Recurrent isolated sixth nerve palsy after consecutive annual influenza vaccinations in a child

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Recurrent sixth nerve palsy in children in the absence of structural or other neurological abnormality is a rare occurrence. We report the case of recurrent isolated sixth (abducens) nerve palsy after consecutive annual influenza vaccinations in an otherwise-healthy 2-year-old boy. Investigations including magnetic resonance imaging of the brain and orbits after each episode failed to reveal any abnormality. The temporal relation to the immunizations supports but does not prove that the influenza immunization regimen was responsible.

Case Report

A previously healthy 17-month-old boy was inoculated with an inactivated influenza virus vaccine preparation (Aventis-Pasteur, Lot# U1804AA) by intramuscular injection. Three weeks later, when he was otherwise well and did not appear to be in pain, his mother noted that he was esotropic. There was no history of antecedent febrile illness, trauma, or family history of strabismus. Ophthalmological examination revealed a 45° esotropia in primary gaze increasing to a 65° esotropia in right gaze and orthotropia in left gaze.

Examination of ductions revealed marked limitation of abduction of the right eye and full ductions of the left eye, consistent with right lateral rectus paralysis. Cycloplegic refraction revealed +1.5 D spherical error for each eye. The remainder of the ophthalmic examination, including dilated fundus examination, was normal. A complete neurological examination was unremarkable. Magnetic resonance imaging (MRI) was performed, including T1, T2, fluid attenuation inversion recovery (FLAIR), and fat-saturation imaging (MRI) was performed, including T1, T2, FLAIR, and non-enhanced imaging used 1-mm slice resolution of the brain and orbits. Fast imaging using steady-state acquisition sequencing was used to achieve submillimeter resolution in assessing the course of the sixth nerve from the ventral medulla into the cavernous sinus and orbit. Neuroimaging did not reveal any abnormality.

Part-time occlusion therapy of his left eye was instituted, and repeat examination at 4 months revealed a 15° esotropia in primary gaze with improved abduction of the right eye. Subsequent examinations revealed orthotropia in primary gaze and a 10° esotropia in right gaze with minimal limitation of abduction of the right eye at 6 months and orthotropia in all diagnostic positions of gaze at 9 months, at which time occlusion therapy was discontinued.

The child was then well until 1 year after the onset of symptoms when, 3 weeks after receiving his annual influenza vaccination (Sanofi Pasteur, Lot# U2174GA), his esotropia recurred. He otherwise appeared well and did not appear to be in pain. He exhibited a 10° -20° incomitant esotropia with limitation of abduction of the right eye. The patient was orthotropic in levoversion. The remainder of the ophthalmic examination was unremarkable. A neurological examination and MRI of the brain and orbits without gadolinium failed to reveal any abnormalities. Repeat examination at 6 weeks demonstrated a 10° esotropia with improved abduction of the right eye. Subsequent examination at 12 weeks demonstrated orthotropia in primary and left gaze, and a 10° esotropia in right gaze. The residual motility deficit failed to resolve over the subsequent 7 months.

Discussion

Because our patient exhibited an isolated sixth (abducens) nerve palsy occurring 3 weeks after annual influenza vaccination during 2 consecutive years for which imaging studies failed to reveal any abnormality and because he failed to exhibit any evidence of underlying disease, his recurrent right sixth nerve palsy is either cryptogenic or was precipitated by influenza vaccination.

Isolated recurrent sixth nerve palsy is a rare entity in children; a retrospective review of the cumulative diagnostic index spanning 15 years at Boston’s Children’s Hospital Medical Center revealed only 2 (1.6%) of 123 children diagnosed with sixth nerve palsy exhibiting recurrent sixth nerve palsy in the absence of other abnormalities or illnesses.1 Knapp and Gottlob2 also have reported 2 cases of benign recurrent sixth nerve palsy in the absence of any identifiable precipitating event. Boger and colleagues3 reported a series of 6 children with benign recurrent sixth nerve palsy. The average age at the time of occurrence was 3.4 years, and the total number of episodes ranged from 2 to 5 spanning from 3 months to 4.5 years. Forty percent of episodes, either primary or recurrent, were...
associated with antecedent febrile illness, and the remainder were cryptogenic. Five of six patients enjoyed complete spontaneous recovery, whereas 1 patient exhibited a persistent palsy that was treated with strabismus surgery at 6 months after recurrence. Likewise, our patient exhibited incomplete recovery after recurrence. Plausible etiologies for incomplete recovery in this patient include residual sixth nerve palsy, loss of sensory fusion with resultant secondary strabismus after recovery of ductions, or fibrosis with contracture of the antagonist medial rectus with resultant esotropia.

There have been several reports of isolated sixth nerve palsy in children after immunization. Werner and colleagues describe the case of a 15-month-old girl who developed a left sixth nerve palsy 10 days after receiving the mumps-measles-rubella (MMR) vaccine. The ophthalmoplegia gradually resolved over several months but occurred during an upper respiratory tract infection. Recovery occurred over several months. McCormick and colleagues reported the occurrence of an isolated left sixth nerve palsy in a 13-month-old girl 1 week after receiving the MMR vaccine; the palsy resolved over several months, then spontaneously recurred, followed by eventual resolution. Werner and colleagues also reported the case of an 8-month-old girl who developed a left sixth nerve palsy 6 weeks after diphtheria-pertussis-tetanus (DPT) immunization. The motility disturbance gradually resolved over the next 6 months. The following year the ophthalmoplegia recurred 3 months after DPT booster immunization, followed by resolution of the sixth nerve palsy over 2 months.

Although inactivated (killed) influenza inoculation has been associated with adverse ocular effects, including bilateral conjunctivitis, pruritus, pain, periorcular edema, and blurred vision, we are unaware of any previous association between influenza vaccination and ocular motility disturbance.

In the absence of antecedent trauma, the etiology of an isolated sixth nerve palsy should be sought in all cases, whether or not there has been a recent vaccination, given the association with potentially life-threatening or debilitating intracranial lesions. A thorough neurological examination should be performed in all cases. Any abnormality should prompt thin-section (1–2 mm) MRI of the brain and orbits with and without the administration of gadolinium.

To our knowledge, this is the first description of recurrent sixth nerve palsy in a child associated with influenza vaccination. The temporal relation to the immunizations supports but does not prove that the influenza immunization regimen was responsible.

### Literature Search

A PubMed search was performed using the following keywords: *Influenza AND (each of the following), abducens nerve, sixth cranial nerve, VIth cranial nerve, sixth nerve, VIth nerve, cranial nerve six, or cranial nerve VI*. The search spanned from at least 1949 to December 2008 (including some citations for articles published before 1949 but appearing in indexes published in 1949 or later).

### References