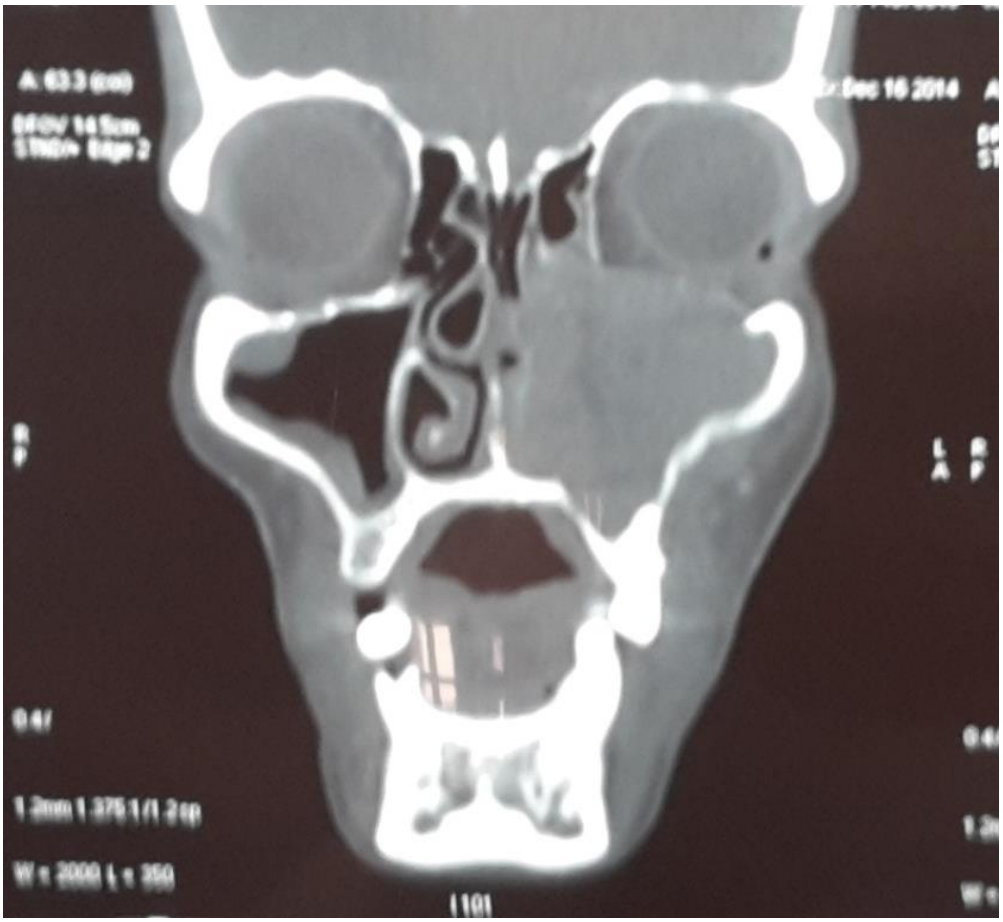


***Figure 3**: Large tumor cells with vesicular nucleus and prominent central nucleoli (40×)*

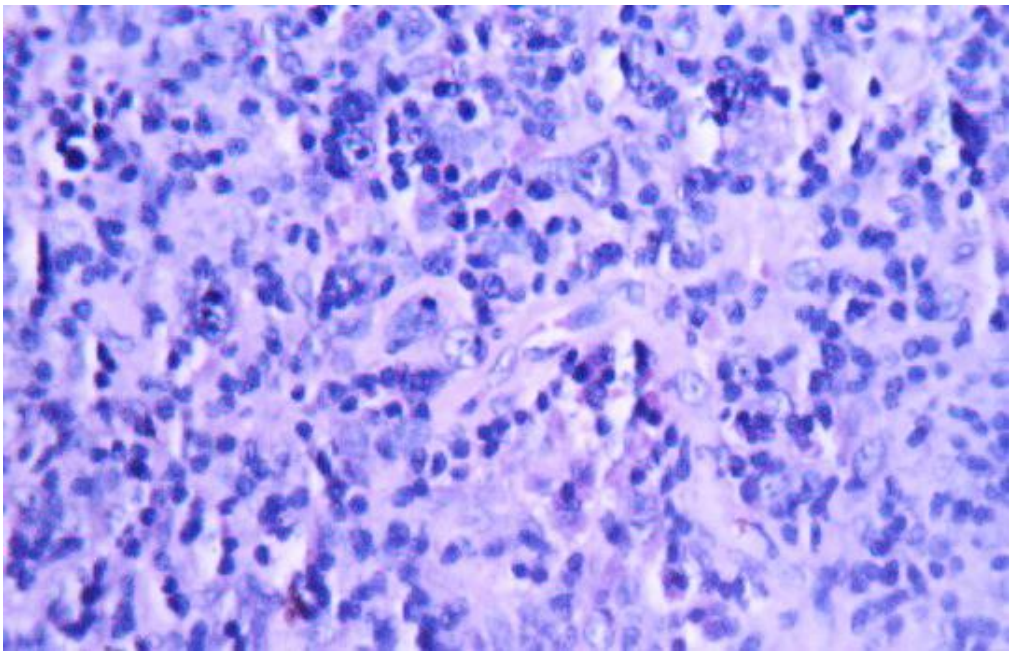
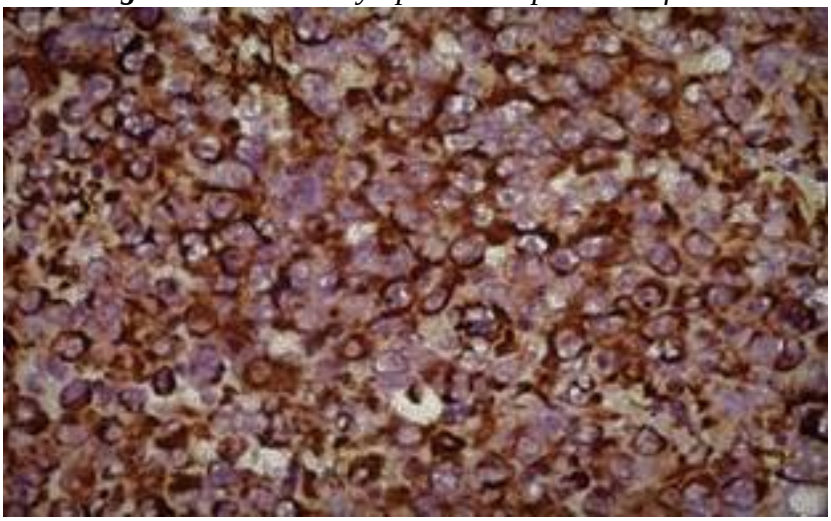


***Figure 4**: Positive Cytoplasmic expression of CD 138*



Discussion

"Non Hodgkin's lymphomas (NHL) are a heterogenous cluster of neoplasms affecting the lympho reticular system". [8] NHL of the sinonasal tract are the rarest constituting about 3% to 5% of all malignancies, with NHL comprising about 60% of all lymphomas. B cell lymphoma are predominantly seen in the paranasal sinuses and malignant cells with positive T-cell markers are predominantly seen in the nasal cavities. [3] In the western countries lymphomas of the maxillary sinus are frequently seen when compared to Asian population where nasal cavity lymphomas are more common.[3] However in our case the lesion was involving the maxillary sinus which extended to the nasal cavity. Plasmablasticlymphoma (PBL) is a atypical aggressive form of Non hodgkins lymphoma, accounting for approximately 2.6% of all AIDS-related lymphomas (ARLs).[1-6-7] "In the largest literature review of 228 patients with PBL, 157 patients (69%) were HIV-positive and 71 (31%) were HIV-negative".[7]

The aetiology of NHL is unclear but it is proposed that viral infections such as human herpes virus-8, Epstein-Barr virus and hepatitis C virus, [1-6] , and immunosuppressive diseases such as HIV, Hashimoto's thyroiditis, Helicobacter pylori gastritis, Ritcher's syndrome and Sjogren's syndrome may be the causative factors for the neoplasm.[1] "Chromosomal translocations play a key role in the pathogenesis determining oncogenic activation or the inactivation of tumor suppressor genes, with the subsequent malfunction of the mechanism of genomic rearrangement in lymphoid cells". [5]

