Isolated Peripheral Nerve Sheath Tumours of the Orbit

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Summary

Fifty-four cases of peripheral nerve sheath tumours within the orbit are reviewed. Benign neurilemmomas or neurofibromas occurred in 93% of patients and had an equal incidence. There was a family history or other signs of systemic neurofibromatosis in one-quarter of those with solitary neurofibromas, but in none of the patients with neurilemmoma.

Symptoms and signs were generally those of an orbital mass lesion and pain or sensory loss was unusual, occurring more frequently with malignancy.

Within the orbit, most peripheral nerve sheath tumours affect the first division of the trigeminal nerve and extension of some tumours through the superior orbital fissure limits their surgical resection. Despite incomplete resection of some tumours, with up to 23 years follow-up there have been no recurrences requiring further surgery. A postoperative sensory deficit occurred in only 32% of patients with benign neurilemmomas and 72% with neurofibromas.

The majority of peripheral nerve sheath tumours comprise benign neurofibromas or neurilemmomas and malignant nerve sheath tumours are relatively rare.

In the absence of systemic neurofibromatosis, peripheral nerve sheath tumours are uncommon throughout the body and form only about 2–4% of orbital neoplasms.^{1–3} Orbital peripheral nerve sheath tumours have been reported in several small series and as solitary case-reports, some with unusual features—for example, intramuscular location of a tumour,⁴ multiple tumours in a single orbit^{5–7} or malignant tumours.^{1–3, 8–11}

The clinical features and management of 54 peripheral nerve sheath tumours of the orbit are reviewed in this paper: Plexiform neurofibromas are excluded from this report, being a group of diffuse tumours with distinctive presentation and behaviour.

Patients and Methods

Fifty-four patients with isolated orbital peripheral nerve sheath tumours were seen between 1969 and 1989, less than 2% of about 3,500 patients seen in the Orbital clinic.

A detailed clinical history was taken from each patient, with particular attention being directed to a personal or family history of neurological or dermatological abnormalities. All patients had complete ophthalmic evaluation and also assessment by a neurologist, for the systemic stigmata of neurofibromatosis (using criteria of Crowe and others).¹²

Radiological investigation generally included plain orbital radiographs, computerised orbital tomography (after 1974) and orbital venography (before 1974). Orbital B-mode ultrasound investigation was used only rarely.

Results are compared by analysis of vari-

Table I Age and symptoms at presentation for 54 patients

Characteristics or Presenting symptoms	Type of orbital tumour		
	Benign neurofibroma	Benign neurilemmoma	Malignant sheath tumour
Sex	12M, 13F	8M, 17F	3M,1F
Age (years)			
Mean, SD	40, 17	41, 16	(36)
Median	38	41	—
Range	8 to 66	21 to 82	17 to 55
Duration of first symptom (years)			
Mean, SD	7.9, 11.0	3.2, 5.2	3.0, 1.8
Median	2	1	3.2
Range	0.2 to 32	0.2 to 20	0.7 to 5
Swelling/lump	15 (60%)	14 (56%)	3 (75%)
Proptosis	12 (48%)	13 (52%)	2 (50%)
Visual change	4 (16%)	5 (20%)	—
Ptosis	4 (16%)	2 (8%)	—
Diplopia/squint	3 (12%)	2 (8%)	—
Ache	3 (12%)	3 (12%)	1 (25%)
Visual obscurations	2 (8%)	1 (4%)	—
Epiphora	—	1 (4%)	—
Redness	—	—	1 (25%)

M denotes male, F denotes female, SD denotes standard deviation

ance, the 'Student' t statistic and the Chi-squared statistic.

Results

The sex incidence and the ages at presentation are similar in three diagnostic groups (Table I; Fig. 1).

The presenting symptoms for neurofibromas, neurilemmomas and malignant nerve sheath tumours are similar (Table I). However, the duration of first symptom at presentation is significantly greater for neurofibromas than for neurilemmomas

($P < 0.05$), but that for benign neurilemmomas and malignant nerve sheath tumours are similar ($P < 0.9$).

