Skew deviation. Strabismological diagnosis and treatment alternatives

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Abstract

Background: We undertook this study to analyze diagnostic and treatment alternatives in patients with skew deviation (SD).

Methods: This is a prospective, observational and longitudinal study of patients with SD. The study took place in a third-level medical center during the period from September 2007 to May 2008. Strabismological exploration, multidisciplinary diagnosis and treatment alternatives were analyzed.

Results: Ten patients presenting SD were studied. Diagnoses were multiple sclerosis, arteriovenous malformation, epilepsy, hydrocephalus, ischemic encephalopathy, cortical atrophy, hypoplasia of corpus callosum and thalamic hemorrhage. Psychomotor retardation was present in 80%. Other diagnoses were Cogan apraxia, Parinaud syndrome, see-saw nystagmus, Foville syndrome, and hemiplegic alterations. Related strabismuses were exotropia (5), esotropia (3), hypertropia (2), and dissociated vertical deviation (1). Lesions of II, III and VII cranial nerves were found.

Conclusions: Complete strabological study allows a better diagnosis of the lesion and consequently relapsing disease in order to achieve a better treatment according to each patient. Optical rehabilitation and botulinum applications are especially indicated.

Key words: skew deviation, strabismus, ocular motility disorders, diplopia.

Introduction

Skew deviation (SD) is an infrequent strabismus that manifests as a vertical strabismus with hypertropia in one eye; however, this position changes according to gaze rotations and it does not present the patterns associated with cranial nerve paralysis. Skew deviation can be caused by a lesion of brainstem, cerebellum or asymmetrical lesion of vestibular projections from otolithic receptors in utricle. The most evident characteristic of this disorder is the change on vertical deviation according to gaze direction, so one eye can express hypertropia when abducted and present hypotropia in adduction. Several patterns have been described, but SD vertical strabismus does not match with manifestations from muscular hyperfunction; for instance, in hypertropia adduction from upper oblique muscles, hyperfunction will show divergence at infraduction and torsional changes in eye fundus. Therefore, its association with other strabismuses can be difficult to diagnosis because true lower oblique muscle hyperfunction can be related with SD. SD may have several causes including brainstem damage, cerebellum damage, acute lesion in posterior cranial fossa (such as infarction), multiple sclerosis, tumors, trauma, abscesses, hemorrhages, syringobulbia secondary to neurosurgery and in peripheral vestibular lesions.1,2 Patients with healthy cerebellar nuclei have recovery possibilities that allow SD manifestation reduction; therefore, strabismic exploration should be done carefully in order to appropriately diagnose the lesion, its extension and severity. Here we specify SD causes and correction possibilities of associated strabismus as rehabilitation.

Materials and Methods

We carried out a prospective, observational, longitudinal and descriptive study of patients with SD diagnosed between September 2007 and May 2008 in the Strabismus Department of a third-level National Hospital in Mexico. Patients were...
examined for strabismus and imaging studies and laboratory tests were requested. Multidisciplinary diagnosis was carried out using the services from Neurology, Pediatrics and Neurosurgery. SD was diagnosed because of vertical deviations (unilateral or bilateral), comitant, noncomitant, alternating and from abnormal response to vestibulo-ocular reflex with head tilting to left and right. Strabismus study of nine gaze positions was carried out to confirm diagnosis of associated strabismuses, including oblique muscle alterations. Treatment alternatives were established after diagnosis and results were analyzed.

## Results

We included ten patients with SD in our study: six females and four males. Average age was 11.5 years ± 13.6 (range: 1-33 years). Available neurological diagnoses were psychomotor retardation in seven patients, epilepsy in four patients, arteriovenous malformation in two patients, corpus callosum hypoplasia in two patients, and the following were reported as a single event: multiple sclerosis, hydrocephalus, ischemic encephalopathy, microcephalia, cortical atrophies. Hemiplegia was found in two patients. Associated ocular alterations were horizontal nystagmus in three cases and see-saw in two cases manifested in lateral versions, Cogan apraxia, Parinaud’s syndrome, horizontal conjugate movement paralysis, ptosis from lesion of cranial nerve III. Associated strabismus was present in seven cases, exotropia in five patients, esotropia in three patients, frontal hypertropia in two patients and one patient presented dissociated vertical deviation (DVD). Cranial nerve lesions were found in three patients, involving cranial nerves II, III and VII (Table 1).

