Spectrum of Biopsy Proven Extraocular Muscle Tumours of Non-Thyroid Origin

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ABSTRACT

Objective: To describe different types of primary extraocular muscle (EOM) tumours based on the results of imaging studies, peroperative clinical picture and their histopathological diagnosis.

Study Design: Case series.

Place and Duration of Study: Al-Shifa Trust Eye Hospital, Rawalpindi, from July 2001 to January 2017.

Methodology: A retrospective analysis of 640 diagnosed orbital tumours was carried out using non-randomised sampling technique, and the prevalence of primary EOM tumours was determined. Based on the results of imaging studies, the clinical picture observed during surgery (orbitotomy) and the histopathological diagnosis, primary EOM tumours were divided into different types, accordingly.

Results: Nineteen (n=19) primary EOM tumours (frequency of 2.96%) had 12 types of histopathological diagnoses, and were categorised into inflammatory tumours (n=8, 42%), vascular tumours (n=4, 21%), lymphoproliferative tumours (n=3, 16%), neurogenic tumours (n=2, 10.5%) and myogenic tumours (n=2, 10.5%). The recti were involved more frequently than obliques (n=15, 78.94% and n=4, 21.06%, respectively). All the patients presented with proptosis of varying degree with some degree of globe rotation and had surgical excision/appropriate management. Visual acuity was not affected in any of the patients. Four (n=4, 21.05%) tumours were malignant (NHL, ASPS, myeloid sarcoma and rhabdomyosarcoma) and these patients underwent chemotherapy and/or radiotherapy.

Conclusion: Biopsy-proven primary EOM tumours were devisable into five broad categories. Patients with primary EOM tumours presented with proptosis and impaired ocular motiliy. The primary EOM tumours involved both the recti and the obliques and were excised surgically with favourable outcomes in most cases.

Key Words: *Biopsy, Extraocular muscle, Tumour, Proptosis.*

INTRODUCTION

Cranial mesoderm which surrounds the developing eye gives rise to extraocular muscles.[1] Each orbit has seven muscles: four recti, superior and inferior obliques and a levator palpebrae superioris.[2] Thyroid orbitopathy is the most common cause of extraocular muscle abnormalities. However, various vascular, inflammatory, neoplastic, infective, metabolic and neuromuscular disorders could affect the extraocular muscles morphology and their functions.[3]

Primary extraocular muscle (EOM) tumours are rare.[3] Their exact incidence is difficult to calculate as they could be secondary to a generalised orbital disease, such as infiltrating tumours and non-specific orbital inflammatory syndrome.[4] The authors believe that this study presents the largest case series on biopsy-proven primary extraocular muscle tumours, reported in the international literature to date. The authors have also reported a case of alveolar soft-part sarcoma, involving the EOM primarily.

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METHODOLOGY

The study was conducted from July 2001 to January 2017. A retrospective analysis of 640 diagnosed orbital tumours was carried out. The frequency of primary extraocular muscle tumours was determined. The clinical features of the included patients and their subsequent management were reported. The sampling technique was non-randomised sampling. The Institutional Ethical and Research Committee approved the study.

All the patients included in the retrospective analysis underwent orbitotomy after the necessary imaging studies and the diagnoses were confirmed on histopathology. The patients with radiological and histopathological evidence of having a primary extraocular muscle tumour were included in the current case series. Based on the results of imaging studies, the peroperative clinical picture, and their histopathological diagnosis, the primary extraocular muscle tumours were categorised into five different categories, accordingly. Patients with an orbital neoplasm, which could not be confirmed as a primary extraocular muscle tumour on imaging studies or histopathology, were excluded from the current case series.

Attempts were made to preserve the structure and the function of the involved extraocular muscle as much as possible that was followed by subsequent necessary management. Moreover, in some cases, it was seen that the eye was deviated opposite to the direction of the action of the involved muscle with primary EOM tumour, necessitating further intervention to correct the ocular deviation. The function of the muscle with primary EOM tumour gradually returned to normal or near normal with time in some cases.

Frequency of categorical and mean +SD values of quantitative variables was determined.

RESULTS

Of the 640 orbital neoplasms, there were 19 primary extraocular muscle tumours with frequency of 2.96%. The 19 different (n=19) tumours had 12 types of histopathological diagnoses, which have been divided into five broad categories, following the usual classification system for the orbital tumours, as shown in Table I.

