# Etiology and treatment of pediatric sixth nerve palsy

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**PURPOSE** To describe the causes and treatment of sixth (abducens) nerve palsy in a series of pediatric patients.

**METHODS** This was a 14-year retrospective study of sixth nerve palsy in children under 14 years of age. Outcomes studied included horizontal deviation, degree of limitation of abduction, and head turn. Patients were treated with botulinum toxin injection at the time of diagnosis; surgery was indicated if treatment with botulinum toxin was unsuccessful. Success was defined as final deviation of orthotropia with no head turn or diplopia.

**RESULTS** Sixth nerve palsy was diagnosed in 15 patients (10 boys; mean age, 4.1 years) between 1995 and 2008. Involvement was bilateral in 2 cases and unilateral in 13 (7 right eyes). Causes included neoplasm (4 cases), trauma (2), idiopathic (3), congenital (2), viral (2), and inflammatory (1). Neoplastic causes were associated with other neurologic signs. Recovery was spontaneous in 5 cases (2 idiopathic, 1 traumatic, 1 congenital, and 1 inflammatory). Botulinum toxin was successful in 7 of 10 patients treated, with follow-up surgery required in the remaining 3 cases. The final result was good in all cases. In all 15 patients, mean time from diagnosis to resolution was 39 months (range, 5 to 170 months).

**CONCLUSIONS** Neoplasms were the most frequent cause of sixth nerve palsy in our patient population. Recovery was spontaneous in one third of the patients. Most required treatment with botulinum toxin, which was successful in most cases. Surgery was successful after a single procedure. (J AAPOS 2010;14:502-505)

Acquired sixth (abducens) nerve palsy occurs more frequently in children (<18 years) than in adults, and the etiology is reported to be more easily established in children.[1-3] The leading cause varies in different studies, with neoplasm most common in some, and trauma (or idiopathic) in others. The incidence of congenital and inflammatory sixth nerve palsy is somewhat lower.[1,2,4] Acquired sixth nerve palsy is usually an isolated finding except in cases of intracranial neoplasm, where it is usually associated with other neurological signs and symptoms.[1,2,4] The outlook for recovery with or without treatment is directly related to etiology: palsy that is neoplastic in origin has the worst prognosis for bilateral involvement and severity of limitation of abduction.[1,5,6]

In this report, we determined the causes and treatment of acute and chronic sixth nerve palsy in a series of children in our institution. Treatment ranged from no treatment to botulinum toxin injection with or without follow-up surgery.

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*Presented at the 85th Congress of the Spanish Society of Ophthalmology, Santander, Spain, September 2009.*

*Submitted March 5, 2010.*

*Revision accepted September 19, 2010.*

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*1091-8531/$36.00*

*doi:10.1016/j.jaapos.2010.09.009*

## Patients and Methods

We performed a retrospective study of cases of pediatric sixth nerve palsy diagnosed between 1995 and 2008 in the ocular motility section of the Hospital General Gregorio Marañón and at a private clinic. The study was performed in accordance with the principles set out in the Declaration of Helsinki. All patients under 14 years old were reviewed.

In patients <2 years of age, the deviation was measured at 33 cm, while in older children, distance deviations were recorded. Horizontal deviation was measured using the simultaneous prism and cover test and in younger children, the Hirschberg test was applied by converting degrees to prism diopters, with 1° equivalent to 1.75$^{\Delta}$ following Prieto Diaz and Souza Diaz.[6] For children <3 years of age, head turn was subjectively examined by observing the position of the face and head with the patient looking at a luminous point 3 m distant; children ≥3 years of age fixated on Snellen optotypes. Following the classification of Gómez de Liaño,[7] limitation of abduction was rated from 0 (no limitation) to −3 (if the eye did not reach the midline). Patients not sent by the neurologist were referred immediately to the neuropediatrics section to complete the study.

Botulinum toxin was injected at diagnosis if the palsy was secondary to neoplasm or trauma. In cases of idiopathic palsy and those resulting from inflammation or infection, botulinum toxin was injected after at least 3 months if the patient's condition did not improve. If treatment with botulinum toxin was ineffective, surgery was indicated at least 1 year after the onset of paralysis, provided it was not contraindicated by other specialists.

Sixth nerve palsy was considered acute if it had been present ≤4 months and chronic if it had been present >4 months. All cases with limitation of abduction from −2 to −3 were considered as complete palsy, and cases with limitation of abduction of −1 were considered as partial palsy. A good outcome was defined as orthotropia with no head turn or diplopia.

