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Clinical Manifestations of Orbital Mass Lesions at the Jules Stein Eye Institute, 1999–2003

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■ **BACKGROUND AND OBJECTIVE:** To describe the clinical manifestations, diagnoses, treatments, and outcomes of orbital mass lesions at a tertiary care referral center.

■ **PATIENTS AND METHODS:** All cases of newly diagnosed or referred orbital tumors at the Jules Stein Eye Institute from 1999 to 2003 were reviewed retrospectively. Demographic and clinical data were extracted from the electronic oculoplastics registry of the Division of Orbital and Ophthalmic Plastic Surgery.

■ **RESULTS:** Three hundred sixty-nine cases of orbital mass lesions were evaluated (167 males and 202 females; mean age = 48 years). The most common presenting symptoms were mass/proptosis, pain, swelling, inflammation, and diplopia. The most common categories of diagnosis were cystic or structural lesions, benign tumors, inflammatory processes, neuronal processes, and fibrous processes. Increasing age was associated with an increased incidence of primary and metastatic malignant tumors. Half of all cases required surgical intervention consisting of excision, debulking, or exenteration; 20% to 30% of cases were managed conservatively.

■ **CONCLUSIONS:** The differential diagnosis of orbital mass lesions differs across age groups. No clinical sign or symptom is specific for the underlying diagnosis and the biological behavior of the abnormal process may be misleading. Therefore, a careful diagnostic approach that considers the benefit of imaging studies must be undertaken. Almost 50% of these mass lesions can be managed with nonsurgical intervention.

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INTRODUCTION

Orbital tumors comprise a diverse group of neoplasms, infiltrations, and malformations. Previous studies describe the prevalence of orbital tumors and space-occupying lesions, demonstrating wide disparities due to the differences in local referral patterns, the method of classification, and the special interests of the investigators.[1-5] Attempts to correlate clinical features of orbital tumors with specific diagnoses by analyzing signs, symptoms, and imaging characteristics have been made in the past.[1] Although narrow categorization of this heterogeneous group is difficult, these correlations have yielded general classification guidelines for orbital tumors.

Orbital mass lesions have various underlying pathological processes that may fall under the expertise of different medical specialties, each with their own management biases. The purpose of this study is to describe the clinical manifestations, diagnoses, treatments, and outcomes of orbital mass lesions that were referred to a tertiary care ophthalmic referral center during a 5-year period.

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TABLE 1

Symptoms and Signs at Presentation of 369 Patients With Orbital Mass Lesions at the Jules Stein Eye Institute, 1999–2003

Sign/Symptom	% of Patients*
Mass/proptosis	30
Pain	27
Swelling	24
Inflammation	20
Diplopia (in any gaze position)	15
Pressure/headache	7
Ptosis	7
Epiphora/local eye symptoms	7
Facial numbness	2
Visual disturbances/transient visual obscurations	2
Recent progression	1.5
Enophthalmos	1.0
Incidental finding	0.3

**Percentages add up to more than 100% because patients could have more than one sign or symptom.*

PATIENTS AND METHODS

This study is a retrospective, noncomparative, interventional cases series. The oculoplastic registry (electronic medical record) of the division of Orbital and Ophthalmic Plastic Surgery at the Jules Stein Eye Institute was reviewed to identify all patients evaluated for an orbital mass lesion or orbital tumor from January 1, 1999, to October 1, 2003. The study complied with the policies of the local institutional review board. Data regarding diagnosis, clinical examination, imaging and treatment modality, and outcome were recorded and analyzed.

Statistical Analysis

Statistical analysis was performed using the two-tailed paired samples *t* test to evaluate pretreatment and posttreatment data such as visual acuity, intraocular pressure, and exophthalmometry measurements. The one-sample *t* test was used to examine changes in proptosis in follow-up visits. The independent samples *t* test was used to compare numerical variables among different groups of signs, symptoms, diagnoses, or treatment modalities. Chi-squared nonparametric analysis was used to explore associations between clinical signs and specific diagnoses. Pearson bivariate correlation was employed to analyze the contribution of age, visual acuity, intraocular pressure, color vision, and extent of exophthalmos with treatment outcome. Snellen acuity measurements were converted to the logarithm of the minimum angle of resolution.

