Superior oblique myokymia

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Abstract

Superior oblique myokymia (SOM) is a rare condition of unclear etiology. We discuss the history, etiology, clinical features, differential diagnoses, management, and prognosis of SOM. We conducted a meta-analysis of all 116 cases published since SOM was first described in 1906. The age at examination was 17–72 years (mean: 42 years). There was a right-sided preponderance in 61% of cases (P < 0.02) that was statistically significant in females (63%, P < 0.04) but not in males (59%, P = 0.18). The pathophysiology of SOM may be neurovascular compression and/or ephaptic transmission. Although various pharmacological and surgical approaches to SOM treatment have been proposed, the rarity of the condition has made it impossible to conduct clinical trials evaluating the safety and efficacy of these approaches. Recently, topical beta blockers have managed SOM symptoms in a number of cases, including the first case treated with levobunolol. Systemic medications, strabismus surgery, and neurosurgery have been used to control symptoms, with strabismus surgery carrying a moderate risk of postoperative diplopia in downgaze. Although there is no established treatment for SOM, we encourage clinicians to attempt topical levobunolol therapy before considering systemic therapy or surgery.

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1. Introduction

Superior oblique myokymia (SOM) is an uncommon monocular condition of unclear etiology that results in episodes of oscillopsia and diplopia. Currently, there is no established treatment protocol for SOM, although multiple pharmacological and surgical approaches have been proposed. We review what is known about the etiology, clinical features, patient demographics, and treatment of SOM. We also present a meta-analysis of all 116 reports of SOM that have been published since Alexander Duane first described the condition in 1906.

2. History

In 1906, Duane described a case of what he termed “unilateral rotary nystagmus” where the patient described seeing “one object rising vertically out of the other” and then “appear to dance up and down.” Hoyt and Keane later proposed the basic diagnostic criteria for the condition in 1970 and introduced the term “superior oblique myokymia” (SOM). In the 1970s, SOM was defined as a “unicocular rotary microtremor.” Subsequent studies, mostly case reports,
expanding the characterization of SOM as “monocular, high-frequency, low-amplitude, torsional, and involuntary contractions of the superior oblique muscle that result in oscillopsia and diplopa”.

3. **Etiology**

The etiology of SOM is unknown. Ephaptic transmission (direct transmission across adjacent neural cell membranes that bypasses synapses) has been proposed as a likely contributor. Other conditions, including ocular neuromyotonia, epilepsy, and facial nerve diseases (including hemifacial spasm and facial synkinesis) are also believed to result at least in part from ephaptic transmission. SOM has also been linked with neurovascular compression syndromes that are characterized by recurrent attacks of symptoms from pulsatile nerve compression by an artery. Vascular compression occurs when there is an absence of the cerebrospinal fluid layer between the trochlear nerve and an adjacent blood vessel on neuroimaging. It is theorized that the compression leads to segmental demyelination of the nerve transition zone covered by oligodendrocytes, leading to subsequent ephaptic axonal transmission. Successful treatment of SOM using membrane stabilizers such as carbamazepine, gabapentin, and memantine further supports the hypothesis that ephaptic transmission contributes to the disorder.

There has been speculation on a possible link between multiple sclerosis and SOM, with 2 reported cases in patients with a family history of multiple sclerosis. An additional published case described a patient whose SOM episodes were triggered by prolonged exposure to heat such as bathing. This phenomenon, known as Uhthoff's phenomenon, can be exacerbated by fatigue, the chronic time course of the condition, and the resolution of symptoms following microvascular decompression. However, SOM can occur spontaneously and have no previous trauma or known neurovascular compression. Neurovascular compression may lead to SOM, but not all SOM cases result from neurovascular compression. Hence, SOM cannot be truly defined as a neurovascular compression syndrome, as it is not always caused by direct cranial nerve irritation by vessels.

4. **Clinical features and meta-analysis**

SOM episodes may last seconds or hours and can occur several times a day. Triggers include fatigue, stress, and mood.
Superior oblique myokymia: Case report.