## Results

The chart review identified 15 patients (10 boys; mean age, 48.5 ± 34.5 months; range, 1-108 months). Only 2 patients had bilateral involvement (1 due to neoplasm, 1 due to trauma), and 13 had unilateral involvement (left eye, 6; right eye, 7). The palsy was of neoplastic origin in 4 patients, traumatic in 3 patients, idiopathic in 3 patients, congenital in 2 patients, viral in 2 patients, and inflammatory in 1 patient (diagnosed with meningoencephalitis). Additional cranial palsy was diagnosed in 3 of the 4 cases associated with malignant neoplasm (1 in the seventh cranial nerve, 1 in the third cranial nerve, and 1 with bilateral involvement of the fourth cranial nerve). The remaining case, which was not associated with other cranial nerves, was a benign tumor (clivus chordoma) that presented with headache. Only 3 patients presented associated neurological signs: 1 of the patients with a neoplasm had headache, another of the patients with a neoplasm had headache and ataxia, and the patient with inflammation had papilledema. The degree of limitation of abduction, head turn, and the magnitude of the deviation are given in e-Supplement 1 (available at jaapos.org). The mean deviation in primary position was $37.3^{\Delta} \pm 17.8^{\Delta}$ (range, $10^{\Delta}$-$90^{\Delta}$).

Of the 15 patients, 5 recovered spontaneously (mean recovery time, 3.6 ± 3.1 months): 1 with traumatic origin after 1 month, 1 with idiopathic origin after 2 months, 1 with congenital origin after 3 months, and 1 with inflammatory origin after 9 months. A patient with an idiopathic palsy had 2 recurrences before fully recovering after 3 months.

Botulinum toxin was administered in 10 cases (Table 1), with the mean time from diagnosis to injection of the toxin 10.4 ± 6.9 months (range, 2-18 months). Three patients underwent surgery 35 ± 19.9 months (range, 22-58 months) after the onset of paralysis (Table 1). Muscle transposition or weakening of the contralateral medial rectus associated to a recession-resection procedure in the affected eye was not performed. The 3 patients who underwent surgery received botulinum toxin: 1 with 1 injection in both eyes 8 months after onset, 1 with 2 injections in the medial rectus muscle of the affected eye 18 months after onset, and 1 with 4 injections in both eyes 18 months after onset. The final result was good in all the cases in the sample. Mean time from diagnosis to resolution in all 15 patients was 39 ± 45.1 months (range, 5-170 months).

## Discussion

Although the literature contains several studies of the incidence and causes of pediatric sixth nerve palsy, published figures are contradictory.[1,2,4] Holmes and colleagues[4] reported that the most common pediatric cranial nerve palsies affecting ocular motility involved the fourth nerve, followed by the sixth nerve, and the third nerve. They identified 12 cases of pediatric sixth nerve palsy over a period of 14 years. The most common associated etiology was idiopathic (4 of 12, 36%), followed by traumatic (3 of 12, 27%). None of the cases were associated with neoplasm. We diagnosed 15 cases of childhood sixth nerve palsy over 14 years; most were secondary to neoplasm (4 of 15, 26.6%) or trauma (3 of 15, 20%), or were idiopathic (3 of 15, 20%). Both our series and that of Holmes and colleagues[4] have very few cases, unlike the series of Kodsi and Younge,[1] Harley,[8] and Lee and colleagues[2] (Table 2). Holmes justifies the small number of cases by the type of study (population based); the other studies included children attended at a tertiary hospital similar to ours. The series cannot be compared since population-based studies might yield

Table 1. Treatment and results

| Patient | Botulinum toxin (IU) | Time to toxin (mo) | Time to surgery (mo) | Surgery | Follow-up (mo) |
|---|---|---|---|---|---|
| 1 | LE 7.5 | 9 | — | | 19 |
| 2 | OU 7.5 | 18 | — | | 170 |
| 3 | OU 5.0 | 2 | — | | 7 |
| 4 | No | No | — | | 12 |
| 5 | OU 2.5 | 18 | — | | 80 |
| 6 | No | No | — | | 10 |
| 7 | LE 2.5 | 2 | — | | 7 |
| 8 | 4 OU 5.0 | 18 | 58 | Rc/Rs MR/LR LE 5/8.5 | 60 |
| 9 | 2 RE 5.0 | 18 | 25 | Rc MR OU 5.5 | 32 |
| 10 | OU 5.0 | 8 | 22 | Rc/Rs MR/LR LE 4/5 | 36 |
| 11 | No | — | — | | 15 |
| 12 | No | | — | | 30 |
| 13 | No | | — | | 5 |
| 14 | RE 5.0 | 7 | — | | 12 |
| 15 | RE 7.5<br>LE 2.5 | 4 | — | | 150 |

*IU*, international units; *LE*, left eye; *LR*, lateral rectus; *MR*, medial rectus; *OU*, both eyes; *RE*, right eye; *Rc*, recession; *Rs*, resection.