RESULTS

Three hundred sixty-nine cases were identified with the diagnosis of orbital mass lesions in our outpatient clinic. Of these patients, 167 were males and 202 were females. The mean age was 48 years with a range of 2 months to 93 years. The most common presenting symptoms were pain, swelling, proptosis, inflammation, and diplopia (Table 1). The lateralization of orbital tumors was equally distributed between right and left eyes. Upper eyelid involvement was more common than lower eyelid involvement.

Individual diagnoses of the orbital tumors fell into several categories (Table 2). Benign lesions was the most prevalent group (25%); within this group, cavernous hemangioma was the most common specific diagnosis. The second most common category was orbital inflammation (22.5%); idiopathic was the most common diagnosis within this group, followed by dacryoadenitis, myositis, and fibrosis. The third most common category was malignant lesions involving the orbit (19%); squamous cell carcinoma was the most common specific diagnosis within this group, followed by basal cell carcinoma, malignant melanoma, adenocystic carcinoma of the lacrimal gland, and sebaceous carcinoma. Mucosa-associated lymphoid tumors was the most common specific diagnosis in the category of lymphoid diseases, comprising almost two-thirds of the group. In the category of fibrous/osseous and cartilaginous diseases, fibrous dysplasia and osteoma were the most common diagnoses. In the category of neuronal diseases, meningioma and neurofibroma accounted for more than two-thirds of the specific diagnoses. Three cases of metastatic orbital lesions were diagnosed: prostate cancer, breast cancer, and renal cell carcinoma.

Diagnoses were analyzed by age group (Table 2). In children younger than 2 years, we found that capillary hemangioma was the most common, followed by lymphangioma. In children and adolescents (3 to 20

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TABLE 2

Clinical Onset and Diagnosis of Non-thyroid Orbital Disease at the Jules Stein Eye Institute, 1999–2003

	Onset of Disease (Y)				
Disease/Diagnosis	**0–2**	**3–20**	**20–60**	**60–95**	**Total**
Hemangioma	7	5	21	6	39
Pleomorphic adenoma	–	–	5	5	10
Fat/lacrimal gland prolapse	–	–	1	3	4
Lipoma/dermatolipoma	–	4	–	2	6
Mucocele	–	–	3	3	6
Dacryops/lacrimal cyst	–	–	1	1	2
Lacrimal duct papiloma	–	–	–	1	1
Organizing thrombus	–	–	1	–	1
Choristoma/dermoid/cyst	1	5	11	2	19
Normal/neuralgia	1	1	1	–	3
Total benign	**9**	**15**	**44**	**23**	**91 (25%)**
Infection (cellulitis/abscess)	–	1	3	4	8
Idiopathic inflammation	–	8	29	10	47
Sclerosing inflammatory tumor	–	–	–	3	3
Dacryoadenitis	–	1	11	4	16
Granuloma/sarcoid	1	–	–	4	5
Eosinophilic granuloma	–	2	–	–	2
Blepharochalasis	–	–	1	–	1
Amyloidosis	–	–	1	–	1
Total inflammatory	**1**	**12**	**45**	**25**	**83 (22.5%)**
Adenocystic carcinoma lacrimal	–	–	3	4	7
Adenocarcinoma	–	–	2	–	2
Basal cell carcinoma	–	–	2	9	11
Squamous cell carcinoma	–	–	8	10	18
Sebaceous carcinoma	–	–	1	5	6
Malignant melanoma	–	–	6	3	9
Extension of intraocular neoplasm	–	–	–	2	2
Hemangiopericytoma	–	–	–	3	3
Sarcoma	–	–	1	2	3
Metastasis	–	–	1	2	3
Paranasal carcinoma	–	–	1	–	1
Rhabdomyosarcoma	1	–	–	–	1
Neuroblastoma/esthesio	–	–	1	1	2
Merkel cell tumor	–	–	1	–	1
Total malignant	**1**	**0**	**27**	**41**	**69 (19%)**
Varix/venous lake	–	–	8	2	10
Arteriovenous shunt/malformation	–	1	4	2	7
Lymphangioma	3	5	5	1	14
Total active vascular	**3**	**6**	**17**	**5**	**31 (8.5%)**
Meningioma	–	–	9	5	14
Neurofibroma	1	2	1	–	4
Schwannoma	–	–	6	–	6
Neuroma	–	–	1	1	2
Total neuronal	**1**	**2**	**17**	**6**	**26 (7%)**
Mucosa-associated lymphoid tumors	–	–	5	10	15
Lymphoma	–	–	2	6	8
Total lymphoid	**0**	**0**	**7**	**16**	**23 (6%)**
Fibrous dysplasia	–	5	5	4	14
Osteoma	–	1	3	1	5
Osteosarcoma	–	–	1	–	1
Total fibrous/osseous/cartilaginous	**0**	**6**	**9**	**5**	**20 (5%)**
Glioma	–	–	3	–	3
Meningioma	–	–	2	–	2
Arachnoid cyst	–	–	3	–	3
Total optic nerve	**0**	**0**	**8**	**0**	**8 (2%)**
Other/miscellaneous	–	–	17	1	18 (5%)
Total, all types	**15**	**41**	**191**	**122**	**369**