Fig. 1 – Image obtained during neurosurgical decompression of the trochlear nerve. A: Branch of superior cerebellar artery (arrowhead) strangulating the origin of the trochlear nerve (arrows). B: Artery cushioned from nerve after interposition of a Teflon graft. Modified with permission from Fam MD, Scott C, Forster A, Kamel MH. Microvascular decompression for superior oblique myokymia: Case report. British Journal of Neurosurgery. 2014; 28:552-5.

Changes, but episodes may also occur spontaneously. There are few symptoms other than diplopia, unilateral oscillopsia, and the sensation of abnormal eye movement.

The unilateral, high-frequency (up to 50 Hz), low-amplitude (<4° in both planes), torsional, nystagmoid movements of SOM are distinctive. Electromyography demonstrates prolonged high-voltage discharges. On examination, there are usually no other physical findings of note, but Wertenbaker reported an audible phenomenon when placing the stethoscope over the affected eye in 2 patients. He described the finding as “an irregular, rapid, machine gun sound.” On ocular motility testing, there may be a slight weakness of the superior oblique muscle while it is at rest. In these cases, a small hypertropia in the SOM eye will change to a hypotropia during a myokymic episode.

To better characterize what is known about the epidemiology and clinical features of SOM, we reviewed all 116 cases published since SOM was first described in 1906 (Table 1). The age at the time of examination ranged from 17–72 years, with a mean of 42 years (Table 2). The meta-analysis supports the clinical teaching that patients presenting with SOM are often young adults who are otherwise healthy and that SOM more commonly affects the right eye. We did not, however, confirm previous suggestions that women are more likely to be affected than men. Approximately half of all reported cases have been female (52%; Table 1).

SOM was unilateral in all reported cases, and there was a statistically significant right eye predominance, with 61% (71/116) of SOM being right-sided (P = 0.016, chi-squared test) (Table 1). This right-sided SOM predominance remains unexplained. In 1 MRI study, all the 6 cases of symptomatic SOM occurred in the right eye. Even with advanced MRI imaging techniques allowing for 3-dimensional visualization of 92% of the right and left trochlear nerves, there do not appear to be any anatomical asymmetries of the trochlear nerves or superior cerebellar arteries that could explain the SOM asymmetry. We further found that the right-sided predominance was statistically significant in women (63%, P = 0.039), but not in men (59%, P = 0.18; Fig. 3). Between males and females there was no difference in the age of presentation, and more than half of patients presented between the ages of 31–50 years, regardless of sex (Fig. 4).

5. Differential diagnosis

The features of SOM are so distinctive and remarkable that it is rarely confused with other conditions, especially if the symptoms and signs match the classic presentation; however, it is helpful to consider the differential diagnosis, both to help with cases that have a less typical presentation and also to provide further insight into the etiology of the condition.

Myokymias are localized, involuntary, fine, continuous contractions that propagate through the affected striated muscle. Eyelid myokymia is the most common type of facial myokymia. Patients experience involuntary fine contractions of the orbicularis oculi muscle. Eyelid myokymia can be confused with SOM, especially as it can cause oscillopsia in some cases. Like SOM, eyelid myokymia is commonly unilateral, transient, and intermittent, occurring in otherwise healthy individuals, frequently triggered by fatigue, stress, or excessive caffeine intake. Episodes of eyelid myokymia occur intermittently for several hours over a few days but can persist for several weeks to months before resolving spontaneously.

The Heimann-Bielschowsky phenomenon is a dysconjugate monocular vertical eye movement that develops in an eye with reduced vision. The phenomenon is characterized by unilateral, coarse, low-frequency, pendular vertical oscillations. It has no neurologic implications. The Heimann-Bielschowsky phenomenon can be distinguished from SOM by the amplitude and frequency of oscillations: SOM has low amplitude (<4°) and high frequency (up to 50 Hz), whereas the Heimann-Bielschowsky phenomenon has high amplitude (up to 30°) and low frequency (<5 Hz).

