Case Report

Extra Nodal Mucosa Associated Lymphoid Tissue Lymphoma of Orbit-A

Manzoor Ahmad Bhat

ABSTRACT

A case of primary extra nodal orbital mucosa associated lymphoid tissue lymphoma is
reported for its rarity and a controversial scenario with no clear cut guidelines for post excision treatment. The patient was referredtous in the post excision setting for treatment with
radiotherapy, but we put the patient on close follow alone. Patient is alive, with no morbiditiesand disease free for last eight years.

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INTRODUCTION

Orbital lymphomas or ocular adnexal lymphomas are lymphomas occurring in the conjunctiva, lacrimal gland, eyelid and ocular musculature i.e., in adnexae, while as lymphoma arising in the eye proper are called ocular lymphomas. These should be treated as separate entities due to the differences in presumed etiology, investigations, management and outcomes[1]. All of these are extra nodal because the origin is not in any lymphoid structure. Lymphomas are the most frequent orbital tumors[2] with majority (84%) of low grade type and rest of high grade type; among low grade ones more than half (57%)are of mucosa associated lymphoid tissue (MALT) histology[3]. Mucosa associated lymphoid tissue lymphoma is a subtype of non-Hodgkin's lymphoma with its own specific pathology, histology and clinical features. It is distinct because it involves lymphoid proliferation in mucosa-associated lymphoid tissue rather than lymph nodes but the optimal initial management of primary orbital associated mucosal lymphoma(POAML) has not been fully elucidated [4]. It was described as a discrete form of lymphoma in 1994 in the Revised European-American Lymphoma (REAL) classification as one subtypes of marginal zone B-cell lymphomas (MZL)[5], as well as in World Health Organization Classification of Lymphoid Neoplasms 2016 [6].

Extra nodal mucosa associated lymphoid tumors make approximately 40% of cases in ocular adnexa with majority presenting in stage I and II. The natural history includes prolonged survival without widespread dissemination and suggests a role for radiotherapy or surgery in management[7]. As these tend to remain localized for long periods of time, localtreatment (surgery or radiotherapy) is effective at long term controlof disease[6].

The controversy in the management of local early stage disease is that if excision alone is done then possibility of local recurrence is there and if radiotherapy is used either as single modality or post excision, it is bound to cause late and long term sequelae which become all the more important because these patients usually have a long survival. Hence avoiding inducing morbidity should be the prime aim in such situations.

Author Affiliations

Manzoor Ahmad Bhat
Associate Professor,

Repartment of Radiotherapy
(Radiation Oncology)
Government Medical College
Srinaga,Kashmir 190010

Correspondence:
Dr Manzoor Ahmad Bhat
Associate Professor,

Repartment of radiotherapy
(Radiation Oncology)
Government Medical College
Srinaga,Kashmir 190010
Email:bhatmanzoor@hotmail.com
Cell: 9419075354

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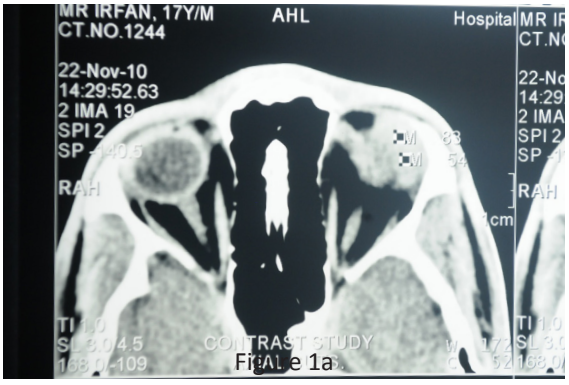

Figure 1a

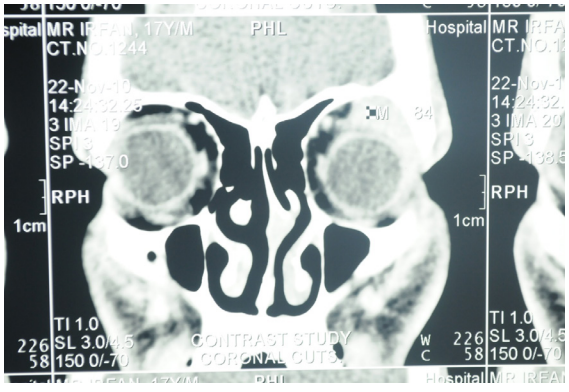

Figure 1b

Case report

A 20 years old male presented to our department on September 29, 2011.He had returned from Post- Graduate Institute of Medical Education and Research (PGIMER) Chandigarh where he had been subjected to excision of mass lesion of left lacrimal gland on September 10, 2011. The lesion was seen on contrast enhanced computerized tomography(CECT) scan orbits performed before surgery on 22 November 2010, see figure 1a, b and reported as a moderately enhancing solid mass in left orbit (anterolateral wall) outside eyeball.