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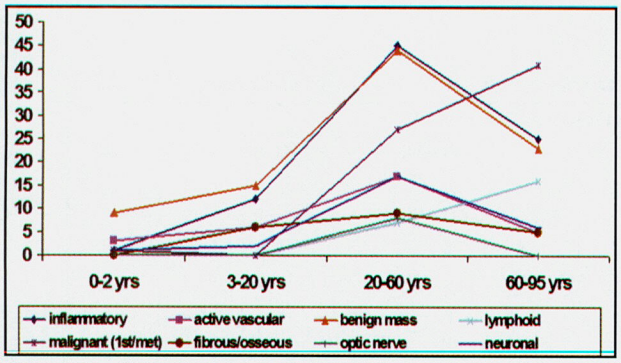

Figure. Number of orbital mass lesions in different age groups at the Jules Stein Eye Institute from 1999 to 2003.

years), benign mass lesions were the most common, followed by orbital inflammation. In adults aged 20 to 60 years, the most common diagnosis was idiopathic inflammation, followed by benign lesions, of which hemangioma was the most prevalent; these diagnoses comprised nearly 50% of all orbital tumors in this age group.

More than one-third of idiopathic inflammation in this age group occurred in the lacrimal gland fossa and often coexisted with the diagnosis of dacryoadenitis. Other common diagnoses in adults aged 20 to 60 years were orbital varix, lymphoma, mucosa-associated lymphoid tumors, and sphenoid wing meningioma. The incidence of most orbital tumors in this study increases into adulthood and then declines in the elderly age group, with the exception of malignant disease and lymphoid processes, which increase in incidence in the elderly (Figure).

Visual acuity and intraocular pressure in primary and up gaze remained unchanged during the follow-up time for the entire cohort. Two percent of patients had subjective visual complaints on presentation. On clinical examination, these patients had a mean visual acuity of 20/30 that was not significantly different in comparison to patients with no visual complaints. Malignant primary and metastatic orbital lesions did not show decreased visual acuity on presentation. However, significantly decreased visual acuity on presentation was more common among patients with optic nerve involvement or optic nerve sheath tumors. Motility disturbances occurred in 34.5% of patients. Diplopia in any position of gaze occurred in 14.8% of patients and confrontational visual field defect in 8%; neither of these findings were associated with any specific diagnosis.

There were no specific clinical signs or symptoms that were more common among patients with malignant disease. Most patients had normal fundus examination on presentation (92%). Several patterns of optic nerve or posterior pole involvement were noticed (Table 3). None were related to any specific diagnosis or provided clues to the location of the tumor in relation to the optic nerve and globe.

Seventeen patients (4.6%) had bilateral disease; all but one had benign lesions or an inflammatory process. The one exception was a 77-year-old woman with metastatic breast carcinoma who developed bilateral orbital involvement and enophthalmos. Enophthalmos was present in three additional cases with the diagnosis of orbital varix, adenocarcinoma, and idiopathic inflammation. The degree of proptosis for the entire cohort decreased significantly by 1.0 ± 1.1 mm from 18.7 to 17.7 mm ($P < .001$; one-sample t test), reflecting surgical treatment by excision or medical treatment with steroids for idiopathic inflammation, chemotherapy/radiation for lymphoma and antibiotic/drainage for infectious diseases of the orbit (Table 4).

Treatments were specific to individual diagnoses. More than half of the cases in this study required diagnostic or therapeutic surgical intervention; these data are summarized in Table 5. Of note, 29 patients (8%) were diagnosed prior to referral and therefore may have not required further surgical intervention.

