Benign acute cerebellitis[1]

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Two patients are described as examples of a benign acute cerebellar syndrome. Each had abnormal ocular oscillations and truncal ataxia after an upper respiratory infection. One had myoclonus of the head and neck; the other had ataxic dysarthria. Each exhibited a lymphocytic pleocytosis of the cerebrospinal fluid. Historically similar cases have been identified as *benign postviral encephalitis*. No viral etiology was identified in these two patients or the reference cases. No other underlying pathology proposed for this syndrome has been proven in these two cases. In addition, the physical findings of each patient are most closely associated with isolated cerebellar dysfunction. Therefore, the authors prefer to label these cases, *benign acute cerebellitis*.

Index terms: Cerebellar diseases · Encephalitis · Eye movements · Myoclonus

Cleve Clin J Med 54:91–94, March/April 1987

The combination of opsoclonus and myoclonus was originally described in 1913 by Orzechowski[1] in the context of benign encephalitis. Since that time many authors have documented series of abnormal spontaneous eye movement with myoclonic jerking, ataxia, dysarthria, and other cerebellar signs. All have been classified as *benign postviral encephalitis*. The same clinical syndromes, however, have been seen in many adults and children with much less benign conditions, including infections, hemorrhage, hydrocephalus, demyelinating disease, and neoplasia. The following two cases are examples of those within the spectrum of these historical descriptions in the adult population.

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0891-1150/87/02/0091/04/$2.00/0

Case 1

Patient 1, a 30-year-old woman, had severe head and eye jerking, difficulty walking, and nausea. These symptoms had progressed over the preceding two weeks, with the onset one month after an episode of bronchitis. CT scans of the head with and without contrast enhancement performed at an outlying hospital were normal. Spinal fluid analysis showed 1 RBC/mm^3, 1 WBC/mm^3, and a protein content of 34 mg/dL.

When she was admitted to the Cleveland Clinic Hospital, her vital signs were stable and she was afebrile. There was no nuchal rigidity. Her lungs were clear and cardiac auscultation revealed no abnormality. There was no breast mass or thyromegaly, no abdominal organomegaly, or palpable adenopathy. She had had a cesarean section nine months earlier.

A mental status examination showed she had anxiety and no deficit in cognitive function. A cranial nerve examination revealed chaotic conjugate horizontal and vertical jerking of the eyes (10 per second) that was uncontrollable but decreased in frequency very briefly when the eyes were fixed. The extraocular movements were full, and end-gaze nystagmus was sustained. The optic discs were normal in appearance. The remainder of the cranial nerves were intact. There was prominent myoclonic jerking of the head and neck. No palatal myoclonus was present. Motor strength and sensory function were unimpaired. When she sat, marked truncal titubation was noted, which was exacerbated when she stood. Tandem gait was impossible. There was no limb ataxia. Deep tendon reflexes were brisk with flexor plantar responses.

Laboratory evaluation consisted of the following: Hematology and chemistry profiles, including liver enzymes, were normal. Toxicology screen was negative. CT scan of the brain with and without contrast enhancement was normal. Brain T1- and T2-weighted MR images were normal. Westergren sedimentation rate was 3 mm/h. Serum protein electrophoresis and antinuclear antibody profiles were normal. Lumbar puncture was performed (one week after the initial sample) revealing the following: Opening pressure was 150 mm H_2O. There were 18 WBC/mm^3 that were 94% lymphocytes, the protein content was 44 mg/dL, and the glucose level was 59 mg/dL. IgG synthesis and myelin basic protein were not elevated. There was no oligoclonal banding. Cytologic examination showed no abnormalities.

Visual and auditory brain-stem evoked potentials were not delayed. Chest radiographs and abdominopelvic CT scans were normal. Cervical cytologic examination showed no abnormalities. A monospot test was negative. Twenty-four-hour urine catecholamine levels showed a slight elevation of homovanillic acid (HVA), and the vanillylmandelic acid (VMA) level was normal, consistent with salicylate use. Serum catecholamines were not elevated.