The histopathology was reported as mucosa associated lymphoid tissue(MALT) Lymphoma,
CD20 positive and CD5 negative.

The patient was advised at PGIMER Chandigarh to go for treatment with post excision radiotherapy but the patient had expressed his desire to return to kashmir and get treatment here. After registration in our department we did a baseline workup of the patient which included a thorough history and physical examination.

Laboratory tests like complete blood counts with differential and platelet count, liver and kidney function tests, LDH levels, peripheral blood film, contrast enhanced computerized tomography of the head, neck, chest, abdomen and pelvis. All these investigations were within normal limits. A bone marrow biopsy was also done and reported as normal.

A post excision follow up magnetic resonance imaging of brain and bilateral orbits was done on December 10 2011 which showed findings suggestive of post operative changes in the region of left lacrimal gland without evidence of any mass lesion.

Treatment options of radiotherapy or close follow-up (no initial therapy) with benefits and drawbacks of each were discussed with the patient and his father. The family agreed and accepted the option

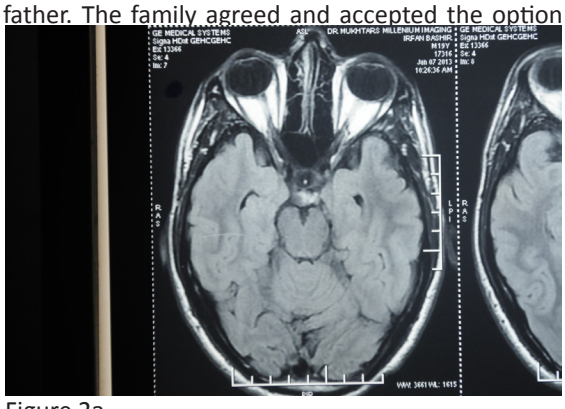

Figure 2a

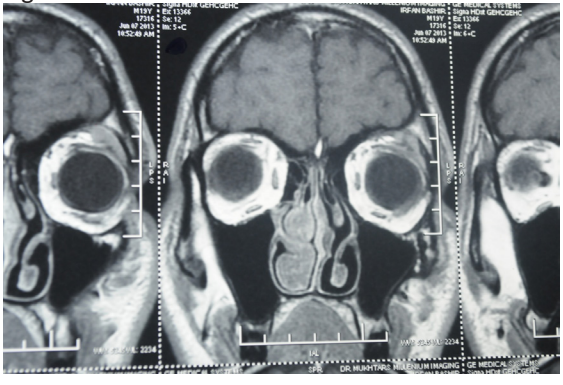

Figure 2b

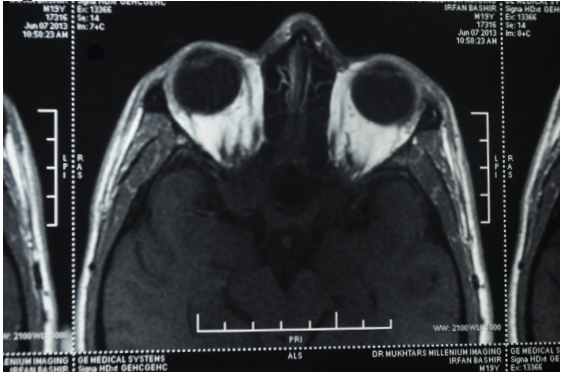

Figure 2c

of close surveillance for the patient. The patient is on follow-up of our department and till date he is disease free clinically and radiologically. His last magnetic resonance imaging head and neck was done in June 2013 and was reported as normal, see figure 2a, b, c. The patient is on regular 06 monthly follow up with us.

DISCUSSION

Patients with primary ocular adnexal mucosa associated lymphoid (POAML) tumor are first subjected to a biopsy to establish diagnosis and subtype and then a examination with imaging and bone marrow biopsy to establish the stage of the disease. The majority of patients with POAML have stage IE disease (Stage I is disease confined to orbit and E indicates extra nodal involvement) [3]. Various treatment modalities are available for the management of patients of POAML, however, currently no treatment guidelines exist because no prospective clinical trials have been conducted to evaluate various therapeutic options or define the optimal treatment approach forthese patients. All therapeutic strategies are associated with unique short- and long-term efficacy and toxicities, which need to be carefully weighed. The final treatment decision requires a multidisciplinary approach, taking into account the extent of the disease, the impact of the lymphoma on the eye and visual function, and finally patient- and disease-related prognostic factors. Thus, the optimal initial management of POAML has not been fully elucidated[4].