### Case 1

We report the case of a 27-year old female who presented partial, simple, visual, epileptic seizures that generalized to tonic-clonic seizures, associated with left occipital arteriovenous malformation with deep drainage. The patient is being treated for epilepsy and presents psychomotor retardation. At 16 years old she suffered malformation rupture and required surgical management, remaining in a coma for 2 months. Postoperative neuroimaging shows left occipital encephalomalacia and left paramedian mesencephalic infarction. Upon discharge, the patient presented right hemilateral dystonia, right hemiparesis, bilateral facial paralysis with higher right representation, permanent alternating SD, exotropia and right hypertropia. There was right homonymous hemianopia with reduced sensitivity in the left half of the visual field. Visual acuity was as follows: right eye (RE) 20/60, left eye (LE) 20/25. Diplopia was not present. Surgery was carried out to correct exotropia and hypertropia with extended retroinsertion of both lateral rectus muscles and superior right rectus muscle (Figure 1).

### Case 2

We report the case of a 5-year old girl with congenital strabismus, premature delivery at 34 weeks and thalamus hemorrhage managed in intensive care unit for 30 days. The patient presented with mild psychomotor retardation. Visual acuity was 20/40 (RE), 20/20 (LE). She presented difficulty with horizontal gaze following lateral movements and short saccades. Examination revealed limited frontal nystagmus with endodeviation and right hypertropia. Right lateral vision increased right hypertropia and left lateral vision showed left hypertropia. Recommended

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Cause</th>
<th>Strabismus</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>27</td>
<td>A-V malformation, epilepsy</td>
<td>Exotropia</td>
<td>Surgery</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>5</td>
<td>Premature thalamic hemorrhage</td>
<td>Esotropia + Cogan syndrome</td>
<td>Botulinum toxin</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>33</td>
<td>MS</td>
<td>Esotropia + Parinaud syndrome</td>
<td>Botulinum toxin</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>2</td>
<td>Hydrocephaly</td>
<td>None at the start</td>
<td>Surveillance</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>2</td>
<td>Congenital rubella, neuroinfection, epilepsy</td>
<td>Exotropia</td>
<td>Botulinum toxin</td>
</tr>
<tr>
<td>6</td>
<td>M</td>
<td>1</td>
<td>Microcephaly, epilepsy</td>
<td>Esotropia and DVD</td>
<td>Occlusive</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>3</td>
<td>Hypoplasia of corpus callosum</td>
<td>Exotropia</td>
<td>Botulinum toxin</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>5</td>
<td>Epilepsy</td>
<td>None at the start</td>
<td>Surveillance</td>
</tr>
<tr>
<td>9</td>
<td>F</td>
<td>33</td>
<td>A-V malformation</td>
<td>Paralysis of III nerve</td>
<td>Botulinum toxin</td>
</tr>
<tr>
<td>10</td>
<td>F</td>
<td>4</td>
<td>Hypoplasia of corpus callosum</td>
<td>Exotropia</td>
<td>Surgery + prisms</td>
</tr>
</tbody>
</table>

F, female; M, male; DVD, dissociated vertical deviation; A-V, arteriovenous; MS, multiple sclerosis.
treatment was botulinum toxin in medial rectus muscles to treat esotropia and temporary occlusion of left eye to treat amblyopia.