The clinical signs for benign and malignant nerve sheath tumours are almost exclusively those of an orbital mass: Thus, about 75% of the benign tumours caused non-axial displacement of the globe and over 90% caused proptosis (from 1–12 mm). An anterior orbital mass was palpable and eye movements were restricted in about two-thirds of patients. Visual function was reduced in 9/50 (18%) cases, some with choroidal striae (six cases), papilloedema (three cases) or optic atrophy (two cases). There was a detectable trigeminal sensory loss in 6/50 (12%) of the benign, in contrast to 2/4 (50%) of the malignant, nerve sheath tumours.

Benign nerve sheath tumours typically have a smooth contour on CT scanning (Fig. 2) and expand neighbouring orbital walls (25/30 cases; Fig. 3). Extension to the superior orbital fissure (Fig. 4) was evident in 11/27 (41%) scans. However, flattening of the globe was unusual (5/28 scans) and tumour calcification was not evident in any of the scans (at soft-tissue settings). The intraorbital distribution of neurofibromas and neurilemmomas, as determined radiologically or surgically (Fig.

Fig. 1. Age at presentation for 54 patients with isolated peripheral nerve sheath tumours of the orbit.

Fig. 2. Axial CT scan demonstrating a smoothly-contoured benign neurilemmoma in the intraconal space, displacing the optic nerve medially.

5), shows a significant departure from random: Lesions are superiorly-located significantly more often than inferiorly in most spaces within the orbit ($P < 0.001$; Fig. 5). Similarly, posteriorly ($P < 0.05$) and in the middle one-third intraconally ($P < 0.01$), laterally-located tumours are more common than medial. The nerve(s) of origin for neurofibromas is more readily identifiable than that for neurilemmomas (Table II).

Tumours were mainly resected through lateral orbitotomy (Table II), although complete resection was achieved with only 72% of neurilemmomas and 46% of neurofibromas ($P < 0.05$). Orbital neurofibromas extending intracranially, too extensive for resection, were present in two patients, double neurofibromas in two others and multiple neurofibromas in three patients.

Intraoperative complications were few and included minor leaks of cerebro-spinal fluid from the superior orbital fissure (one case) or orbital roof (one case) and damage to branches of the ophthalmic artery (two cases).

The postoperative results and complications are presented in Table III.

Fig. 3. Extraconal neurofibroma expanding the roof of the orbit, shown on a reformatted coronal CT scan.

Discussion

Benign peripheral nerve sheath tumours comprise a variable proliferation and mixture of axons, Schwann cells, supporting endoneural cells and vascular elements.¹⁻³ Neurilemmomas (Schwannomas) are generally well-defined, often eccentric from the nerve of origin, and show a predominance of spindle-shaped Schwann cells; these latter cells often displaying palisading of nuclei (Antoni A pattern) or a less organised pattern (Antoni B). Axons are infrequent within, and often pass eccentrically through, the main mass of a neurilemmoma. Neurofibromas more commonly arise within nerves and display more endoneural proliferation, thus expanding and forming an intimate relation to the parent nerve. When there is multiple involvement of adjacent nerve branches, the effect is to produce a composite mass of thickened nerve bundles and, as such, the tumours are usually referred to as 'plexiform'. Neurofibromas and, to a lesser degree, neurilemmomas can undergo degeneration, manifest as myxoid or cystic change and haemorrhage; inflammatory cell infiltration may occur with this degeneration. Malignant nerve sheath tumours are infrequent.¹¹

Epidemiology and Presentation

Orbital neurilemmomas and neurofibromas comprised less than 2% of patients seen in the Orbital clinic at Moorfields Eye Hospital and about 5% of the orbital tumours; this latter figure being somewhat higher than other smaller studies.^{1,3} The sex incidence and age distributions (Table I) agree with those for other series.¹⁻³ The equal incidence of neurofibromas and neurilemmomas is, however,

Fig. 4. Axial CT scan showing a neurofibroma extending posteriorly towards the superior orbital fissure (arrow).