Square wave jerks are high-frequency, low-amplitude eye movements occurring in association with a central neurologic lesion causing fixation instability. Square wave jerks are often asymptomatic, but patients may describe objects as “jumping from side to side.” whereas SOM
commonly results in “shimmering” and objects “bouncing up and down.”21,49,110 Square wave jerks are distinguished as horizontal and saccadic,39,86 whereas SOM movements are torsional and nystagmoid.12,21,42,93 Symptoms of SOM mimic those of other disorders resulting from neurogenic hyperactivity, leading to intermittent extraocular muscle spasms. One example is ocular neuromyotonia, a condition characterized by spontaneous episodic contractions of one or more extraocular muscles.5,23,29,32,71,77 Often associated with radiation injury. While both SOM and ocular neuromyotonia are associated with paroxysmal strabismus and diplopia lasting 10–30 seconds occurring multiple times a day and resolving spontaneously,5 the tempo of a neuromyotonic movement is considerably slower and would not likely be confused with SOM. Ocular neuromyotonia may be either monocular or binocular,28,29,67,77 whereas SOM is strictly monocular (Table 1).12,21,42,105 We identified 2 reported cases of ocular neuromyotonia affecting the superior oblique muscle producing daily episodes of intermittent vertical diplopia, often with torsion.77 One of the cases was diagnosed as SOM; however, subsequent examination revealed episodes triggered by eccentric gaze, overaction of left superior oblique muscle, and inability of affected eye to elevate on adduction.77 The authors proposed that this case may have represented transition from SOM to ocular neuromyotonia. Both ocular neuromyotonia23,28,71 and SOM27,80,93 will respond to carbamazepine.

Fig. 2 — High-resolution MRI of the trochlear nerve in superior oblique myokymia (SOM). A: Axial plane magnetic resonance image using 3-dimensional Fourier transform constructive interference in a steady state. Image shows the right medial superior cerebellar artery branch (arrow) in direct contact with the trochlear nerve (arrowhead), in a patient with right SOM. B: Corresponding noncontrast 3-dimensional time-of-flight magnetic resonance angiography sequence confirms the presence of arterial compression of the trochlear nerve (arrow). MRI = magnetic resonance imaging. Image and legend reproduced with permission from Yousry I, Dieterich M, Naidich TP, Schmid UD, Yousry TA. Superior oblique myokymia: Magnetic resonance imaging support for the neurovascular compression hypothesis. Annals of Neurology. 2002; 51:361-8.

6. Management

There is no definitive treatment for SOM. The uncertain mechanism and variable time course make it difficult to evaluate the results of treatment even in individual cases. In addition, the low prevalence of the condition makes it difficult to generate conclusive evidence on the effectiveness of any 1 approach. Several therapies have been tried with varied success, including topical beta blockers, carbamazepine, phenytoin, baclofen, gabapentin, clonazepam, mirtazapine, memantine, botulinum toxin injections, and surgery.7,8,10,19,27,80,83,106 Botulinum toxin injection may lead to temporary symptomatic relief, but it is difficult to isolate treatment to the superior oblique muscle without involving adjacent extraocular muscles.83 Williams and colleagues106 found that 80% of 20 SOM patients had a favorable response to systemic medical therapy (including carbamazepine, baclofen, propranolol, and phenytoin).

There has been growing evidence for the efficacy of beta blockers in SOM, with reports of successful use of systemic propranolol as well as topical timolol and betaxolol.7,8,31,38 One proposed explanation for the effectiveness of beta blockers is the reduction of blood pressure amplitude,91 which could alleviate symptoms from the pulsatile compression of the trochlear nerve by a nearby artery. Alternatively, beta blockers may reduce neuronal sensitivity to the local ephaptic stimulus. Controversy remains as to whether the efficacy of topical therapy is a direct, local effect or secondary to systemic absorption.7,8 Given the overlap of SOM with ocular neuromyotonia, we speculate that some cases of ocular neuromyotonia may respond to topical therapy, though we have not yet had the opportunity to offer this treatment.