Case 3

We report the case of a 33-year-old female who 6 years previously had been diagnosed with multiple sclerosis, optic neuritis 3 years ago, and endodeviation 2 years ago corrected with botulinum toxin. For the past year she has suffered from left-central facial paralysis and right hemiplegia. Magnetic resonance showed new demyelinating lesions and enlargement of previous lesions. Visual acuity was 20/70 (RE), 20/30 (LE) with frontal horizontal nystagmus, limited voluntary elevation and depression with nystagmus movements. Disability scale was reported as 8. The patient is being treated with immunomodulators. SD with hypertropia is observed in bilateral abduction and see-saw nystagmus in lateral versions.

Case 4

We report the case of a 2-year-old boy who had ventriculoperitoneal shunt surgery due to hydrocephalus. There is mild psychomotor retardation. The patient presents correct position at the front, remaining in depression and elevation. Alternating SD is observed with hypotropia of adducted eye in horizontal conjugate movement with lateral gaze nystagmus (Figure 2).

Case 5

We report the case of a 2-year-old boy diagnosed with congenital rubella and cytomegalovirus infection. There is mild psychomotor retardation with epilepsy. The patient presents 35 prism diopters (PD) exotropia at the front with alternating hypertropia of abducted eye. Exotropia was treated with botulinum toxin in both lateral rectus muscles.

Figure 1. Case 1 patient, right and left versions are observed and reflex movements when head is tilted to the front.

Figure 2. Patient (Case 4). Strabogram.
Case 6
We report the case of a 1-year-old boy with ischemic encephalopathy from neonatal asphyxia. There is microcephaly and epilepsy. Diagnosis is esotropia with angle variation, DVD, nystagmus, and bilateral unstable eye fixation. Examination reveals SD with eye hypertropia in bilateral abduction. Alternating occlusion is indicated.

Case 7
We report the case of a 3-year-old girl diagnosed with corpus callosum hypoplasia, variable exotropia of 10-30 PD with SD during head tilt over right shoulder with higher eye hypertropia in bilateral abduction when tilting head over right shoulder. Exotropia was treated with botulinum toxin in both lateral rectus muscles.

Case 8
We report the case of a 5-year-old boy whose mother reported toxemia of pregnancy. The child presents epilepsy and mild psychomotor retardation. He presents SD with eye hypertropia in bilateral abduction.

Case 9
We report the case of a 33-year-old woman with transsphenoidal surgery carried out 2 months before symptoms, indicated on hypophysis adenoma. She presented intraoperative hemorrhage from internal carotid-dependent aneurysm. After hemorrhage she presented left blepharoptosis, 45 PD exotropia, limited bilateral horizontal conjugate movement and SD with higher right eye hypertropia at abduction and see-saw nystagmus. Visual acuity was 20/20 in both eyes. Botulinum toxin was applied in both lateral rectus muscles to treat exotropia.

Case 10
We report the case of a 4-year old female who was born prematurely with corpus callosum hypoplasia. The patient presented SD with eye hypotropia in bilateral abduction, higher in the right eye and exotropia. Retrinosertion of both lateral rectus muscles was carried out along with retnosertion of right inferior rectus muscle. Optical correction included 6 PD.

Discussion
SD strabismus occurs generally after a lesion in neurovisual coordination centers and pathways, especially vestibular. Normal adaptation mechanisms allow us to turn, tilt and rotate our head without movement of the world around us. This function is mostly conditioned by our subjective perception of the vertical plane. Therefore, when our head rotates in a particular plane, one of the semicircular canals in the inner ear detects acceleration and sends signals to corresponding extracocular muscles. In addition to this vestibular-ocular pathway (that allows retinal image stabilization even during head movement), ascending information is also provided (thalamus-cortical projections) for spatial perception as well as descending perception (vestibulospinal projections) to maintain head and body posture (vestibulospinal reflexes).2