Fig. 5. Distribution of benign nerve sheath tumours within the orbital spaces. (A) Neurofibromas affecting 59 sectors in 24 patients; (B) Neurilemmomas affecting 50 sectors in 25 patients.

a significant ($P < 0.05$) departure from a quoted ratio of 2:1;¹ this possibly reflecting exclusion of plexiform neurofibromas from the present series.

Patients with benign orbital neurofibromas and neurilemmomas generally give a long history of progressive symptoms due to the orbital mass; the duration of symptoms is significantly longer with neurofibromas (Table I), although the reason for this is unclear.

Although Rootman³ suggests changes of sensory nerve function to be 'frequently noted' with neurofibromas, in the present series disturbance of trigeminal nerve function is uncommon with benign tumours and appears to occur more frequently with malignancy. Seven of the 25 patients (28%) with orbital neurofibromas had a family history and/or systemic signs of neurofibromatosis, in contrast to none of the 25 patients with neurilemmomas ($P < 0.01$).

Clinical and radiological signs for nerve sheath tumours, benign or malignant, are typically those of a slowly-expanding orbital mass¹³ and only few signs—such as trigeminal sensory loss or destruction of bone¹¹—tend to favour malignancy.

Benign nerve sheath tumours occurred significantly more often in the upper half of the orbit (Fig. 5), this probably being a manifestation of the greater number of sensory nerves in this location. The nerves of origin were evident for 63% of neurofibromas, 32% of benign neurilemmomas and 50% of malignant nerve sheath tumours (Table II).

Surgery for Benign Tumours and its Complications

Surgical resection of nerve sheath tumours

Table II Surgical characteristics for 54 patients

Surgical characteristics	Type of orbital tumour		
	Benign neurofibroma	Benign neurilemmoma	Malignant sheath tumour
<i>Approach to Resection and Surgical Findings</i>			
Lateral orbitotomy	14/25 (56%)	17/25 (68%)	1/4 (25%)
Anterior orbitotomy	7/25 (28%)	8/25 (32%)	3/4 (75%)
Frontal orbitotomy	1/25 (4%)	—	—
Exenteration	1/25 (4%)	—	—
None (too extensive)	2/25 (8%)	—	—
Extension to SOF	8/24 (33%)	6/25 (24%)	2/4 (50%)
Resection complete	12/25 (48%)	19/25 (76%)	1/4 (25%)
<i>Evidence for Nerve of Origin at Surgery or Postoperatively</i>			
Supratrochlear (ST)	2/23 (9%)	1/25 (4%)	1/4 (25%)
Supraorbital (SO)	6/23 (26%)	4/25 (16%)	—
Lacrimal (L)	1/23 (4%)	1/25 (4%)	—
ST + SO nerves	3/23 (13%)	—	—
ST, SO + L nerves	2/23 (9%)	—	—
Corneal	1/23 (4%)	—	—
Zygomatico-temporal	—	2/25 (8%)	—
Infraorbital	—	—	1/4 (25%)

