

Aetiology and outcomes of adult superior oblique palsies: a modern series

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Abstract

Purpose To establish the contemporary aetiology of adult superior oblique palsy (SOP).

Materials and Methods A retrospective consecutive case series of 150 persons diagnosed with SOP between 1 January 1999 and 31 May 2005 at a neuro-ophthalmology centre in the West Midlands, the United Kingdom. Interrogating two different hospital databases identified all cases. A case note review was performed on all participants to determine demographics and aetiology based on diagnostic criteria, neuroimaging used, and outcome.

Results We identified 133 unilateral isolated, 7 unilateral associated with other cranial nerve involvement, and 10 bilateral cases of SOP. Eighty-six were acquired, 51 congenital, and 13 undetermined. Of the unilateral isolated cases, 38.3% were considered to be congenital, 29.3% followed trauma, 23.3% were presumed to be vasculopathic in origin, and no cause could be established in 7.5%. All presumed microvascular-associated palsies resolved within 6 months of presentation. Unilateral SOPs associated with other cranial nerve palsies were commonly caused by trauma (71.4%), followed by tumour and undetermined causes (both 14.3%). Trauma was the most frequent cause of bilateral SOP (50%), followed by tumours and undetermined causes (both 20%), with congenital causes being uncommon (10%).

Conclusion We present a contemporary aetiological spectrum for adult SOP, with the lowest incidence of undetermined cases published in the medical literature. Neuroimaging did not change the management for the vast majority of cases and should be prompted by atypical presentations.

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Introduction

Since Bielschowsky¹ recognized fourth cranial nerve palsies as the commonest cause of paralytic vertical ocular misalignment, there have been several published series on the aetiology of superior oblique palsy (SOP) (Table 1). Some predate the advent of modern neuroimaging.^{1–4} Rucker^{2,3} and Rush and Younge⁴ did not classify their subjects into the generally recognized major categories: congenital, traumatic, ischaemic, other, and undetermined. Although Richards *et al*⁵ acknowledged congenital causes, they excluded this group from their results. Other studies that have recognized the congenital group have not used fully representative populations; Von Noorden⁶ presented a surgical cohort with a mean age of 24.7 years, and Keane⁷ presented an in-patient series of an office-based diagnosis.

It is generally accepted that maintaining close medical review of all isolated SOP in presence of microvascular risk factors is appropriate, although there is insufficient evidence in the literature to support this. This was our local practise during the study period and neuroimaging was employed only when progressive cranial nerve involvement was present (ie no longer isolated) or where there was no recovery.

The purpose of our study was to determine the up-to-date aetiological distribution of adult onset SOP according to stringently defined categories. We also wished to establish the time

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Table 1 A summary of published data compared to this series

Series		No. of cases	Congenital	Trauma	Presumed microvascular	Undetermined	Tumour	Other
Rucker, ² 1958–1964	Mayo, USA	84	—	27.4%	15.5%	33.0%	8.3%	15.5%
Rush and Younge, ⁴ 1966–78	Mayo, USA	172	—	32.0%	18.6%	36.0%	—	7.6%
Von Noorden, ⁶ 1973–84	Houston, USA	270	39.5%	34.0%	—	23.2%	—	2.9%
Richards and Younge, ⁵ 1978–88	Mayo, USA	578	—	29%	18%	32%	5%	16%
Keane, ⁷ 1970–93	Los Angeles, USA	215	1%	52%	4%	—	8%	34%
This series, 1999–2005	United Kingdom	150	34.7%	32.7%	20.7%	8.7%	2.7%	0.7%

period of symptoms to stabilization and explore the role of neuroimaging in the management of SOP. By characterizing the contemporary presentation of SOP, in a representative adult population, both clinician and patient will benefit from a more detailed understanding of the current natural history of this condition.

Materials and methods

Consecutive patients with SOP presenting to the Birmingham and Midland Eye Centre, a regional neuro-ophthalmology centre, between 1 January 1999 and 31 May 2005 were identified using the orthoptic department database, cross-validated with the neuro-ophthalmic database. The study was registered with the Sandwell and West Birmingham NHS Trust clinical effectiveness department.