Vestibular Pathway
Vestibular information reaches the pontocerebellar angle and enters laterally to the medulla oblongata at the pons level towards the bulbo-vestibular nuclei complex, which contains four major nuclei and other minor nuclei. The superior nucleus projects motoneurons from homolateral trochlear nucleus and from III homolateral and contralateral nerve. The lateral nucleus projects in its ventral portion to III nerve. Medial nucleus (the largest of vestibular complex) projects through medial longitudinal fascicle (MLF) to motoneurons and internerve neurons of III homolateral and contralateral nerve and also projects on motoneurons of IV nerve and finally forms the medial vestibulospinal tract towards supraspinal and central-cervical nuclei. Therefore, its participation in vestibulo-ocular and position compensated reflexes can be inferred. Inferior nucleus contributes to vestibulospinal pathways and integrates input from cerebellum. Within small nuclei, group Y projects to III nerve especially for control of vertical gaze. Through the commissura fiber system, both vestibular complexes project and receive crossed inhibitory inputs. Almost all primary vestibular inputs end homolaterally in flocculus, nodule, uvula and dentate nucleus of cerebellum and, from there, inhibitory regulatory impulses respond to medial and descending vestibular nuclei controlling the activity of secondary vestibular neurons. Fastigial nucleus receives information from flocculus and sends outputs to medial and lateral vestibular nuclei. Cortical areas are related to vestibular coordination through reticulo-thalamic pathway and posterior commissura nuclei, interstitial nucleus of Cajal (iC), which is an important structure for vertical control of eyes and head and an essential component in neural integration related with speed-position for vertical and oblique movements and nucleus of Darkschewitsch. When vestibular stimulation neurons access the thalamus, they seem to correspond to the lateral position of the posterior ventral nucleus and through the cerebellum into anterior ventral nucleus.3,4 This results in the fact that different elements participating in vestibulo-ocular reflex control may experience a lesion with manifestations different than SD. In this study, SD was diagnosed associated with cranial nerve lesions according to brainstem lesion, internuclear ophthalmplegia and nystagmus. We also found association of non-paralysis nystagmus as esotropia, exotropia and even DVD.
Strabismuses observed were congenital and were associated with embryonic infections, brain malformations, etc., as well as acquired from diverse traumatic or surgical causes, vascular accidents and vascular and demyelinating diseases.

Clinical observation of SD shows a failure in the adaptive mechanism of vestibulo-ocular control where a head position change should be compensated by gaze. Usually, when we tilt our head to the right our eyes meet that movement in an angled plane if compared to a horizontal line, which is compensated with reflex hypertropia of the eye on the lower position (the right eye in this case) and hypotropia of the eye in the upper position (the left eye in this case). At the same time, the eye in the lower position should present incyclotorsion and the eye in the upper position should present excyclotorsion. Therefore, semicircular anterior canals send stimuli to ipsilateral superior rectus muscle and contralateral inferior oblique muscle. Posterior semicircular canals stimulate ipsilateral superior oblique muscle and contralateral inferior rectus muscle, and both canals send simultaneous inhibiting stimuli to their antagonist. However, if one has a lesion, it loses the inhibiting function causing hyperstimulation in the antagonist muscle and, therefore, an apparent hyperstimulation of extraocular muscles generating changes observed in SD. Therefore, SD diagnosis, regardless of true hyperfunction of oblique muscles, should be performed considering an altered response to vestibular reflex of head tilting and rotation.

Ocular Tilt Reaction

Experimental studies in monkeys have demonstrated that electric brainstem stimuli can cause vertical deviation, with one eye looking upwards and the other looking downwards with conjugate cyclotorsion of the eye deviated downwards. This response was named ocular tilt reaction (OTR), which demonstrated SD alteration effects manifested as perception (subjective vertical plane tilting), ocular motor (torsion or SD) and postural (head tilting). OTR can be “complete” (tonic or paroxysmal) or present only some components, especially SD.