At some point in their clinical course, 20.6% of the patients in this study received steroids with or without nonsteroidal anti-inflammatory drugs. In general, this group of patients were cases of idiopathic inflammation, myositis, or dacryoadenitis. In this study, 9.2% of the patients underwent radiation therapy for orbital lymphoma or mucosa-associated lymphoid tumors, idiopathic inflammation, squamous cell or basal cell carcinoma, malignant melanoma, lymphangioma, adenocystic carcinoma of the lacrimal gland, osteosarcoma, neurofibroma, and malignant infiltrative diseases.

Chemotherapy was the treatment for nine patients with malignancy. Infectious cases were treated with oral antibiotics, intravenous antibiotics, or both with surgical drainage in cases of abscess formation. Sclerosing therapy was used in cases of disfiguring lymphangioma.

Imaging by computed tomography and magnetic resonance imaging demonstrated specific characteristics in each group of diagnoses. Based on these imaging findings, 23 patients (6.2%) had a change in referral

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TABLE 3

Funduscopic Examination in 369 Patients With Orbital Mass Lesions, 1999–2003

Fundus Examination	Prevalence	Diagnoses
Normal	340 (92%)	
Swollen disc	3 (0.8%)	Idiopathic inflammation, meningioma, adenocystic carcinoma
Optic atrophy	18 (4.9%)	Idiopathic inflammation, meningioma, fibrous dysplasia, hemangioma, squamous cell carcinoma, neurofibroma, maxillary carcinoma, optic nerve glioma, schwannoma, angiofibroma, fibrous histiocytoma
CRVO	1 (0.3%)	Arachnoid cyst
Subretinal fluid	1 (0.3%)	Carotid cavernous fistula
Choroidal folds	2 (0.5%)	Rhabdomyosarcoma, hemangioma
Venous engorgement	4 (1.1%)	Idiopathic inflammation, carotid cavernous fistula, hemangiopericytoma

CRVO = central retinal vein occlusion.

TABLE 4

Mean Values ± Standard Deviation (Range) of Visual Acuity, Intraocular Pressure, and Degree of Proptosis of 369 Patients With Orbital Mass Lesions, 1999–2003

Characteristic	At Presentation	At End of Follow-up	*P**
Visual acuity†	20/40 (20/15–HM)	20/35 (20/15–HM)	NS
IOP (mm Hg)			
Primary gaze	15.7 ± 4 (8–40)	15.8 ± 3.1(8–20)	NS
Up gaze	21.5 ± 7.3 (1–40)	17.8 ± 4.2 (12–26)	NS
Color vision‡ (Ishihara)	11/14		
Proptosis affected eye (mm)	18.7 ± 3.4 (9–30)	17.7 ± 3.3 (12–27)	< .001
Time to biopsy/excision§ (mo)	17 (0–120)		
Follow-up time (mo)	9.1 (1–108)		

HM = hand motions; NS = not significant; IOP = intraocular pressure.
**P value was calculated using paired samples t test.*
†*Visual acuity calculations were performed using logarithm of the minimal angle of resolution.*
‡*Color vision by Ishihara color plates was examined only at presentation.*
§*From initial diagnosis (not necessarily at presentation).*

diagnosis, and 60 patients (16.3%) had a change in suspected diagnosis. Imaging characteristics of orbital tumors and pitfalls in the diagnosis of orbital tumors will be the subject of a future article.

DISCUSSION

Our survey describes clinical symptoms of patients with orbital mass lesions who were treated at the Jules Stein Eye Institute from 1999 to 2003. In general, the prevalence of specific diagnoses of orbital tumors by age is similar to previous studies (Table 6).[1-5] In addition, we did not find specific clinical signs that clearly implicated a specific diagnosis. In many orbital mass lesions, a diagnosis and treatment plan should not be attempted without a complete evaluation, including history, clinical examination, and imaging studies. However, in many cases (eg, typical idiopathic orbital inflammation or infections) the clinical presentation and examination are often sufficient to initiate treatment.