NHL are commonly seen in the second and fifth decades of life. It approximately affects patients around the age of 40 years and has slight male predominance (3:2). [1] The peak occurence for the oral types occurs at 41 years (range 7–86 years) and for extraoral types occurs at 46 years (range 11– 86 years).Both are more common in males (the M⁄F ratio is 5.7:1 for the oral type and 4:1 for the extra-oral type).[6] Maxilla is more frequently involved than the mandible[1] with palate and gingiva accounting for almost 70% of lesions in Maxilla.[8] The most frequently affected sites of NHL are the gastrointestinal tract, lymph nodes, and skin. Other uncommon sites include the CNS, paranasal sinus, mediastinum, lungs, liver, and testes. [6-7]Bone marrow involvement has been reported in 30% in both HIV positive and negative patients.[7]

Squamous cell carcinomas are usually ulcerative thus differing from lymphomas which are seen submucosally. [3-9] Clinical signs and symptoms of lymphomas of the paranasal sinuses includes a mass in the nasal cavity, facial pain, headache, paresthesia, recurrent sinusitis, epistaxis , nasal obstruction and discharge, eyelid swelling, diplopia and proptosis if orbital invasion has occurred. [3-9] Early diagnosis of primary NHL of the paranasal sinuses was difficult in our patient, because this lesion developed in the sinus and expanded towards the nasal cavity not causing symptoms in the early stages. Symptoms appeared only after reaching a considerable size and involvement, and they mimicked other nasal or head and neck diseases.

Radiological imaging is an important diagnostic tool which determines the extension of the tumor, bony destruction, mucosal thickening, and preference of biopsy site and route. CT is the best

imaging modality for demonstrating fine bony details. Among the paranasal sinuses the maxillary sinuses are the most commonly affected, followed by the ethmoidal , frontal sinuses and the sphenoid sinuses being the rarest. [9]In our case the medial and anterior walls of the maxillary sinuses were destroyed extending to the ethmoid sinuses and nasal meatuses which was easily detected in CT.

Plasmablastic lymphoma is characterised by a monomorphic proliferation of large, round or oval cells, with copious cytoplasm and eccentrically placed nuclei, a single prominent central nucleolus or multiple peripherally located nucleoli, growing in a diffuse pattern. Apoptotic bodies and mitotic figures are common and large number of macrophages with tingible bodies are easily demonstrable, leading to a starry-sky' appearance. [6-7] The malignant cells in PBL are consistently immunoreactive for CD138, a member of the transmembrane heparin sulphate proteoglycan family,that plays a role in plasma cell adherence to bone marrow stromal matrix. [6]

Therapy for PBL patients includes a amalgamation of chemotherapy⁄ or radiotherapy with alkylants. The prognosis is usually poor, apart from the primary site of occurrence (oral and extraoral) and the clinical scenario (HIV infection or immunocompetence). [6]Monoclonal antibodies directed against antigens and interferon injection has also been used. [5- 8]A large literature review of treated cases of PBL shows an overall response rate (ORR) to chemotherapy of 77%, with 46% of patients achieving a complete response (CR) and 31% a partial response (PR). Patients with PBL who were not treated with chemotherapy invariably died with a median survival of 3 months. Cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP) and CHOP-like regimens have been used in half of the patients reported to date. [7]

Lymphomas in the paranasal sinuses have a poor prognosis, when compared with lymphomas in other sites in the body. [2-6-9]In a recent review of the literature, patients with PBL and HIV infection were found to have an overall survival of 14 months when compared to 9 months in HIV negative patients. A possible justification for this finding is that the use of Highly active anti retroviral therapy (HAART) restores immune surveillance to battle the tumor more efficiently. Other factors such as extent of disease and performance status also increased the overall survival of the patients. [6-7-10]

Conclusion

Plasmablastic lymphoma is a unique, aggressive type of NHL which commonly affects the oral cavity of HIV positive patients. The clinical and histopathological features are frequently vague, thus making accurate diagnosis quite cumbersome in the absence of a comphrensive assimilation of clinical, morphological, phenotypic and molecular features. [6-10] An early diagnosis of NHL of nasal cavity and paranasal sinuses might be even more demanding because of its extra-oral localization, which is necessary for its adequate and successful management, thereby improving the prognosis, and quality of life in such patients.

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