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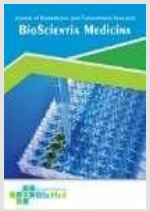

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Orbital Lymphoma: Clinical Features and Management at Dr. M. Djamil General Hospital in 2018

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A B S T R A C T

Background: Orbital lymphoma is found in 50-60% of ocular adnexal lymphomas, with approximately 90% of orbital lymphomas being Non-Hodgkin's lymphomas. Clinical features may include proptosis, ptosis, limitation of eye movement, and salmon patch lesions on the conjunctiva. If an orbital tumor is present, an accurate histopathological examination is important in the management of orbital lymphoma. Because of nonspecific clinical signs and symptoms, some diagnostic delays may occur. The purpose of the study was to evaluate the clinical features, diagnostic approach, and treatment choice in orbital lymphomas. **Methods:** We identified patients diagnosed with orbital lymphoma in an outpatient clinic in Dr. M. Djamil General Hospital from January to December 2018. Patients' medical records were reviewed retrospectively. **Results:** The patient group consisted of 6 patients (five males and one female) with a median age of 58 years. Proptosis and orbital swelling were the leading clinical symptoms, mainly found unilateral (five cases). The diagnosis was confirmed by a surgical biopsy. One histology result showed lymph node hyperplasia, which didn't suit the clinical manifestation and got re-reviewed. All histology results then showed non-Hodgkin's lymphoma with the small lymphocytic type (100%). Five patients received systemic chemotherapy with the CHOP regimen protocol, and one patient refused to get further chemotherapy treatment. **Conclusion:** When unmatched orbital symptoms with histology results are present, re-reviewing the histology result is essential. Once the diagnosis is established, systemic chemotherapy is indicated and can proceed so there will be no delay in treatment

1. Introduction

Orbital lymphomas are rare, comprising only 1% of all non-Hodgkin's lymphoma. However, lymphomas are the most common primary orbital tumor in adults 60 years of age and older.[1,2] Orbital lymphoma is usually unilateral but can be bilateral, and females are more dominant than males. Clinical features of orbital lymphoma that are commonly found are proptosis with slow mass growth, painless, insidious onset, causing inferior displacement of the globe, eyelid swelling, and ptosis. A lymphoid lesion of the conjunctiva, known as a salmon-patch appearance, appears as conjunctival edema, pink-colored, free from its base, located in the substantia propria of the conjunctiva.[3,4,5]

An accurate histopathological examination is an important diagnostic step in the management of orbital lymphoma. Specimens are taken by means of an open biopsy, or a fine-needle aspiration biopsy (FNAB) can also be performed on an orbital mass suspected of being a lymphoma.[6] The diagnosis of lymphoma is established when diffuse immature cells and mitotic active lymphocytes are found. Orbital lymphoma mostly originates from B lymphocytes. Most published journals find that 85% of lymphoma cases in the eye are small cell (low grade), and another 15-20% are large cell (high-grade) tumors.[6,7,8] Our study aimed to explore the diagnostic and therapeutic

approach as well as the clinical course of lymphomas involving the orbit.

2. Methods

A retrospective review of orbital tumors treated at the outpatient clinic of Ophthalmology in Dr. M. Djamil General Hospital from January to December 2018 retrieved 6 cases of non-Hodgkin's lymphomas that presented clinically in the orbital region. The initial clinical staging included a computed tomography or magnetic resonance imaging scan of the orbital region to localize the tumor site and extension. Based on imaging findings, a surgical biopsy under general anesthesia was planned. Histologic diagnosis was performed by the Department of anatomical pathology. Once the diagnosis was confirmed, patients were staged according to the Ann Arbor classification. As radiation oncology was unavailable in our institution at that time, patients were sent to the oncologist for further treatment planning.

3. Results

Six patients were included in this analysis. Of the 6 patients, five were men (83.3%), and one was a woman (16.7 %), with a median age of 58 years old (range 44 to 84 years old). The most common presenting signs and symptoms were proptosis in five patients (83.3%) and periorbital tumor mass in one patient (16.7 %). One patient (16.7%) was found to have bilateral disease. The tumor was located in the supraorbital region in five patients (83.3%) and the infraorbital region in one patient (16.7%). Table 1 displays patient characteristics. Orbital computed tomography was used in all patients to evaluate the extent of the disease.

Table 1. Patient characteristics of orbital lymphomas (n = 6)

Characteristic	Number of Patients	%
Age (years)		
Median	58 (years)	
Range	44-84 (years)	
Gender		
Male	5	83.3
Female	1	16.7
Clinical symptoms		
Proptosis	5	83.3
Periorbital mass	1	16.7
Orbital imaging study		
Computed tomography	6	100
Surgical treatment		
Surgical biopsy	6	100
Complete surgical removal	1	16.7
Treatment		
Chemotherapy	5	83.3

Initial treatment consisted of a surgical biopsy under general anesthesia in all patients using anterior orbitotomy approaches. One patient with involvement of the lacrimal gland received complete surgical removal as the primary treatment. Histopathological examinations were performed from biopsy specimens of all 6 patients, and all matched the small lymphocytic type. One patient previously underwent a re-reviewed histology examination because of unsuitable clinical signs and histopathology results (reactive hyperplasia or lymphoid). However, because the clinical course of the patient suggests an orbital

lymphoma, and it seemed inconsistent with the histopathological results, the histopathological results were then re-reviewed. The second histopathological examination showed the results of non-Hodgkin's lymphoma of the small cell type. Immunohistochemical analysis was not performed because it was unavailable in our institution at that time. There are five patients treated by using the CHOP regimen, resulting in good outcomes.