There were 11 (n=11; 57.8%) males and eight (n=8; 42.2%) females. The mean age was of 22.52 ±17.06 years, ranging from 4 to 64 years. All the patients were Pakistanis by nationality and represented different ethnic groups (Punjabi, Sindhi, Baloch and Pakhtoon). The recti were involved in 15 cases (n=15; 78.94%) as compared to the oblique muscles, which were involved in just four cases (n=4; 21.06%). The medial and the inferior quadrants were involved more frequently than the other quadrants. Except for one patient with angiolymphoid hyperplasia, where the involvement of the orbital floor was also seen, the rest of the patients had an isolated single-muscle involvement only. In addition, one patient presented with spontaneous intramuscular haemorrhage. Besides, those patients were included in the current case series who presented with proptosis and globe rotation of varying degrees. However, the visual acuity was not affected in any of the patients. In addition, no patient in the current study showed any signs of muscle shrinkage secondary to cranial nerve palsy, congenital fibrosis or post-inflammatory fibrosis.

Inflammatory tumours in the form of fungal granulomas, nonspecific granulomas, and idiopathic orbital inflammatory disease were the commonest and represented 42% (n=8) of the diagnosed cases. Seemingly, the inflammatory tumours had a male preponderance and were seen in five (n=5, 63%) male and three (n=3, 37%) female patients. Besides, all the patients with fungal granuloma underwent systemic antifungal therapy with itraconazole following orbitotomy.

Vascular tumours like cavernous haemangioma and angiolymphoid hyperplasia were the second most common entity, involving 21% (n=4) of the diagnosed cases with primary EOM tumours. Moreover, vascular tumours were found equally in both male (n=2, 50%) and female (n=2,50%) patients in the current case series.

The lymphoproliferative lesions, like extranodal marginal zone lymphomas, myeloid sarcoma (Figure 1) and the pseudolymphoma (Figure 2) were found in 16% (n=3) of the included patients. In addition, the lymphoproliferative tumours were more common in females (n-2, 67%) than males (n=1, 33%).

Neurogenic and myogenic tumours were found in two patients (n=2; 10.5%) each. Neurogenic tumours were seen in male patients (n=2,100%) only; whereas, myogenic tumours involved male (n=1, 50%) and female (n=1, 50%) patients equally.

Four (21.05%) of the 19 tumours were malignant in nature (NHL, ASPS, Myeloid Sarcoma and Rhabdomyosarcoma) and underwent appropriate chemotherapy and/or radiotherapy. One child (n=1; 5%) with rhabdomyosarcoma, died because of the metastatic disease, after two years. One child (n=1; 5%) with fungal granuloma developed an intracranial lesion, which was found to be of tuberculous in origin, after the neurosurgical intervention. Eleven (n=11; 57.8%) out of the 19 patients had some degree of loss of muscle function after the treatment.

DISCUSSION

Lacey *et al*. reported 31 (n=31) biopsy-proven EOM tumours, which included 16 (n=16) cases of primary

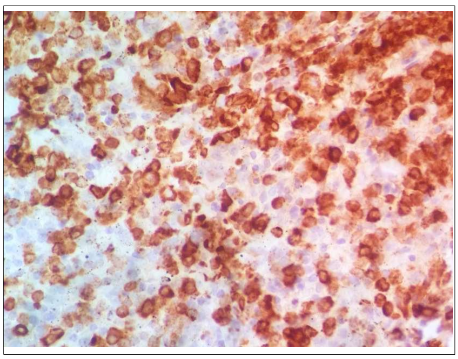

Figure 1: The figure shows positive staining for myeloperoxidase but negative staining for B and T cell markers in a myeloid sarcoma patient.

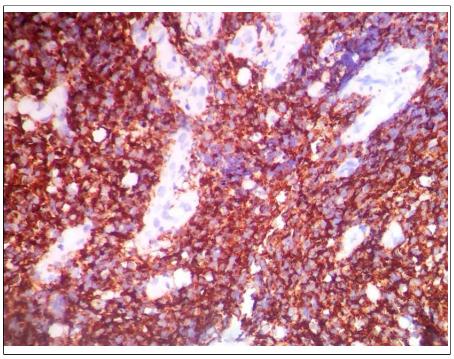

Figure 2: Positive CD 20 staining of B cells in psuedolymphoma patient.