We recently found that intermittent, topical levobunolol 0.5% controlled SOM symptoms. In those 2 cases, as little as 1
### Table 1 – Review of eye preference and sex in SOM from 116 reports in the literature since 1906

| SOM report author and year published | Left SOM | Right SOM | | | |
|-------------------------------------|----------|-----------|---|---|
| | | | | | |
| | Female (F) Age (y) | Male (M) Age (y) | L total | Female (F) Age (y) | Male (M) Age (y) | R total |
| Duane (1906) | 24-year F | — | 1 | — | — | 0 |
| Hoyt and Keane (1970) | 25-year F | — | 1 | 32-year F | 43-year M | 4 |
| Susac et al (1973) | 52-year F | 17-year M | 3 | 54-year F | 59-year M | 4 |
| Roper-Hall and Burde (1978) | 39-year F | 58-year M | 5 | 45-year F | — | 1 |
| Breen et al (1983) | — | 26-year M | 1 | — | — | 0 |
| Keltner (1983) | 48-year F | — | 1 | — | — | 0 |
| Neetens and Martin (1983) | — | 43-year M | 1 | — | — | 0 |
| Lee (1984) | — | 62-year M | 2 | — | — | 0 |
| Palmer and Shults (1984) | — | 29-year M | 1 | 45-year F | 31-year M | 2 |
| Stauntenaier (1988) | — | — | 0 | 36-year F | — | 1 |
| Ruttum and Harris (1988) | — | — | 0 | — | — | 0 |
| Aizawa et al (1989) | — | 30-year M | 1 | — | — | 0 |
| Morrow et al (1990) | — | — | 0 | — | 33-year M | 2 |
| Tyler and Rulz (1990) | 22-year F | — | 1 | — | — | 0 |
| Leigh et al (1991) | 69-year F | — | 2 | 60-year F | — | 1 |
| Thurston and Saul (1991) | — | — | 0 | — | 21-year M | 1 |
| Komai et al (1992) | — | — | 0 | — | 50-year M | 3 |
| Kettner and Casselman (1993) | 17-year F | — | 1 | — | — | 0 |
| Bibby et al (1994) | 50-year F | — | 1 | — | — | 0 |
| Mehta and Demer (1994) | 28-year M | — | 1 | 31-year F | — | 1 |
| Wertenbaker (1994) | — | — | 0 | 37-year F | — | 1 |
| Heaven et al (1995) | 44-year F | — | 1 | — | — | 0 |
| Kosmorsky et al (1995) | — | — | 0 | 38-year F | — | 1 |
| Geis et al (1996) | 40-year F | — | 1 | — | — | 0 |
| Samii et al (1998) | — | — | 0 | — | 50-year M | 1 |
| Hayakawa et al (2000) | — | — | 0 | 20-year F | — | 1 |
| Scharwey et al (2000) | — | — | 0 | — | — | 0 |
| Hashimoto et al (2001) | — | — | 0 | 50-year F | — | 1 |
| Tomak et al (2002) | — | 49-year M | 1 | 41-year F | — | 1 |
| Yousry et al (2002) | — | — | 0 | 39-year M | — | 1 |
| Yousry et al (2002) | — | — | 0 | 45-year F | 32-year M | 3 |
| Kattah and Fitzgibbon (2003) | — | — | 0 | 36-year M | — | 1 |
| Suzuki et al (2003) | — | — | 0 | 43-year M | — | 1 |
| Hashimoto et al (2004) | 49-year M | 1 | — | — | 0 |

*continued on next page*
A drop of levobunolol every 3 weeks reduced the intensity of, but did not eliminate, the myokymic movements, as documented on video before and after treatment.\textsuperscript{110} One patient with a 6-decade history of symptoms was ultimately able to discontinue topical therapy without recurrence, whereas the other patient, who had experienced episodes for multiple times per day for the prior 13 years, controlled symptoms with only 1\textsuperscript{2} twice-daily applications of levobunolol every 1\textsuperscript{2} months.