The patient was made comfortable with trimethobenzamide, meclizine, and clonazepam. A trial was started of methylprednisolne 1 g daily for two days, then prednisone 60 mg tapered off over 18 days, with no significant decrease in the opsoclonus or myoclonus. The patient was discharged on the 15th hospital day.

Follow-up six weeks later revealed occasional (4/min) jerking of the eyes and similar myoclonic jerking of the head. There was no titubation. Tandem gait was only slightly impaired. Review of acute and convalescent viral titers for echovirus, Coxsackie virus, Epstein-Barr virus, and cytomegalovirus showed no immune response.

Case 2

Patient 2, an 18-year-old man, was seen in consultation for progressive oscillopsia, gait instability, nausea, and slurred speech of two weeks duration. This followed a febrile upper respiratory syndrome by one week. CT scans of the head with and without contrast enhancement were reviewed and thought to be normal.

When he was admitted to the Cleveland Clinic Hospital there were no signs of persistent respiratory symptoms. He was afebrile, there was no nuchal rigidity, the chest was clear, and cardiac examination normal. There was no abdominal organomegaly and no palpable adenopathy. The genitals were normal.

Mental status was normal with no memory or cognitive dysfunction. Cranial nerve examination revealed low amplitude, high frequency (15/sec) conjugate involuntary jerking of the eyes, primarily in the horizontal plane. Extraocular movements were full, and there was fine, sustained end-gaze nystagmus. The optic discs were normal. The remainder of the cranial nerves were intact. Motor and sensory tests were normal. There was mild truncal titubation exaggerated by closing the eyes. Tandem gait was mildly impaired. Repetition of syllables revealed a spastic dysarthria. There was minimal limb ataxia. Deep tendon reflexes were symmetrical, with flexor plantar responses.

Laboratory evaluation included the following: Hematology and chemistry profiles, including liver enzymes, were normal. Toxicology screen was negative, including the heavy metal screen. CT scan of the brain with and without enhancement was normal. Brain T1- and T2-weighted MR scanning was normal. Westergren sedimentation rate was 1 mm/h. Lumbar puncture showed an opening pressure of 140 mm H_2O, 30 WBCs that were 96% lymphocytes, a protein content of 58 mg/dL, and a glucose level of 55 mg/dL. IgG synthesis and myelin basic protein were not elevated. There was no oligoclonal banding. Cytologic examination showed no abnormalities.

Visual and auditory brain-stem evoked potentials were not delayed. Chest was clear on the radiograph. The heterophile antibody screen for mononucleosis was negative. Twenty-four hour urine catecholamine levels were not elevated.

The patient was given trimethobenzanide for comfort. Prednisone 100 mg was administered for two days, and the dose was tapered off over 14 days. He had only mild resolution of his symptoms, and he was discharged on the seventh hospital day.

Follow-up four weeks later revealed no dysarthria or ocular oscillations. There was mild impairment of tandem gait. There was no elevation of antibody titer to echovirus, Coxsackie virus, Epstein-Barr virus, or cytomegalovirus.

Discussion

Both patients exhibited abnormal eye movements that are described as a continuum called *lightning eye movements*. This group of disorders includes opsoclonus, ocular flutter, and ocular dysmetria. Patient 1 was representative of historical prototypes with opsoclonus and myoclonus. Patient 2 had a less severe form of the syndrome with ocular flutter and dysarthria. Each exhibited marked truncal ataxia and nausea.

Several series and individual cases of adults with ocular dysfunction and cerebellar ataxia have been described in the literature as *benign postviral encephalitis*. As examples, Smith and Walsh,[2] Cogan,[3] and Baringer et al[4] reported series of 2, 8, and 20 cases, respectively. Each case characteristically followed the onset of a febrile illness by hours to several weeks. Neurologic examination revealed bursts of saccadic eye movements in a chaotic pattern in both the horizontal and vertical planes. The element of postural ataxia was uniformly greater than extremity ataxia. The degree of nausea, vertigo, and dysarthria was variable. Absence of fever, headache, and meningismus was the rule at the time of neurologic deterioration. The only significant and consistent laboratory finding was a lymphocytic pleocytosis of the spinal fluid. All of the adult cases spontaneously resolved within weeks to months. In no case was there a positive viral culture or a documented viral immunoglobulin response.