Benign tumors are the common diagnoses at all age groups. In this group, dermoid cyst and heman-

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TABLE 5
Surgical Interventions for Patients With Orbital Mass Lesions, 1999–2003

Surgery	No. (%)
Biopsy–debulking	156 (43.3)
Biopsy–excision	72 (19.5)
Exenteration	11 (3.0)
Drainage	7 (1.9)
Fistula blockage/embolization	3 (0.8)
Optic nerve decompression	3 (0.8)
Enucleation	3 (0.8)
Fine-needle aspiration biopsy	2 (0.5)

gioma (cavernous or capillary) were the most common. These findings are similar to previous reports[1,2,5,6] that described 40% to 80% of all cystic lesions to be dermoid and 30% to 68% of all vasculogenic lesions to be hemangiomas.

We found a relatively high incidence of lymphangioma comprising 20% of all vascular lesions (active and solitary mass) and 4% of total lesions, whereas Shields et al.[6] found an incidence of 10% and 1%, respectively, and Rootman et al.[1] found an incidence of 14% and 2.2%, respectively.

Secondary orbital involvement of ocular adnexal malignancies is more common in older patients. We found squamous cell carcinoma (4.9%) to be the most common adnexal tumor invading the orbit in contrast to Shields et al.,[6] who reported basal cell carcinoma to be more common (2.7%). In this study, the prevalence of orbital involvement by sebaceous carcinoma was relatively common in patients older than 60 years, although they comprise less than 5% of all eyelid malignancies. This high rate of orbital involvement emphasizes the aggressive nature of this process and its tendency toward local invasion. In this study, squamous cell carcinoma also had a tendency toward local orbital involvement, whereas basal cell carcinoma had a low rate of orbital involvement.

For lacrimal gland tumors, inflammatory lesions were the most common, followed by epithelial tumors (pleomorphic adenoma and adenocystic carcinoma). This is similar to a report by Font et al.,[7] who analyzed 120 lacrimal gland cases during a 23-year period, and also to the findings of Johansen et al.[8] and Rootman et al.[1], although they found a higher incidence of epithelial tumors in comparison to inflammatory lesions.[8]

Although our referral patterns provided only three cases of metastatic orbital lesions from breast and prostate carcinoma, these cancers are well-known to metastasize to the orbit.[1,6,9-13] Interestingly, Rootman et al.[1] described a relatively high incidence of fibrosarcoma (3%), which was not as common in other surveys. Lung carcinoma and malignant melanoma are also known malignancies that metastasize to the orbit. In metastatic orbital lesions, up to 42% of cases can be the presenting sign of the systemic cancer.[12]

Overall, the incidence of common primary tumors is similar in all surveys: hemangioma, lymphoma, inflammatory tumor, and neuronal. The most common secondary tumors are basal cell carcinoma, squamous cell carcinoma, meningioma, and paranasal sinus infection or tumor.[2,5,6]

In children younger than 2 years, capillary hemangioma, dermoid cysts, and epidermoid cysts are the most common diagnoses. This finding is similar to the report by Rootman et al.[1] In adolescents, common diagnoses are hemangioma, lymphangioma, dermoid cyst, inflammation, and neurofibroma. Other surveys also found optic nerve glioma, rhabdomyosarcoma, meningioma, and retinoblastoma. In one report[8] optic nerve lesions comprised up to 32% of all orbital lesions in children and young adults younger than 18 years; optic nerve glioma was the most common specific diagnosis in that group. It is possible that in that study, data collection occurred across that country (Denmark) without the selection bias of a tertiary referral center.[3,6,8]

In adults, inflammatory, benign, vascular, neurogenic, and lymphoproliferative diseases are the most prevalent categories of diagnosis. Similar patterns occur in patients older than 65 years, but the incidence of malignant neoplasia or metastases is increased. Demirci et al.[13] examined the frequency of orbital tumors in the older adult population and found malignant lymphoma in 24% of all cases, and an overall frequency of malignant tumors of 63%. We also found an increased incidence of malignant tumors in the older adult population. In fact, both malignant neoplasia and lymphoma were the only tumors that showed increased incidence with older age, whereas the incidence of other diagnoses decreased (Figure). This is in concordance with the increasing incidence of systemic malignant neoplasia and lymphoma with increasing age.[14]

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TABLE 6

Surveys of Orbital Tumors Excluding Thyroid-Related Orbitopathy in All Age Groups

