

Ocular Manifestation As Earliest Presentation Of Non-Hodgkin's Lymphoma, Mimicking Multiple Chalazia: A Rare Case Report

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Abstract

Primary orbital Non-Hodgkin's lymphoma (NHL) is very rare. This 40 year old female patient presented with small multiple smooth swellings on upper and lower conjunctival fornix and in subsequent visits she develops swelling arising from both side lacrimal sac location. MRI brain and orbit suggested multiple oval shaped lesions noted at retro-bulbar, medial and lateral canthus of both eyes and periorbital area without any bony destruction. Biopsy confirmed it to be a case of primary non-Hodgkin's lymphoma. She was given 6 cycles of chemotherapy with CHOP. The patient is now asymptomatic 2 months after the last cycle of the chemotherapy.

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Keywords: Orbital; Primary; Non-Hodgkin's lymphoma (NHL); Chemotherapy.

Introduction

Lymphomas are malignant neoplasm of lymphoreticular system and mainly involve lymph-nodes, spleen and other non-haemopoietic tissues. Eighty percent of lymphomas are B-cell type, while 14% are T-cell type, with natural killer type (NK) forms only 6%.¹ NHL mostly arise in the lymph nodes termed as nodal NHL (N-NHL), but approximately 25-40% arise in tissues other than the lymph node, and therefore termed extra nodal lymphomas (EN-NHL).² The definition of EN-NHL is controversial especially in patients where both nodal and extra nodal sites are involved.³ The common extranodal sites involved are gastrointestinal tract, upper aerodigestive tract, bones, and spine while unusual sites with involvement less than 3% are breast, central nervous system, testis, lung and skin.⁴ Primary orbital Non-Hodgkin's Lymphoma is a rare presentation of extranodal non Hodgkin's lymphoma accounting for less than one percent of NHL.⁵ It affects primarily the lacrimal gland, conjunctiva, eyelid orbit and ocular adnexa.⁶ The diagnosis is difficult and often delayed, because it can present with a wide variety of manifestations that can mimic many ocular conditions. Non-Hodgkin's lymphoma is a heterogeneous group of neoplasm both in their natural history and response to treatment. Here we report a rare case of Primary- NHL involving both eyes orbit and ocular adnexa.

Presentation of the Case

A 40 year old female presented with foreign body sensation in both eyes with increased lacrimation, weight loss, night sweats and intermittent restlessness with palpitation. There was no history of fever, cough, haemoptysis, pain abdomen, lump and bumps anywhere. There was no past history of tuberculosis or contact with tuberculosis and neither she was immunocompromised nor on any immunosuppressive drugs. There was no prior history of exposure to radiation. On general examination, she had mild pallor. On ocular examination, multiple salmon pink colored small swelling was seen in superior and inferior conjunctival fornix in both the eyes [Figure-1(B,C)] and initially treated with topical



Figure 1: (A,B,C): Patient before treatment.

and oral antibiotics with no improvement at all. During subsequent visits she developed swelling in both of her lacrimal sac region [Figure-1(A)]. All the swellings were painless, gradually increasing in size. Her vision, intraocular pressure, fundus findings and pupillary reactions were within normal limits bilaterally. Ocular movements were full and symmetrical in both eyes.

There was no lymphadenopathy or organomegaly found. Neither mediastinal dullness nor any features of superior venacaval obstruction was noted. There was no cranial nerve involvement. Peripheral blood smear showed no abnormal cells. Haemoglobin was 9.3 g/dl, serum LDH was 677 U/l, Urea level 15 mg/dl, Creatinine 0.8 mg/dl. Other routine laboratory tests like blood glucose, liver function test, uric acid, calcium, chest X-ray, echocardiography, and upper gastrointestinal endoscopy were normal. HIV serology was nonreactive. She was further investigated by Contrast enhanced MRI Scan of Orbit along with paranasal sinus (PNS)

and Brain which revealed multiple oval shaped lesions noted at retro-bulbar and medial and lateral canthus of both eyes and periorbital area with patchy contrast enhancement "with true diffusion restriction" suggestive of lymphoproliferative disorder (Figure-3). No space occupying lesion was seen and no evidence of any pseudotumor was noted . Para nasal sinuses were within normal limit. She was provisionally diagnosed as a case of Primary Orbital lymphoma. The incisional biopsy tissue sample was taken from swelling and sent for histopathological examination, which revealed Non-Hodgkin's lymphoma of diffuse large B cell type (Figure-4). She had recieved with 6 cycles of chemotherapy with CHOP (considering her height 4' 11", body weight 50kgs, body surface area 1.44 m2) ;Inj. Cyclophosphamide (750mg/m2 = 1080mg), Inj Doxorubicin (40mg/m2 = 60mg), Inj. Vincristine (1.4mg/m2 = 2mg) and Tablet Prednisolone (100 mg). She had been asymptomatic thereafter and no further recurrence noted on 2 months follow-up and she is still on follow up (Figure 2).