SOF denotes superior orbital fissure

Table III *Postoperative results and complications for 52 patients*

<i>Postoperative results and complications</i>	<i>Type of orbital tumour</i>		
	<i>Benign# Neurofibroma</i>	<i>Benign Neurilemmoma</i>	<i>Malignant sheath tumour</i>
Acuity improved	5/22 (23%)	7/25 (28%)	—
Acuity similar	14/22 (63%)	15/25 (60%)	2/4 (50%)
Acuity worse	3/22 (14%)	3/25 (12%)	2/4 (50%)
+ve Marcus-Gunn	2/22 (9%)	2/25 (8%)	2/4 (50%)
Restricted eye movement	10/22 (46%)	10/23 (43%)	2/4 (50%)
Squint surgery	—	3/23 (13%)	—
Ptosis—early	12/22 (55%)	5/23 (22%)	1/4 (25%)
—late	3/21 (15%)	1/21 (5%)	1/4 (25%)
Ptosis surgery	—	1/25 (4%)	—
Sensory deficit	16/22 (72%)	8/25 (32%)	2/4 (50%)
Fixed mydriasis	4/22 (18%)	6/25 (24%)	1/4 (25%)
<i>Follow-up interval (years)</i>			
All cases of tumour			
Mean, SD	3.8, 6.2	1.9, 2.2	(2.5, 3.8)
Median	0.8	1.2	0.9
Range	0.1 to 23.7	0.1 to 9.5	0.1 to 8.2
Number	23	25	4
Incomplete reaction of tumour			
Mean, SD	6.8, 7.7	2.4, 1.9	(2.4)
Median	6.0	2.8	2.8
Range	0.1 to 23.7	0.1 to 5.0	0.1 to 1.4
Number	11	6	3

#denotes one case of exenteration excluded. SD denotes standard deviation

was possible through an anterior orbitotomy in one-third of cases, although lateral orbitotomy, transfrontal orbitotomy or exenteration was required to excise more extensive or posterior lesions (Table II). The benign nerve sheath tumours were found to extend into the superior orbital fissure in 28% of 47 cases, this limiting the extent of resection. Complete resection was significantly more frequent with neurilemmomas than neurofibromas ($P < 0.05$), this reflecting the localised nature of many neurilemmomas.

Because of the difficulty of surgical dissection near the apex of the orbit, there was a significant, but low, incidence of surgical complications: Two patients developed minor leaks of cerebro-spinal fluid which ceased spontaneously and two other patients developed transient, but marked, neuropraxia of motor nerves—possibly due to peri-operative oedema at the superior orbital fissure.

In most cases, ocular motility and visual function improved after resection of bulky neurofibromas or neurilemmomas (Table III). In six (13%) patients visual function was

reduced after surgery and ten (21%) developed a fixed mydriasis, possibly due to impairment of blood-flow to the optic nerve or ciliary ganglion. One patient developed central retinal artery occlusion after resection of a neurofibroma situated intraconally within the posterior one-third of the orbit. Impairment of the function of extraocular muscles or levator palpebrae, often marked in the early post-operative period, generally recovered over several months; three patients needed further surgery for squint or ptosis.

Although resection of a sensory nerve sheath tumour would reasonably be expected to produce a sensory deficit, this was clinically detectable in only 32% of neurilemmomas and 72% of neurofibromas (Table III). The lack of a clinically detectable deficit presumably arising because these tumours originate on minor branches of sensory nerves, are sited eccentrically from the sensory nerve of origin, or arise on nerves not subserving cutaneous sensorium (for example, autonomic nerves; perhaps the cause of some cases with post-operative mydriasis).

Malignant Nerve Sheath Tumours

The similar duration of symptoms for benign neurilemmomas and malignant nerve sheath tumours (which, in this series, all displayed features of malignant neurilemmomas) would suggest that such malignant tumours are arising *de novo* and not through a malignant transformation within a preceding benign tumour.

Complete resection of malignant nerve sheath tumours was possible in only one of the four patients, the others undergoing diagnostic biopsy or debulking of tumour mass.

Clinical Recurrence of Tumours after Surgical Resection

Even for patients in whom resection of benign nervesheath tumours was known to be incomplete, there has been no evidence of recurrence or continued growth—even to 23 years of follow-up. It is possible that surgical debulking of such (benign) tumours alters the growth pattern, perhaps by removal of tumour growth factors.

One of the patients with malignant nerve sheath tumour died within four months of diagnosis and one patient was lost to follow-up. Two patients are alive and disease-free at one-and-a-half and eight years after resection of tumours of low-grade malignancy.¹¹

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