The otolithic-ocular balance is altered in OTR (from vestibular tone impairment), either from peripheral lesions (stimuli of utricle, semicircular canals or their pathways and vestibular nerve) or from central lesions (in posterior fossa affecting graviceptive pathways that run from medulla oblongata to mesencephalon, MLF and cerebellum, which has an important role in body equilibrium and ocular movements).

Torticollis found in OTR is associated with subjective vertical plane tilting so the patient presents torticollis to perceive his new “vertical plane.” When the patient’s tilted head is straightened by the physician, the patient may respond to vestibular stimulation as if he had been tilted forcibly to the opposite side and compensating pathological mechanisms are evident. For instance, in Case 1, if the patient’s head is straightened from right torticollis towards the front, the patient presents what would occur in left torticollis, and right eye (that would be at a higher position) shows abnormal compensatory hypotropia. We will observe the patient with right frontal hypotropia with SD with an evident overreaction (Figure 1).

OTR rarely produces symptoms and, in general, does not induce disequilibrium. Therefore, torticollis produced by SD is secondary to subjective vertical plane tilting; however, if there is a lesion of IV cranial nerve, torticollis compensates vertical strabismus from superior oblique muscle paralysis. Misdiagnosis would lead to inappropriate management of patients with SD because surgery of extraocular muscles will not correct head tilting from SD. If both processes occur at the same time, it may improve the patient’s paralysis.

It has been suggested that in order to locate a SD-related lesion, ocular torsion direction should match the lower eye, e.g., intorsion of right eye with excyclotorsion of left eye would show left hypotropia and intorsion of left eye with excyclotorsion of right eye would show right hypotropia. Medullary, unilateral pontomedullary and utricular lesions produce ipsilateral SD in general (towards the lower eye), whereas pontomesencephalic and mesodiencephalic lesions or a compromised IC will produce contralateral SD. However, research studies in animals have demonstrated that electric IC stimuli produce temporary ipsilateral OTR and, in contrast, a lesion produces permanent contralateral OTR. This suggests that SD in humans is contralateral if the lesion is inhibitory and ipsilateral paroxysmal if the lesion is excitatory. When SD is associated with internuclear ophthalmoplegia, the higher eye is usually on the affected side, suggesting a rostral MLF lesion after crossing the pons. Central or bilateral mesencephalon lesions may produce alternating SD. Thalamic lesions seem to reflect damage in subthalamic input pathway; for instance, IC compromise associated with thalamic infarction presents ipsilateral hypertropia of the eye.

Lesions of IC and MLF may produce an association between SD and Parinaud’s syndrome as occurs in Case 3 or as observed with III cranial nerve paralysis. Cases presented here with a variety of causes describe lesions at different levels: mesencephalic, thalamic, cortical and at MFL. Causes are also diverse, associated with vascular accidents, multiple sclerosis, hydrocephalus, corpus callosum lesions, ischemic encephalopathy, neonatal cytomegalovirus infection and brain hemorrhage from cranial aneurysm rupture.

According to the different types of vertical deviation, SD has also been classified as comitant, noncomitant and alternating. Comitant SD is the most frequent type and presents as a constant hypertropia in all gaze positions associated with damage of unilateral vestibular nerve information (anterior and posterior...
Strabismus Diagnosis

As shown in presented cases, SD can be associated with other strabismuses, making evaluation and diagnosis difficult. The difficulty in SD diagnosis can also be attributed to temporary SD or patient’s lack of cooperation for following instructions. In Case 9, where Parinaud’s syndrome and lesion of III cranial nerve with frontal exotropia were so evident, SD diagnosis may go unnoticed because see-saw nystagmus lateroversion causes the patient to avoid these gazes. Also, clinical profiles can be confused with IV cranial nerve paralysis with superior oblique muscle hyperfunction or inferior oblique muscle paralysis from a lesion on the posterior semicircular canals (Figure 2).

SD lesion location is important to determine the level of neurological compromise and treatment urgency.