Discussion

Primary Non-Hodgkin's lymphoma (NHL) of the orbit is a rare presentation, representing 8%-10% of extranodal NHL and only 1% of all NHL.^[5] Generally, it has an indolent course. Orbital and adnexal lymphoma is associated with systemic lymphoma in 30-35% of cases [5]. Hence, all patients with ocular lymphoma should have a complete workup to rule

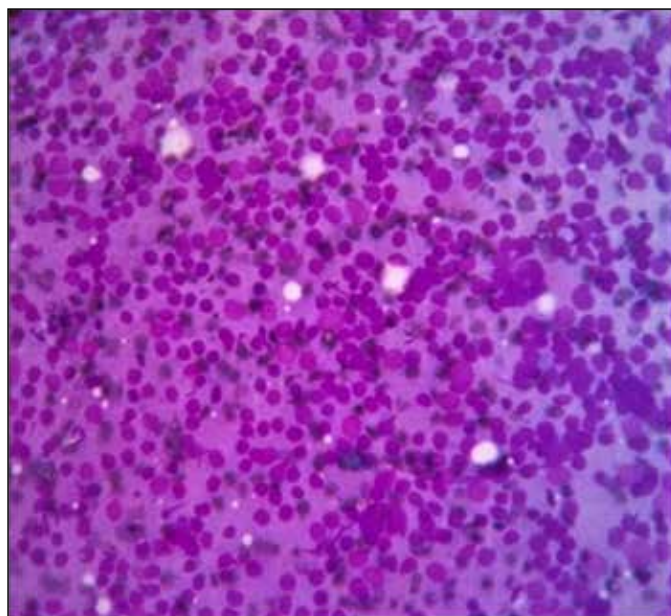


Figure 4: Photomicrograph of histopathological analysis of excisional biopsy specimen from orbital masses showing large atypical lymphoid cells with nuclei having prominent nucleoli suggestive of NHL. H&E stain, [40 x]

out systemic lymphoma. Orbital lymphoma is a lymphoma occurring in the conjunctiva, lacrimal gland, eyelid and ocular musculature. There is another variety known as primary vitreo-retinal lymphoma (PVRL) which is also very rare and 90% of these patients will eventually develop CNS lymphoma and PVRL is best considered as a subset of primary CNS lymphoma. The usual presentation of PVRL is blurred vision with non-resolving uveitis and vitritis.⁷ So NHL in eye can be manifested as conjunctival mass, orbital mass, choroidal infiltration with secondary uveitis and infiltrative optic neuropathy. It may be of following histological types: mucosa associated lymphoid tissue (MALT) histology (57%), follicular lymphomas (19%), diffuse large B-cell lymphomas (DLCL), mantle cell lymphomas, B-cell chronic lymphocytic leukaemia, peripheral T-cell lymphoma, and natural killer cell lymphoma.⁸ Out of which ocular adnexal mucosa-associated lymphoid tissue (MALT) lymphoma (57%) is the commonest one, and it's usually associated with Chlamydia psittaci.⁹ Majority of the orbital lymphomas are of low grade variety (84%) and only 16% are of high-grade histology.¹⁰ Orbital lymphoma may be unilateral or bilateral and up to 20% bilateral presentation is noted. A recent study has shown that ocular lymphoma is more prevalent in women than men.¹¹

It commonly presents with ocular inflammation and swellings and is really a diagnostic challenge for the ophthalmologist. Differential diagnosis of the most common and important periorbital lesions includes multiple chalazia, chronic dacryocystitis, granuloma of orbit and adnexa, lymphangioma, NHL of orbit and adnexa and metastatic deposits. In our case MRI Orbit and brain was suggestive of lympho-proliferative disorder at retro-bulbar medial and lateral canthus and subsequent histopathological examination proven it to be ocular NHL . But further typing by immune- histochemical study can not be done due to



Figure 2: Patient after 2 cycle of chemotherapy



Figure 3: (1,2,3,4) MRI of Brain,Orbit and PNS of the patient (Detail describe in the text)

limitation of resources. Treatment options for ocular NHL include radiotherapy, chemotherapy, excisional biopsy and cryotherapy. Immunotherapy includes anti- CD20 antibody, even with chemotherapy, and radio immunotherapy for patients with CD20 positive NHL.¹² the survival rate is approximately 60% after 5 years. MALT lymphoma has the best prognosis, DLCL prognosis can be improved by early prompt diagnosis and combination chemotherapy. The role of radiotherapy in DLCL is unclear. Combination chemotherapy with CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone) is quite efficacious, while addition of intravenous rituximab (anti CD 20 monoclonal antibody) in the regimen helps in rapid remission with good results.^{13,14} So, total or subtotal excision of the mass followed by radio-therapy and or chemotherapy has a better outcome in patients with large mass However, radiation exposure predisposes to the development of cataracts after 3 – 8 years though The role of radiotherapy in DLCL is unclear. So, from the literature we can conclude that if CD20 is positive then R-CHOP is most efficacious but NHL without CD20 positive patients treatment should be initiated with CHOP regimen. So she was treated with CHOP regimen and responding well with treatment .The size of the swellings reduced significantly after second cycle of chemotherapy (Figure-2) and she had significant improvement of symptoms. The patient is now asymptomatic even after two months of last dose of chemo-therapy and is on follow up.

Conclusion

Lymphoma can occur in the orbit without any systemic manifestations. A palpable painless mass of an eye particularly in elderly female should be suspected as lymphoma. Because early diagnosis of an orbital lymphoma before any bony destruction starts, will improve the prognosis of the patient. R-CHOP chemotherapy regimen is better than CHOP regimen if patient is CD20 positive without any recurrence at follow-up.

Key Messages

Primary Non-Hodgkin's lymphoma of the orbit is rare. Ocular Lymphomas presents as a wide range of clinical manifestation, therefore diagnosis can be challenging. It requires a high degree of clinical suspicion for early diagnosis and differential diagnosis includes different infectious and non-infectious etiologies. It can occur in orbit without any other systemic involvement. If it can be diagnosed early without other nodal or extranodal involvement then treated successfully with CHOP chemotherapy with excellent prognosis.

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