When SOM symptoms are intolerable and unresponsive to medical treatment, extraocular muscle surgery is generally the next step.\textsuperscript{2,10,74,83} Early reports described superior oblique tenotomy or even superior oblique myectomy\textsuperscript{82,83} but these approaches produced an iatrogenic superior oblique palsy, which required subsequent weakening of ipsilateral inferior oblique muscles\textsuperscript{82} and sometimes even the contralateral inferior rectus muscle.\textsuperscript{2} The procedure most commonly used to correct SOM today combines superior oblique tenotomy with an anticipatory inferior oblique myectomy\textsuperscript{2,17,74}; however, even with this approach, Agarwal and Kushner found that 36% of patients reported diplopia in downgaze after surgery, which required further correction with prism glasses or additional surgery.\textsuperscript{2}

Partial weakening of the superior oblique tendon has been proposed as a surgical treatment for SOM.\textsuperscript{37,52} Kosmorsky and colleagues\textsuperscript{52} reasoned that weakening the anterior fibers of the superior oblique tendon (Fig. 5) would reduce or eliminate SOM while preserving at least some superior oblique function. While Harada and Ito’s original article proposed that the

<table>
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<th>Table 1 – (continued)</th>
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<tbody>
<tr>
<td>SOM report author and year published</td>
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<tr>
<td>------------------------</td>
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<tr>
<td>Mickelson et al (2004)\textsuperscript{64}</td>
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<tr>
<td>Webster and Leslie (2004)\textsuperscript{104}</td>
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<tr>
<td>Mikami et al (2005)\textsuperscript{105}</td>
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<td>Foroozan et al (2006)\textsuperscript{26}</td>
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<td>Gupta et al (2007)\textsuperscript{11}</td>
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<td>Hufner et al (2008)\textsuperscript{43}</td>
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<td>Maggioni et al (2007)\textsuperscript{51}</td>
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<td>Jain et al (2008)\textsuperscript{65}</td>
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<tr>
<td>Bek et al (2009)\textsuperscript{5}</td>
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<tr>
<td>Ruttmann and Harris (2009)\textsuperscript{62}</td>
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<td>Meyers et al (2010)\textsuperscript{63}</td>
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<tr>
<td>Abhinav et al (2012)\textsuperscript{1}</td>
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<tr>
<td>Thoorens et al (2012)\textsuperscript{57}</td>
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<td>Kang et al (2013)\textsuperscript{17}</td>
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<tr>
<td>Borgman (2014)\textsuperscript{4}</td>
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<td>Fam et al (2014)\textsuperscript{14}</td>
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<tr>
<td>Wu et al (2014)\textsuperscript{102}</td>
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<tr>
<td>Smith and Comblath (2014)\textsuperscript{88}</td>
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<tr>
<td>Lenci et al (2016)\textsuperscript{48}</td>
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<td>Zhang et al (2017)\textsuperscript{110}</td>
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Table 1—Superior oblique myokymia (SOM): age range at examination

<table>
<thead>
<tr>
<th>Age range (years)</th>
<th>All SOM</th>
<th>Left SOM</th>
<th>Right SOM</th>
<th>Female SOM</th>
<th>Male SOM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (years)</td>
<td>41.72</td>
<td>42.91</td>
<td>40.97</td>
<td>42.53</td>
<td>44.59</td>
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F = female; M = male; SOM = superior oblique myokymia.

There was an overall predominance of right SOM at 61% (P = 0.016).\textsuperscript{a} Cases could not be included if they did not give an individual breakdown of sex and/or eye afflicted.\textsuperscript{b} "Age" denotes the age of clinical presentation.
tendon could be selectively strengthened or weakened, for most surgeons, the name “Harada-Ito” is synonymous with a strengthening procedure. We therefore propose that this be considered a “reverse Harada-Ito procedure.” Kosmorsky and colleagues treated one patient with this approach, nasally transposing the anterior fibers of the superior oblique tendon, and performed eye tracking with magnetic search coils to confirm that the SOM had been eliminated. The procedure successfully preserved vertical eye movements. Hayakawa and colleagues used this approach in one additional patient, utilizing video monitoring to follow eye movements. In their case, the procedure did not eliminate the SOM, but the amplitude was reduced, and symptoms were improved. It is likely that a simple tenectomy of the anterior superior oblique tendon fibers (without placement of a suture) would be equally effective without creating new vertical strabismus or torsional diplopia, though this has not to our knowledge been reported. While a partial weakening of the superior oblique tendon is less invasive than superior oblique tenotomy plus inferior oblique myectomy, patients should be informed that symptoms are more likely to persist if any superior oblique tendon fibers remain attached to the globe.