The local protocol defines SOP as complete or partial paralysis of the superior oblique muscle. The criteria for unilateral SOP were incomitant hypertropia, underaction of the superior oblique muscle and/or overaction of its antagonistic inferior oblique muscle, and excyclotropion $\leq 10^\circ$ as measured with the double Maddox rod test. Bilateral SOP was underaction of both superior oblique muscles and/or overaction of both inferior oblique muscles, and excyclotropia $\geq 10^\circ$. SOP associated with other cranial nerve palsies was included in the study.

Case notes were reviewed recording demographics, aetiology, neuroimaging, interval to symptom-resolution time, and outcome. The aetiology recorded in this study was established by the attending doctor and not by the study investigators. Neuroimaging was not a routine investigation in this series and was at the discretion of the ophthalmologist. Patients under 16 years of age were excluded, as some might have attended the regional paediatric hospital, and have been excluded from the databases searched.

A congenital aetiology was defined as a history of onset of vertical strabismus or corrective head posture dating back to infancy, with a vertical fusion range larger than 6 prism dioptres and no subjective torsion. This was established by either history, inspection of old photographs, and absence of any other contributory

factors, or a combination of these criteria. A traumatic aetiology was defined as having a positive history of head trauma secondary to falls, road traffic accidents, assault, or iatrogenic causes. For example, neurosurgical intervention that resulted in SOP was classified as iatrogenic trauma.

The SOPs presumed to be vasculopathic were identified with the aid of the following local protocol: any non-traumatic acquired SOP has blood pressure and random blood glucose performed. A blood sample is screened for full blood count, urea and electrolytes, erythrocyte sedimentation rate, and C-reactive protein. This is followed up with a fasting blood glucose and lipid profile. Vasculopathic causes included diabetes mellitus, hypertension, and hypercholesterolaemia, with a negative trauma history and normal vertical fusion range. Diabetes was identified if patients were taking insulin, oral hypoglycaemics, using diet to control elevated plasma glucose, or had random blood glucose of ≥ 11.1 mmol/l.⁸ Hypertension was defined if antihypertensive medications were prescribed, or if the blood pressure was elevated on presentation (systolic ≥ 140 mmHg or diastolic ≥ 90 mmHg).⁹ Hypercholesterolaemia was diagnosed if cholesterol was ≥ 5.0 mmol/l at initial assessment.¹⁰ Microvascular categories were confirmed only when the palsy resolved.

SOP as direct result of neoplasm growth was termed tumour. Any idiopathic SOP with none of the above characteristics was categorized as undetermined. The remaining rare causes were termed as others.

Results

One hundred and fifty adults with a diagnosis of SOP were included; 57 women and 93 men with mean age at presentation of 52.5 ± 19.8 standard deviation (SD) years (range 16–87 years). Aetiology and frequency per age group are summarized (Table 2, Figure 1) and show peak incidence in the seventh decade.

Unilateral isolated SOP

The categorization of the 133 unilateral isolated SOP was congenital (38.3%), trauma (29.3%), presumed

Table 2 Aetiology of superior oblique palsy in this cohort (n = 150)

	Unilateral isolated IV nerve palsy	Unilateral multiple cranial nerve palsies	Bilateral IV nerve palsies	Totals
Congenital	51	0	1	52
Trauma	39	5	5	49
Road traffic accident	13	2	5	
Blunt assault	6			
Falls	6			
Occupational	1 (professional boxer)			
Neurosurgical	4	3		
Ophthalmic surgery	2			
ENT surgery	1			
Other	5 ('trauma' recorded (3); post-emesis (1); post-seizure (1))			
Presumed microvascular	31	0	0	31
Hypertension	14			
Diabetes mellitus	1			
Hypercholesterolaemia	1			
Combination	15			
Undetermined	10	1	2	13
Tumour	1	1	2	4
	1 (orbital trochlear schwannoma)	1 (intracranial meningioma)	1 (midbrain glioma), 1 (pinealoma)	
Other	1	0	0	1
	1 (carotid cavernous fistula)			
Totals	133	7	10	150