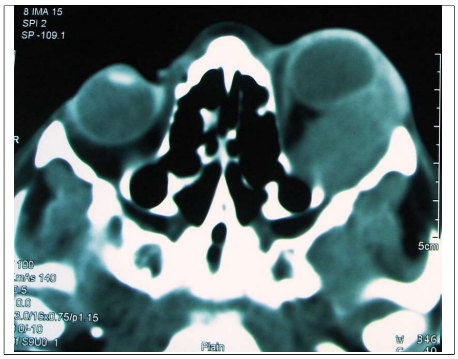

Figure 3: CT scan image showing alveolar soft part sarcoma of left lateral rectus muscle.

Table I: Outcome after treatment of EOM tumours.

SN	Age	Gender	Diagnosis	EOM involved	Treatment	Follow-up and outcome
A. Inflammatory tumours						
1.	21 years	M	Non-specific chronic granuloma	R-Medial rectus	Partial excision of the muscle tumour	4 years. No recurrence. Limitation of medial rectus movements
2.	18 years	F	Pseudotumour / myositis	R-Medial rectus	Biopsy of muscle preceded and followed by steroids	Symptom-free after six years
3.	25 years	M	Fungal granuloma	R-Inferior rectus	Partial excision of muscle tumour followed by nine months treatment with Itraconazole	No recurrence. Inferior rectus limitation gradually improved over 3 years with mild hypertropia persisting
4.	4 years	M	Fungal granuloma with abscess formation	L-Inferior rectus	Partial excision of muscle tumour followed by six months treatment with Itraconazole	Lost to follow-up after 3 years. The child had small degree of hypertopia at the last follow-up.
5.	45 years	M	Fungal granuloma	R-Medial rectus	Total excision of muscle tumour followed by nine months treatment with Itraconazole	No recurrence after two years. Large exotropia persists. Muscle surgery planned.
6.	40 years	F	Non-specific chronic granuloma	R- Medial rectus	Partial excision of muscle tumour preceded and followed by steroids	Symptom-free after one year
7.	08 years	F	Inflamatory psuedotumour	Left superior oblique	The tumour involving distal portion of muscle near insertion was excised in toto preserving the full length of superior oblique.	Tumour-free and symptom free follow up of eight months
8.	18 years	M	Right fungal granuloma orbit and tuberculoma in brain	R-Inferior rectus	Partial excision of muscle tumour followed by nine months treatment with Itraconazole. Neurosurgeon removed the tuberculoma from frontal lobe and antituberculous therapy was given.	Moderate hypertropia persists after four years of follow-up.
B. Vascular tumours						
9.	64 years	M	Cavernous hemangioma	Left-Inferior oblique	Tumour involving the middle third of muscle belly was excised while the muscle was preserved	Symptom-free one year follow-up
10.	15 years	F	Intermuscular hemangioma	Medial rectus	Hemangioma was partially excised and drained	Two years follow-up without any symptom
11.	08 years	F	Angiolymphyoid hyperplasia	Left -lateral rectus	Total excision of the tumour along with the muscle.	Follow-up of two years. Left large esotropia. Muscle surgery for squint planned
12.	38 years	M	Angiolymphyoid hyperplasia	Left-lateral rectus and floor of the orbit	Excision biopsy of the lateral rectus and removal of orbital floor tumour.	Moderate proptosis with mild esotropia persists after one year
C. Lymphoproliferative tumours						
13.	45 years	F	Malignant non hodgkin's lymphoma (extranodal marginal zone lymphoma)	Left-inferior oblique	Partial excision of the tumour. Systemic workup was negative. Local radiation was given.	Tumour and symptom- free after three years
14.	11 years	M	Right granulocytic sarcoma	Right superior rectus	Systemic workup revealed acute lymphoblastic leukemia and child was referred to pediatric oncologist for chemotherapy	Lost to follow-up after six months. Child was with large hypotropia and undergoing chemotherapy at the last follow up
15.	32 years	F	Pseudolymphoma	Right medial rectus	An incision biopsy from medial rectus was taken. Patient is followed up regularly	
D. Neurogenic tumours						
16.	12 years	M	Schwannomma	Left superior oblique	Tumour was excised from the muscle near trochlea.	Tumour and symptom-free after five years of follow-up
17.	2 years	M	Glomus tumour of orbit (paraganglioma) with chronic granulomatous tissue-	Right superior rectus	Excision of the tumour involving the superior rectus.	Complete ptosis, limitation of upgaze after one year of follow-up
E. Myogenic tumours						
18.	05 years	M	Embryonal rhabdomyosarcoma	Right-inferior rectus	Total excision of the tumour along with the muscle followed by radiation and chemotherapy	The child had large hypertropia died with recurrence after two years.
19.	17 years	F	Alveolar soft-part sarcoma of orbit	Left lateral rectus	Lateral orbitotomy revealed a large tumour of lateral rectus muscle which was partially excised. It was followed by chemotherapy and radiation.	Six months follow-up after surgery, radiation and chemotherapy show no recurrence with small degree of esotropia.

muscle involvement while the rest involved the extraocular muscles secondarily, either due to the distant metastasis (n=8) or the local invasion, from the adjacent orbital neoplasms (n=7).[3] The authors in the current study report 19 (n=19) biopsy-proven primary extraocular muscle tumours, making it the largest case series, reported in the international literature to date (Table I).