In cases presented here, congenital and acquired SD causes can be observed as well as the presence of divergent and convergent strabismuses with their amblyopic sensory anomalies. In one case we can observe SD associated with DVD that, according to Brodsky et al., may be a second OTR type such as inverse SD secondary to damage in visual impulses in contrast with graviceptive impulses from inner ear. Brodsky has also proposed that binocular vision loss alters impulses to cerebellum, activating otolithic control in anterior canals that regulates functions of elevator-adductor muscles and manifests as primary hyperfunction of inferior oblique muscles. Brodsky reports about Hoyt’s opinion where he demonstrates SD in 22 seemingly healthy newborns, of which five developed congenital esotropia and therefore mentions that SD may be a precursor of congenital esotropia. Also, he mentions the possibility that non-paralytic strabismuses such as congenital esotropia and DVD have their origin in lesions of long, vestibular or cerebellar pathways.

Brain damage extension determines other paralyses or additional alterations. For example, in Case 1 the patient presents left parieto-occipital encephalomalacia, left thalamic lesion and left pontomesencephalic infarction associated with bilateral SD. All these lesions explain right hemiparesis and facial paralysis. These complex clinical profiles can be observed in patients who suffer from multiple sclerosis with frequent presence of nystagmus, conjugate movement paralysis, convergent strabismuses, etc.

In Case 4 where the patient is controlled through a shunt valve, any neurological relapse may be caused by alterations in cerebrospinal fluid dynamics. Strabismus test shows alternating SD with adducted eye hypertropia without other frontal associated strabismuses and without divergence in depression. However, other neurological response elements are more useful for diagnosis such as vestibular reaction and its association with lateral gaze nystagmus, which is frequent in these cases. By identifying the strabismal profile, it is possible to recognize any change in the patient’s current status, which would suggest a neurological relapse (Figure 2). Association of surrounding lesions according to lesion location may suggest damage extension as in Case 9, where hemorrhage over a small area can produce a major cortical lesion. Also, communication failures within interhemispheric pathways as presented in Case 10 with congenital lesion of corpus callosum or Case 2 with Cogan’s apraxia in following movements suggest brain damage extension.

Fesharaki et al. suggest that acute SD movements violate Listing’s laws, whereas patients with chronic SD respond appropriately. This would suggest that in spite of brain lesion, neuronal adaptation can restore certain functions. Neuronal stimulation in caudal area of paramedian pontine reticular formation (PPRF) and MLF evoke saccades that violate Listing’s law, which suggests that regulatory circuits would run from superior colliculus and above pontine neurons. Caudal nucleus of reticular pontine tegmentum ventral to PPRF receives stimuli from superior colliculus and projects to vermis and fastigial nucleus. Its lesion produces torsional alterations, which suggest its role in Listing’s plane stability.

Treatment

Treatment for these patients should include the following:

- Cause stabilization
- Optic correction to improve visual status
- Sensory management
- Associated strabismus correction

Cases 2 and 6 were treated with occlusive therapy. Surgery possibilities in these patients are limited either from disease evolution as in Case 3 with multiple sclerosis or because of neurological compromise. The use of botulinum toxin to treat
associated strabismuses offers a great improvement, as demonstrated in this study for Cases 2, 3, 5, 7 and 9. If surgery is indicated to correct SD, it is recommended to weaken vertical muscles with the purpose of reducing their movement, and oblique muscle surgery would be recommended especially if they present hyperfunction or to reduce their movements. Multidisciplinary surveillance of these patients is mandatory as well as relapse detection.

In conclusion, SD is a strabismus with a complex clinical profile associated with several neurological pathologies, having a complex diagnosis with varied presentations. The association between severe neurological compromises and SD should alert the ophthalmologist to seek proper and prompt lesion location. Surveillance of lesion will allow diagnosis of neurological relapse or development of new lesions such as in multiple sclerosis. Treatment will be focused towards visual rehabilitation and management of associated strabismus that should be preferably controlled with non-surgical techniques such as with the use of botulinum toxin.

References