Diagnosis	Rootman et al.[1] (N = 1,895)* British Columbia 1976–1999	Shields et al.[6] (N = 645) Wills Eye 1962–1982	Henderson et al.[5] (N = 1,376) Mayo Clinic 1948–1987	Seregard & Sahlin[2] (N = 300) Stockholm 1974–1998	Johansen et al.[8] (N = 965) Denmark 1974–1997	Kennedy[4] (N = 820)	Total†
Cystic/structural lesions	25%	30%	12.1%	12.3%	5.1%	12%	20.9%
Inflammatory	17.2%	13%	5.8%	7.3%	9.0%	17%	15.1%
Lacrimal gland/fossa‡	2.4%	13%	–	17.7%	12.4%	5%	7.0%
Secondary (eye, ocular adnexa, and nasopharynx)	4.6%	11%	11.2%	11.3%	15.6%	6.5%	11.3%
Lymphoid and leukemias	8.2%	10%	8.1%	12.7%	13.4%	14%	12.6%
Vasculogenic lesions	4.8%	6%	9.5%	12.0%	5.4%	10%	8.8%
Fibrous/osseous/cartilaginous/ adipose	2.8%	5.5%	4.5%	1.2%	4.8%	3.5%	4.7%
Peripheral nerves	3.4%	2%	3.9%	3.0%	2.6%	4.5%	4.1%
Optic nerve and meningeal	5%	1.5%	5.5%	1.7%	7.8%	5.5%	6.3%
Rhabdomyosarcoma	0.4%	1%	2.7%	1.0%	0.1%	1%	1.3%
Metastatic	3%	2.5%	–	3.7%	3.7%	3%	3.0%
Unclassified/miscellaneous	6%	2%	–	6.0%	0.3%	2%	3.4%
Normal orbital tissue	–	1%	–	3.3%	4.8%	1%	1.5%

**Number with non-thyroid orbital disease. Rootman et al. also included 2,024 cases of thyroid orbitopathy; these are excluded in the table for comparison analysis. Percentage is presented in relation to non-thyroid orbital disease.*

†Computed as the relative proportion of specific group in all cases (actual numbers were added and divided in total of all series).

‡The reason for the disparity is that most authors included all lacrimal gland and and fossa processes, whereas Rootman et al. included only benign or malignant epithelial lesions of the lacrimal gland.

The most common presenting symptoms in order of occurrence were proptosis, swelling, inflammation, and double vision; these are similar to the presenting symptoms described by other investigators.[1,13] Rootman et al.[1] found swelling in 28% of patients, proptosis in 21%, diplopia in 21%, pain in 20%, visual loss in 18.5%, mass in 16%, ptosis in 10%, local eye symptoms in 10%, and enophthalmos in 1.8%. Despite their conclusions that symptoms may aid in differential diagnosis, and although pain was commonly associated with malignant tumors of the lacrimal gland,[15] we did not find any significant correlation between symptoms and specific diagnosis.

Treatment consisted of several modalities, but it is important to emphasize that only approximately 50% of orbital tumors were amenable to excision, debulking, or exenteration. In our survey, 20% of the mass lesions or orbital conditions would not be treated surgically under any circumstances and did not require tissue diagnosis. Other orbital lesions such as malignant primary or metastatic neoplasms may be more suitable for chemotherapy or radiation. Inflammatory cases usually respond well to steroids or nonsteroidal anti-inflammatory medications; surgery to obtain specific tissue diagnosis is indicated for atypical cases. Infectious processes are treated with specific antibiotic or anti-fungal therapy with or without surgical drainage of localized abscess. Twenty percent to 50% of orbital tumor cases can be managed by observation with periodic clinical examination and imaging studies alone.[8,13]

Any specific survey of orbital tumors can provide only a partial picture of the diagnostic spectrum because of referral bias, special interests, and demographic influences. Therefore, a familiarity with the differential diagnoses within different age groups should guide the clinician. Moreover, clinical features of orbital tumors can suggest a suspected diagnosis, but no clinical sign or symptom is truly specific and the biological behavior of the abnormal process may be misleading. A careful, individualized diagnostic approach must be undertaken in every case. A careful examination and history can point the examiner in a specific direction and can narrow the differential diagnosis, thus allowing more specific examinations and tests. Management of orbital tumors is complex and may necessitate collaborative work of different medical disciplines. Treatment of orbital tumors may involve surgical intervention half of the time; for the other half, radiotherapy, chemotherapy, medical management, or observation alone may be most appropriate.

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