If a reverse Harada-Ito procedure could alleviate SOM, one might expect that a standard Harada-Ito procedure would worsen symptoms. We reported the case of a patient who had no recollection of worsening of her SOM symptoms after a Harada-Ito procedure years earlier; however, the procedure overcorrected her strabismus, exacerbating diplopia, which may have masked any change in her SOM symptoms. The patient stated with confidence that there was no improvement of SOM following the procedure. Unfortunately, there was no documentation of the SOM before and after the Harada-Ito procedure.

Microvascular decompression of the trochlear nerve (Fig. 1) has also been used for treatment of SOM. Fam and colleagues even described it as “the least destructive surgical option for treatment of medication-refractory SOM.” This approach, however, has only been used in patients with specific vascular anomalies identified on imaging of the origin of the trochlear nerve.

While there is a rare association of SOM with brainstem tumors, neuroimaging is not routinely indicated for patients with SOM, as there is a low yield in the absence of trauma or other symptoms or clinical findings. Imaging may be indicated, however, for evaluation of patients whose symptoms are refractory to medical therapy before moving forward with extraocular muscle surgery in order to identify candidates for microvascular decompression.

After reviewing the findings of our meta-analysis as well as the differential diagnosis and treatment options, we developed a flow diagram for evaluation and treatment of SOM (Fig. 6). These recommendations balance the likelihood of response to treatment with the risks and benefits of specific intervention.

7. Prognosis

The clinical course of SOM is variable, ranging from spontaneous recovery to chronic oscillopsia and diplopia resistant
to medical treatment. One of the longest published non-congenital cases of SOM spanned 29 years, but we recently reported a case of a 69-year-old woman who had suffered from intermittent SOM for her entire life (As noted previously, she ultimately responded to a brief course of topical levobunolol).

8. Conclusion

SOM is a rare condition that, at least in some cases, likely results from ephaptic transmission in a damaged trochlear nerve and/or a denervated, misinnervated superior oblique muscle. Considering the risks of surgery and the potential side effects of systemic medical therapy, we encourage clinicians to attempt topical therapy with beta blockers such as levobunolol. If topical therapy fails, systemic medical therapy may be considered. MRI is not indicated for typical cases that respond to medical treatment, but imaging—specifically, high-resolution imaging of the fourth cranial nerve—may be informative. A neurosurgical approach might be considered if a structural abnormality is identified where the nerve exits from the brainstem, although there are only a handful of case reports describing this approach. Extraocular muscle surgery might consist of selective weakening of the anterior fibers of the superior oblique tendon, but a combined superior oblique tenotomy and inferior oblique myectomy are more likely to be effective. The latter procedure should be pursued with the expectation that there is a more than 30% risk of symptomatic, postoperative diplopia that may require prism therapy or additional surgical intervention.

8.1. Method of literature search

MEDLINE, ProQuest, and ScienceDirect were searched utilizing the advanced search function with the Medical Subject Headings (MeSH) terms “superior oblique myokymia,” “trochlear nerve disease,” and “ocular myokymia.” No date or language restrictions were set in order to gather the most complete set of reported cases dating back to the first discovery of SOM in 1906. Reports in other languages were translated electronically. All valid case studies and their references were reviewed to source further SOM research.

9. Disclosures

There are no conflicts of interest to declare.

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Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.survophthal.2017.10.005.

References

53. Kraft SP, Lang AE. Cranial dystonia, blepharospasm and hemifacial spasm: clinical features and treatment, including the use of botulinum toxin. CMAJ. 1988;139(9):837–44