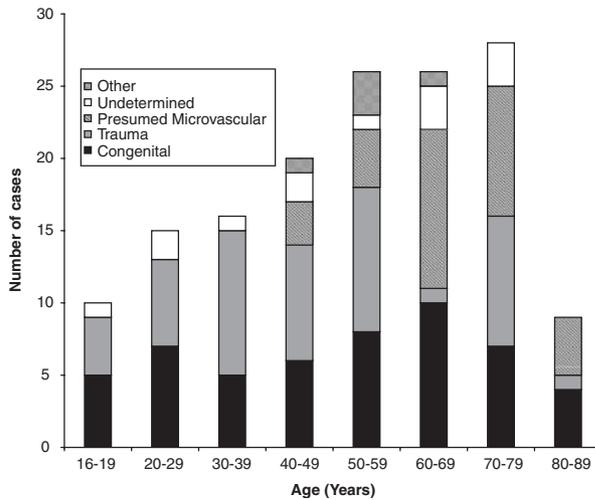


Figure 1 Frequency and aetiology of all superior oblique palsy per decade of life (n = 150).

microvascular (23.3%), undetermined (7.5%), and miscellaneous (1.5%) (Table 2).

Congenital

Fifty-one cases, mean age 51.6 ± 21.8 SD years (range 16–87 years), were congenital. The majority did not have neuroimaging and, of those scanned, five (9.8%) were normal. In all, 47.3% (24/51) had successful surgery and 66.7% (27/51) were managed conservatively.

Trauma

Thirty-nine (29.3%) cases, mean age 47.0 ± 19.7 SD years (range 17–81 years), resulted from trauma (Table 2). In all, 33.3% (13/39) had surgery, 46.2% (18/39) were treated conservatively, and 17.9% (8/39) were lost to follow-up. Nine cases resolved completely within 12 months (mean 4 months, range 4 weeks–12 months).

Microvascular

Presumed microvascular cases accounted for 23.3% (31/133) of SOP (mean age 65.9 ± 10.8 SD years, range 41–85 years, Table 3). The majority (48.4%) were associated with multiple ischaemic risk factors. In all, 45.2% were associated with hypertension alone, 3.2% with diabetes alone, and 3.2% with hypercholesterolaemia alone. In all, 93.5% (29/31) resolved and 6.4% (2/31) were lost to follow-up.

Of the 29 cases that resolved, in 22 (71%), the mean time to resolution was 10.5 weeks (range 3 weeks–6 months). There was no statistical significance (Student's *t*-test) in time to recovery when comparing the group with multiple risk factors with those with hypertension alone. Similarly, the time to recovery was not significantly different across the different age categories (Table 3). Two cases underwent neuroimaging, both were normal and resolution occurred at 3 and 5 months. No

Table 3 The relationship between type of microvascular disease (horizontal values), age per decade of life (vertical values), and time to resolution of superior oblique palsy in the presumed microvascular group (*n* = 31)

Age range (years)	40–49	50–59	60–69	70–79	80–89			
Number in cohort (31)	3 ^a	4	11	9	4 ^b	Mean time to resolution	SD	Resolution range
Hypertension (14)	2	2	5 ^c	3 ^c	2	9.2 weeks	± 5.65	3–16 weeks
Diabetes (1)	0	0	1	0	0	12 weeks	—	—
Hypercholesterolaemia (1)	—	—	—	—	—	13 weeks	—	—
Combination (15)	1	2	5	5	2	10.8 weeks	± 5.04	5–24 weeks
Mean time to resolution	—	10.7 weeks	8 weeks	13 weeks	—			
SD	—	± 2.31	± 4.31	± 6.71	—			
Resolution range	3 weeks	8–12 weeks	3–16 weeks	4–24 weeks	8 weeks			

No statistical significance was found between age and time to resolution, and between type of ischaemic cause and time to resolution.

^aExact time to resolution not recorded in two cases.

^bExact time to resolution not recorded in three cases.

^cSubject in this group lost to follow-up (age 67 and 71 years, respectively).

microvascular cases had surgery, nor were any of the cases an initial presentation of systemic disease.

Tumour

A trochlear nerve schwannoma caused one case of unilateral SOP. A magnetic resonance imaging scan was performed as they presented with pain, diplopia, and proptosis; it diagnosed this intraorbital tumour.