4. Discussion

This study gives a brief profile and characteristics of orbital lymphoma patients at Dr. M. Djamil General Hospital in 2018. Olsen et al. found more cases in men in their study, namely 52% in men and 48% in women. This result differs from the study by Ahmed et al., which found more cases in women than men. In the study of Sjo et al., the majority of orbital lymphomas were found in men. This indicates that there are gender variations in cases of orbital lymphoma.[9,10,11] Regarding the age of onset, Sharma et al. found that orbital lymphoma can appear in the age range of 15 to 70 years, but most of them appear in older age.[4] Olsen et al. found that the average age of patients with orbital lymphoma who came for treatment was 73% over the age of 50 years.[7] The same thing was proposed by Ahmed et al., where the mean age of orbital lymphoma patients in the United States was 66 years.[11] This is in line with the results of this study, where the average age of the patient was 58 years old.

The most common manifestation of orbital lymphoma in this study was proptosis followed by a palpebral mass, and almost all of the manifestations were unilateral. The majority of orbital lymphomas are unilateral, especially in B-cell lymphomas, up to 90%. In contrast, the type of mantle cell lymphoma (MCL) found more bilateral manifestations (43%). The salmon patch appearance is one of the typical features of the conjunctiva found in orbital lymphoma. However, in the medical record, none of these manifestations were found because almost all patients presented with complaints of proptosis accompanied by severe chemosis, so the appearance of the *salmon patch appearance* is difficult to assess. Eckardt et al. found the most common clinical manifestation in their study was a periorbital mass (64%) followed by exophthalmos (45%), ocular pain (36%), and limitation of motion in 1 patient (9%).[12]

Clinical manifestations found are usually nonspecific, depending on the location of the lymphoma. Visual acuity is usually not compromised because infiltration into the eyeball and optic nerve is rare. Almost all orbital and adnexal structures can be involved by orbital lymphoma. More than 50% of orbital lymphoid lesions arise in the lacrimal fossa that originates in the superior anterior orbit of the orbit, leading to the inferonasal displacement of the globe. If the lymphoid lesion originates in the eyelids, it can be found in the dermis or orbicular muscle of the upper eyelid, causing ptosis.[14,15,16]

Histopathological examination in this study showed non-Hodgkin's lymphoma with Small Lymphocytic type in all patients. It is estimated that 85-90% of orbital lymphomas have a low-grade appearance, with the small, monoclonal, and diffuse proliferation of B-cell lymphocytes. Meanwhile, follicular or nodular images are only found in 10-15% of cases.[15,17]

Management performed on this orbital lymphoma patient was chemotherapy with CHOP regimen in 5 patients (83.3%), and 1 patient (16.7%) refused to undergo chemotherapy, so complete removal surgery was performed. Surgical therapy alone is not recommended for the management of orbital lymphoma because of the high risk of postoperative recurrence.[18,19]

Radiotherapy as initial therapy has been reported to be very effective in orbital lymphoma, especially in MALT.[20] Eckardt et al. reported satisfactory results post-radiotherapy and good post-therapy survival rates.[11] However, because there are no radiotherapy facilities at Dr. M. Djamil General Hospital, no orbital lymphoma patients are treated by using radiotherapy.

Systemic chemotherapy is an effective therapy for orbital lymphoma. Chemotherapy is mainly given in the form of a combination of post-surgical and

radiotherapy or given alone in stage III and IV lymphoma. In more aggressive lymphoma, chemotherapy is a more appropriate choice. The orbital lymphoma patients in this study were treated with chemotherapy. The regimens used were cyclophosphamide, doxorubicin, vincristine, and prednisone (CHOP).[12,16]

Despite the effectiveness of radiotherapy or chemotherapy alone, Mallick et al. showed through their study that a combined modality therapy with a combination of CHOP/COP-based chemotherapy and a moderate dose of radiotherapy imparts excellent long-term local and systemic disease control.[21]

5. Conclusion

The clinical profile of orbital lymphoma in this study shows almost similar results to most studies that have been published previously regarding age, gender, laterality, clinical manifestation, and histology finding. The limited facility for performing immunohistochemical examinations did not cause a delay in the treatment of orbital lymphoma. When unmatched orbital symptoms with histology results are present, re-reviewing the histology result is essential. Although radiotherapy is preferred for the management of orbital lymphoma, a chemotherapy regimen is still one of the treatment choices which gives good outcomes to the patients.

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