Table 2. Etiology of sixth nerve pediatric palsy described in the literature and in our study

| | Harley[8] (1968-1979) | Kodsi and Younge[1] (1966-1988) | Lee et al[2] (1993-1997) | Holmes et al[4] (1978-1992) | Our study (1995-2008) |
|---|---|---|---|---|---|
| Neoplasm | 17 (27%) | 18 (20%) | 34 (45%) | 2 (18%) | 4 (26.6%) |
| Elevated ICP | 3 (5%) | 2 (2%) | 11 (15%) | — | — |
| Trauma | 21 (34%) | 37 (42%) | 9 (12%) | 3 (27%) | 3 (20%) |
| Congenital | 5 (8%) | — | 8 (11%) | 1 (8.3%) | 2 (13.3%) |
| Inflammation | 8 (13%) | 5 (6%) | 5 (7%) | — | 1 (6.6%) |
| Miscellaneous | 4 (6%) | 13 (15%) | 4 (5%) | — | — |
| Idiopathic | 4 (6%) | 13 (15%) | 4 (5%) | 4 (36%) | 3 (20%) |
| Postviral | — | — | — | 2 (18%) | 2 (13.3%) |
| Total | 62 | 88 | 75 | 12 | 15 |

*ICP*, intracranial pressure.

different proportions of etiologies when compared with tertiary referral center studies. However, in the large series of Harley[8] and Kodsi and Younge,[1] most cases were secondary to trauma, whereas Lee and colleagues[2] reported most cases as secondary to neoplasm (Table 2). These latter authors recommended early neuroimaging as soon as sixth nerve palsy was diagnosed, even with isolated clinical findings; other authors believe that neuroimaging is not necessary in all cases, especially in the absence of other neurological findings.[1,4] In our series, the 4 cases associated with neoplasm had other neurological symptoms: 3 had palsy of other cranial nerves and 2 had headache and ataxia. Inflammation and infections, such as meningoencephalitis, Gradenigo syndrome, cerebellitis, brain abscess, varicella, Tolosa-Hunt syndrome, and herpes zoster ophthalmicus, have also been reported to be directly involved in pediatric sixth nerve palsy, although some findings are anecdotal.[1,8-11]

Kodsi and Younge[1] have reported that pediatric sixth nerve palsy was idiopathic in a high proportion of patients (14.8%). In our study, we observed a similar rate (20%), although other studies[4] found higher rates (36%). This variability may be partially attributed to the observation that idiopathic palsy is a diagnosis of exclusion, and the intensity of evaluation may have varied from 1 center to another.[12,13]

Spontaneous recovery from sixth nerve palsy depends on several factors: etiology, involvement (unilateral/bilateral), and the degree of limitation of abduction.[5] Patients with neoplasm and idiopathic palsy have the worst prognosis.[1] Of the 15 cases in our series with varied (nonneoplastic) etiologies, 5 recovered spontaneously; moreover, recovery was complete in under 3 months, excepting 1 case, inflammatory in origin, in which recovery was required 9 months. Kodsi and Younge[1] reported a mean recovery of 2.3 months.

One of our patients had idiopathic palsy of the right eye that recovered spontaneously. The condition recurred in the same eye. Neuroimaging was unremarkable, and the patient's condition was classified as recurrent idiopathic or benign palsy even though it did not share all the characteristics of this type of palsy, namely, onset before 14 months of age, greater involvement of the left eye, and recent vaccination. However, the condition did share other characteristics with this type of palsy, including higher frequency in females and recurrence within a year of the first episode.[14] In another case with 2 recurrent episodes, no neuroanatomical abnormalities were detected by magnetic resonance imaging during the first episode, although the second episode was associated with headache, and clivus chordoma was detected in by magnetic resonance imaging. Therefore, we believe that it is important to repeat studies if a sixth nerve palsy recurs or fails to resolve.

Our treatment of choice was botulinum toxin in 10 of the 15 cases. Holmes and colleagues[15] performed a prospective multicenter study of acute traumatic palsy (<6 months) and found that the incidence of spontaneous recovery was similar to that of recovery with botulinum toxin. However, they recommended intervention in childhood to achieve fusion more quickly to prevent amblyopia.

It is widely accepted that the indicated surgical procedure for treating total sixth nerve palsy is muscle transposition; recession-resection of the horizontal rectus muscles is appropriate in cases of partial palsy, although patients would likely have to undergo more than 1 intervention.[6,16] Potential surgical complications, such as ischemia of the anterior segment in muscle transposition, must be taken into account.[17] The younger the patient and the more recent the palsy, the better postsurgical abduction will be.[6] In our series, the procedure of choice in the 3 patients who underwent surgery was recession-resection in 2 and bilateral recession of the medial rectus muscles in 1. Surgery was successful in all 3 cases.

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