The signs and symptoms of patients, with primary extraocular muscle tumours in the current study, were comparable with the findings of Lacey *et al*.[3] However, contrary to the conclusions from Lacey *et al*.,[3] carotid-cavernous dural shunts, congenital and acquired fibrosis of the extraocular muscles, systemic associations especially neurofibromatosis, systemic inflammatory/ autoimmune disorders and the amyloid deposition in the extraocular muscles, were not seen by the authors in this case series.

In this study, a male preponderance was noted (58%, n=11), which was also seen in the study conducted by Mannor *et al*.[5] Contrary to this, Lacey *et al*.[3] and Scott and Siatkowski,[6] showed a female preponderance. The average age in the current study (mean age 22 years 5 months) was less (4-5th decade) than the one reported in the studies, conducted by Lacey, Scott and Siatkowski and Moriarty *et al*.[3,6,7]

Vascular malformations of the extraocular muscles, in the absence of haematological abnormalities, can lead to spontaneous intramuscular haemorrhage.[8] The authors saw this phenomenon in one of the studied patients. Moreover, in the current study, the clinical features of the primary malignant non-Hodgkin's lymphoma that involved the left inferior oblique muscle were consistent with the findings of Hornblass *et al*.[9]

The rhabdomyosarcoma arises from the primitive pluripotential mesenchymal tissue that is present in the soft tissue of the orbit. They may very rarely arise from the extraocular muscle as well.[10] Porterfield and Zimmerman studied 55 cases of orbital rhabdomyosarcomas and came across just three cases arising from the extraocular muscles.[11] The current study also reports a case of embryonal rhabdomyosarcoma, arising from the right inferior rectus muscle, in a 5-year boy, who died within two years of diagnosis, due to the recurrent and aggressive nature of the tumour.

The alveolar soft-part sarcoma (ASPS) constitutes 1% of all the soft tissue sarcomas that affect the young adults. The ASPS has a female preponderance and involves the head and the neck region predominantly. Orbital involvement of ASPS is very rare.[12] Abrahams *et al*. reported a case of orbital ASPS, which replaced the complete insertion of the inferior rectus muscle.[13] Khan and Burke also reported a case of orbital ASPS, which was indistinguishable from the medial rectus muscle, and was surgically excised.[14] The authors in this study also report a case of alveolar soft-part sarcoma for the first time, which involved the left lateral rectus muscle primarily (Figure 3). The clinical, histopathological and the immunohistochemistry features of the reported ASPS were identical to those already published.[12]

The most common infective process that affects the extraocular muscles is the contiguous involvement of an extraocular muscle from the bacterial sinusitis.[3] However, this was not seen in this case series. The function of an extraocular muscle can be affected by various pathological processes that result in their enlargement or shrinkage.[3] The primary extraocular muscle tumours can produce a mass effect, resulting in the displacement of the globe and/or other structures, as well as compromise their function,[3] as seen in this case series.

At times, the diagnostic dilemmas arise for clinicians, while dealing with swellings associated with chronic progressive muscular dysfunctions. Besides, the primary extraocular muscle tumours do not see a reduction in size following the steroid therapy. Therefore, in these cases, a biopsy is mandatory to rule out malignancy. The primary tumours of the extraocular muscles that have a widespread involvement may respond well to the radiotherapy sessions in divided doses, chemotherapy or palliative debulking.[3,15]

This is the largest case series on biopsy-proven primary EOM tumours. Besides, the patients of the current study are under rigorous follow-up to address the morbidity associated with the disease/treatment, as well as for rehabilitation, to improve their quality of life.

CONCLUSION

The primary EOM tumours had an institutional prevalence of 2.96%, classified into five broad categories. All the patients with primary EOM tumours presented with proptosis and impaired ocular motility; whereas, ll the primary EOM tumours involved both the recti and the obliques, and were removed surgically with favourable outcomes in most cases.

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