

Transient opsoclonus-myoclonus syndrome secondary to neuroblastoma

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ABSTRACT

We report a 2½-year-old girl who presented with acute history of fluctuating level of consciousness in the form of drowsiness, extreme irritability, and involuntary abnormal movements in the form of shaking of the whole body. She was treated with acyclovir empirically, contemplating herpes simplex virus encephalitis. Overtime she improved substantially. The opsoclonus, myoclonus, and ataxia disappeared without treatment. However, 6 weeks later she presented again with classic opsoclonus-myoclonus syndrome. The investigations revealed neuroblastoma. This case illustrates that transient opsoclonus-myoclonus may occur with neuroblastoma and should not be assumed to be due to viral cause. Thus, a thorough search for occult neuroblastoma should be initiated even if opsoclonus-myoclonus resolves spontaneously.

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The opsoclonus-myoclonus syndrome was first reported by Kinsbourne in 1962,¹ and hence was named Kinsbourne disease. This later was named infantile polymyoclonia in 1968.² Opsoclonus-myoclonus syndrome is also labeled myoclonic encephalopathy of infancy.³ The disorder usually presents at one month to 4 years, with a mean age of 18 months, and has equal gender distribution. The onset can be acute or

subacute. Opsoclonus in the form of rapid eye movements conjugate or dysconjugate is present. It persists in sleep or eye closure. Chaotic myoclonic jerks of limbs, polymyoclonus, is another important feature and may even involve the trunk. External stimuli such as light, noise, or movement increases the myoclonia. In addition, these children have a common finding of irritability. The disorder is mostly due to a paraneoplastic condition or post infectious cause. We report a child with transient opsoclonus-myoclonus, which was assumed to be due to a viral illness, which reoccurred 6 weeks later. The child was then found to have a neuroblastoma.

Case Report. A 2½-year-old female child was admitted to hospital with a 7-day history of irritability, excessive crying, and fluctuating level of consciousness. This was followed 3 days later by shaking of the body and 2 days of inability to walk. There was no history of trauma, drug intake, preceding diarrhea, or vomiting. She was the youngest of 11 siblings and was fully immunized. She had a normal birth and development, and her past medical history was unremarkable. The weight, height, and head circumference were at the 50th centile, and systemic examination was normal. The blood pressure was within normal range and remained so during the hospitalization. On examination she was conscious, responding to the surroundings, but irritable. She had chaotic eye movements, dysarthria, finger nose ataxia, and trunk ataxia. Ophthalmic examination was normal. There were no pyramidal signs, and deep tendon reflexes were normal. A working diagnosis of acute cerebellar syndrome/ataxia likely post viral was made and differential diagnosis of drugs, trauma, tumor, degenerative, pseudo ataxia (seizures), vasculitis, and mitochondrial cytopathies were considered. Detailed investigations were carried out. Her complete blood count was white blood count (WBC) 7.02, hemoglobin 10.3, platelets 398, erythrocyte sedimentation rate 7, liver function tests, bone profile and urea/electrolytes were normal. Antinuclear antibody, double stranded DNA, and rheumatoid factor were negative. Serum ammonia was 67 mmol/l, lactate 2.37 mmol, and tandem mass spectrometry (TMS) were normal. An unusual presentation of herpes encephalitis was also considered. An MRI brain and EEG were normal. Cerebrospinal fluid had 5 WBC/cum (lymphocytes) and 204 red blood cells. There was



Figure 1 - Chest x-ray showing the widening of the mediastinum on the left side.



Figure 2 - Magnetic resonance image of a) chest and b) neck showing a tumor in the superior mediastinum on the left side.

no xanthochromia. The protein was 0.32 G/L, glucose 3.3 mmol/L, and polymerase chain reaction (PCR) for herpes simplex were negative. She was treated with acyclovir for 10 days and then discontinued once PCR was negative (result received after 10 days). The child's abnormal movements disappeared completely within 2 days of presentation to our hospital. The patient was discharged within 10 days and was starting to bear weight and continued to improve on follow-up. Six weeks later she was readmitted with excessive crying, irritability, decreased oral intake, drooling, and shaking of the body. On examination she was conscious, alert but irritable, had severe body ataxia, chaotic eye movements (opsoclonus), polymyoclonia, no weakness, brisk deep tendon reflexes, and down going plantars. At this time, the diagnosis of opsoclonus-myoclonus syndrome (Kinsbourne disease) was made and she was investigated for neuroblastoma. Facilities for estimation of urinary vanillylmandelic acid and homovanillic acid were not available in the hospital and hence were sent abroad, and unfortunately the tests were not performed as the urinary pH was found acidic. A chest x-ray, abdominal ultrasound, metaiodobenzylguanidine (MIBG) scan, MRI brain and MRI body (chest), and vasculitis work up were carried out. The abdominal ultrasound was normal and chest x-ray revealed a wide superior mediastinum (Figure 1). The MIBG scan showed uptake in the neck region close to the salivary glands. The MRI chest revealed a mass lesion in the lower neck and upper mediastinum on the left side (Figures 2a & 2b). Vasculitis profile was normal. An open biopsy was carried out and histopathological diagnosis was neuroblastoma, to be differentiated from ganglioneuroma. Chemotherapy was started, and the clinical condition of the child improved soon after this.

Discussion. This child presented with opsoclonus-myoclonus, a recognized manifestation of neuroblastoma. It may be the presenting feature in 2% of neuroblastomas.⁴ Opsoclonus-myoclonus syndrome is believed to be a paraneoplastic syndrome of autoimmune origin, although its exact etiology remains controversial.⁵ Although children with opsoclonus-myoclonus and neuroblastoma have decreased mortality, they suffer from increased neurologic morbidity.⁶ The occurrence of opsoclonus in childhood is a notable clinical sign and should always prompt the search for a precipitating neural-crest tumor, particularly neuroblastoma. Spontaneous resolution of opsoclonus-myoclonus is known to occur with viral etiology.⁷⁻⁹ In neuroblastoma, recurrence of the syndrome is known to occur many years after the tumour resection.^{10,11} The tumour itself has a high incidence of spontaneous regression. However, the spontaneous resolution of symptoms in a

short time is unusual. No previously reported case was found to have a spontaneous recovery of symptoms and then to recur shortly afterwards. This child developed a full-blown opsoclonus-myoclonus syndrome 6 weeks after the initial presentation. She was not treated with any medication that may have affected the symptoms. One might argue that the opsoclonus-myoclonus is due to a viral etiology. However, it will be unlikely that the neuroblastoma would develop in one month's time. We believe that this patient had myoclonus-opsoclonus due to neuroblastoma. Therefore, it is worth noting that spontaneous resolution of the symptoms may occur in the presence of neuroblastoma, and not unique to the syndrome due to post-viral cause. We encourage physicians to search aggressively for neuroblastoma in any patient presenting with opsoclonus-myoclonus even if the symptoms disappear quickly and spontaneously. Our patient remains in remission after the surgery.

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