After diagnosis, a common approach for the initial management of POAML, especially for localized disease, consists of radiotherapy which is a safe and effective treatment and leads to very high local control rates of 85% to 100%. These outstanding results have to be balanced against frequent treatment-related toxicities and substantial risk of distant recurrence (10%-25%) over at least 10 years after treatment[2] in addition to recurrent disease at local initial and distant sites[5]. Although acute effects of radiation are mild and can be managed symptomatically, including the most common, acute conjunctivitis, however, the most common late toxicity is cataract formation. All patients, in whom the lens received direct radiation developed cataracts of different degrees if follow-up was long enough[8] with lens opacities usually appearing three to nine years after radiotherapy. Use of radiation in elderly patients may not be an issue with respect to developing a cataract because they tend to develop cataract over time even without radiation. But our patient was a young boy and avoiding a radiation-induced cataract inclined us for not applying radiotherapy especially since a complete surgical excision had already been done and a long life expectancy was expected.

As a yet another treatment option, investigators in Italy reported the detection of Chlamydia psitacci(Cp) DNA in 80% of POAML and its regression by Cp eradicating antibiotic therapy in some patients[9]. However given the variable prevalence of Cp infection in patients with OAML, empiric antibiotic treatment without prior testing for chlamydial infection cannot be generally recommended[10]. Prospective trials with standardized objective response criteria and longer follow-up will be necessary to further evaluate the role of antibiotics in the treatment of OAML in different geographic regions.[2] The role of chemotherapy in the treatment of localized low-grade disease is questioned in many series [3]. Most of the patients with low-grade tumors have disease localized to the orbit, hence are treated with local therapy limiting the systemic side-effects. Long-term outcome data suggest that local recurrence is the predominant cause of treatment failure, occurring in up to 29% of patients with 100% local control achieved with radiotherapy alone [3].Role of CNS prophylaxis has been evaluated by Restrepo et al[11] but they concluded that it is unnecessary in patients with POAML.Tanimoto et al[12] evaluated a no initial therapy or a “watch and wait” policy in patients with POAML. After a median follow-up of 7.1 years, 69% did not require treatment because there was neither disease progression nor transformation in them. These patients clearly benefited from a conservative management approach, although a minority (47%) of the patients showed a less favorable disease course. Clinical studies on no initial therapy for localized POAML are limited, and the reasons why most of the patients did not progress for a long period are unclear. Recently, while cytogenetic studies have revealed that patients with mucosa associated lymphoid tumors have multiple karyotypic abnormalities, t (14; 18) or t (11; 18) translocation at diagnosis, and these karyotypic abnormalities are useful for predicting the response to therapy and their prognosis[12], there are no reports of cytogenetic or molecular genetic studies in relation to the prognosis of patients with POAML[13]. If prediction of the clinical outcome of each patient is possible, more suitable therapeutic decisions including no initial therapy for each patient may be applicable. Mannami et al[14] observed 12

patients with stage I POAML for a median duration of 50 months. None of the patients progressed during this time period. Spontaneous regression has been recognized in low grade malignant lymphomas[15] and its occurrence in conjunctival mucosa associated lymphoma supports that observation alone is a treatment option after excisional biopsy for histopathological diagnosis[16]. Radiation still remains as a treatment option for residual lesions, but in light of these lesions' tendency to spontaneously regress, the role of radiation should be reevaluated. Survival in selected patients with localized POAML in the ocular adnexa does not appear to be worse when no initial therapy is substituted for local radiotherapy [5].With the prediction of long median survival, quality of life is an important issue for patients who wish to avoid early and late therapy-related complications. Extended follow-up will be required to assess the impact of no initial therapy on overall survival and freedom from requiring treatment. In conclusion, the treatment options for POAML are many but no definite guidelines exist. Although after histopathological diagnosis the most commonly used and effective treatment is radiotherapy, however keeping in mind the sequelae of radiation especially in situations where a long survival is expected and the fact that many authors have shown that such low grade lymphomas undergo spontaneous regression, a no initial therapy or a wait and watch policy seems to be an appropriate and acceptable approach in some of these patients. In our case the patient was a young 20 year boy who was still studying in college and obviously his parents were very much concerned regarding the disease making a comeback, but they were equally bothered for the long term side effects of treatment especially if the eye would be irradiated. Hence they took a long time to decide after the option of wait and watch with close follow up alone was given to them, to which they finally agreed. Now after a gap of more than eight years with the boy at present aged 29 years, working as a government teacher, married and having two children of his own and now reluctant even to accept that he has any disease or needs any further evaluation, I feel the decision of wait and watch proved absolutely right for this patient. Also,since the survival figures are the same when radiotherapy is used versus no initial therapy inclines towards a more conservative approach, using radiotherapy as salvage in cases of a local recurrence. The fact remains that criteria for selection of patients for such an approach need to be clearly elucidated.

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