Others

One case of unilateral SOP was associated with pain and proptosis, and was caused by a carotid cavernous fistula. This was successfully embolized.

Undetermined

Ten cases (mean age 48.5 ± 22.3 SD years, range 18–77 years) had no systemic pathology identified; three resolved (resolution time: 6 weeks, 3 months, 3 months) with no neuroimaging. Four unresolved cases had normal brain and orbit magnetic resonance imaging. Three cases were lost to follow-up.

Unilateral SOP associated with other cranial nerve palsies

Multiple cranial nerve palsies were recorded in seven cases (mean age 48.8 ± 16.1 SD years, range 31–76 years) (Table 2). The majority of cases were caused by trauma (71.4%), one was caused by an intracranial meningioma, and one case was undetermined. All non-isolated underwent magnetic resonance imaging.

Bilateral SOP

Ten cases had bilateral SOP (mean age 42.7 ± 16.3 SD years, range 19–59 years) (Table 2). Half were caused by trauma, two cases by tumour, two were undetermined, and one was congenital in origin. All bilateral cases had magnetic resonance imaging.

Conclusion

This study describes the causes of isolated unilateral, non-isolated unilateral, and bilateral SOP presenting to a regional neuro-ophthalmic unit between 1999 and 2005. The most common categorizations for isolated unilateral SOP, according to our definitions, were ‘congenital’, ‘trauma’, and ‘microvascular’.

We report 23% of unilateral SOP having a presumed microvascular aetiology; this is higher than previously reported (Table 1) and is likely to reflect an ageing population with better detection of cardiovascular risk factors. By definition, microvascular cases are of undetermined origin until they resolve and the coexistence of microvascular disease with SOP does not rule out sinister pathology. If there are no other symptoms or neurological deficits, it is appropriate to maintain close medical review checking for signs of progression or resolution. This series identified 93.5% of presumed microvascular palsies resolving within 2–3 months (mean 10.5 weeks; all within 6 months) with 6.5% lost to follow-up. The exact recovery latency cannot be determined from this study as recorded time is determined by the timing when the follow-up appointment occurs (typically 3–4 weeks). There was no statistical difference in recovery rate when comparing different age groups or different microvascular risk factors (Table 3). Our recommendation would be to observe suspected microvascular cases, employing

neuroimaging when progressive cranial nerve involvement is present or where there is no recovery at 6 months.

There were no cases of undetermined origin that had positive neuroimaging. However, three undetermined cases were lost to follow-up, despite contacting family doctors about non-attendance. There are many rare causes of SOP,^{3,4,7} and in most they are not isolated or present with additional symptoms. Barton's¹¹ series demonstrates that atypical aspects of the patient's history warrants urgent neuroimaging with contrast studies. This was the case in the tumour and other cases where they both presented with SOP, pain, and proptosis.

Bilateral SOPs are uncommon^{4,12} and are typically caused by trauma.¹² In our series, trauma was also the most common cause of bilateral SOPs, accounting for half the cases. It is interesting to note that in the two cases caused by tumour, one was caused by an intrinsic tumour (midbrain glioma) and the other by an extrinsic tumour (pinealoma).

We acknowledge the restrictions of a retrospective design. We minimized the risk of overlooking cases by cross-referencing two separate databases. Using stringent definitions for aetiology can introduce bias and we recognize that vertical fusion ranges in acquired SOP can increase over time. However, microvascular and traumatic causes tend to have a positive history and/or examination that can distinguish them from congenital cases. In this study, details of prior para-infectious symptoms were not routinely sought and this could be an interesting association to explore in the future.

Compared to the literature (Table 1), we report the lowest rate of undetermined SOP, at 8.7% by incorporating the categories of congenital and microvascular causes in our series. As the mean age of the cohort was 52.5 years, with both in-patients and outpatients included, we believe that this is an unbiased adult population. However, as a tertiary centre and an institution-based study, the distribution of aetiology may reflect referral bias and could be different in another geographical location.

This study helps to guide the ophthalmologist in the diagnosis and evaluation of SOP, and provides

contemporary information for informed counselling of patients in the early stages of their clinical course.

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