Where the lesions are that explain the abnormal eye movements is open to debate. It has been postulated that the movements represent dysfunction of the mesencephalic pause cells or their descending controlling factors in the cerebellum.[5–7] The high association of other cerebellar signs, especially dramatic ataxia, strongly implicates cerebellar pathology.

Cerebellar irritation can be caused by a number of underlying processes. These include intracerebral neoplasia, demyelination, cerebral vasculitis, and ingestion of toxic substances, including heavy metals and ethanol. It has also been described in hyperosmolar nonketotic coma.[8] Occult extracerebral neoplasia has also been associated with similar clinical findings, including medullary carcinoma of the thyroid,[9] adenocarcinoma of the breast,[10] squamous[11] and oat-cell lung tumors,[12] adenocarcinoma of the uterus,[13] and squamous cell carcinoma of the tongue.[14] In children, the syndrome has been described in lymphocytic choreomeningitis[15]; Coxsackie, echo, and polio viral meningitides[16]; *Hemophilus influenza* meningitis[17]; hydrocephalus[18]; and intra- and extracranial neuroblastomas.[19]

Ellenberger et al[10] reported the autopsy findings in a patient with opsoclonus and ataxia who was found to have a breast mass. The anatomic findings were limited to the posterior fossa with meningeal inflammation, near absence of the Purkinje cell layer of the cerebellum, neuronal loss in the granule cell layer and dentate nucleus, and perivascular lymphocyte infiltration. There was no evidence of demyelination or cerebral hemispheric involvement. On the other hand, two case reports describe pathologic findings not limited to the cerebellum.[12,20] The exact location of the lesion in these cases, therefore, remains controversial. Indeed, the nature of the symptom complex reported in these two cases is most consistent with cerebellar dysfunction. No other intracranial process was suggested by detailed laboratory assessment.

When an otherwise healthy adult has acute neurologic dysfunction, the physician should give priority to identifying an underlying cause. Toxin and drug ingestion should be excluded. Appropriate scans should be performed to rule out intracranial neoplasm and demyelination. CSF examination, including cultures and IgG quantitation, cytology, and screen for vasculitis and elevated catecholamines should be performed. Serologic viral titers generally do not contribute to the diagnosis. Screening for occult neoplasm should be considered because the remote cerebellar paraneoplastic effects may precede the diagnosis of extracranial neoplasm. Only when the above causes have been excluded can the diagnosis of a benign condition be entertained and the patient reassured. Of note is that our two patients were referred with presumptive diagnoses of multiple sclerosis.

Steroid therapy has been used in children with symptomatic opsoclonus and myoclonus secondary to neuroblastoma. Short courses of steroids were used as a trial in our cases and probably had little effect on the recovery process, because the nature and length of these illnesses closely match those reported in the literature that were not treated.

Summary

With extensive investigations, underlying illnesses were ruled out in these two cases. Lymphocytic pleocytoses determinations confirmed the encephalitis. Each symptom complex could be localized clinically as cerebellar dysfunction. No viral etiology was identified. Each patient has had spontaneous resolution of symptoms. Therefore, in contrast to the past literature that uses the term *benign postviral encephalitis*, we prefer to label these and similar cases as *benign acute cerebellitis*. This nomenclature accurately defines the absence of sequelae and spontaneous recovery. It also dispels the implication of a viral etiology, although preceding viral syndrome is not excluded. The anatomic location suggested by this term is consistent with the clinical findings

associated with the described cases and can be postulated as the site of lesions causing the abnormal eye movements.

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