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Case report

Incidence of tonic spasms as the initial presentation of pediatric multiple sclerosis in Slovenia

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ABSTRACT

Tonic spasms (TS) are involuntary movement patterns that can present in patients with multiple sclerosis (MS). They have been first described decades ago, but are frequently missed and misdiagnosed, particularly in the pediatric MS patients and if appearing ahead of hallmark neurological signs and symptoms of MS.

Slovenia is a country with the population of about 2 million people. In the years from 1992 to 2016, we have treated 57 sequential pediatric patients with MS at our hospital, which is the only tertiary medical institution for treating children with MS in the country. We present the only two MS patients, a 17-year-old girl and a 14-year-old boy, whose first manifestation of MS were TS. This allowed us to estimate the incidence of TS in pediatric MS patients in Slovenia.

1. Case presentations

1.1. Patient one

A 17-year-old girl was referred to University Children's Hospital Ljubljana with a three week-history of recurrent, brief (< 60 s) and painful tonic spasms of the right upper limb and the right side of her face. An unpleasant sensation in the right arm preceded the dystonic posturing, which was triggered by hyperventilation or voluntary movements, such as fast stepping out from the bus or brushing her teeth. Consciousness remained intact throughout the whole event.

The neurological examination was otherwise unremarkable. Her medical and family history did not reveal any relevant details. Routine laboratory blood tests were normal. The electroencephalogram (EEG) was normal during and between the attacks, making the epileptic tonic seizures less plausible explanation for her symptoms. Tonic spasms spontaneously resolved four weeks after the first presentation. She was referred for brain MRI, which was performed three months later, which revealed multiple areas of white matter T2 hyperintensities in the periventricular and subcortical areas, including a lesion in the left cerebral peduncle (Fig. 1). None of the lesions displayed gadolinium enhancement. Brain MRI raised the suspicion of a demyelinating disease of the CNS. Laboratory studies showed positive serum antinuclear antibodies, CSF pleocytosis with lymphocyte predominance and the presence of oligoclonal bands in CSF. All other tests were normal. Serologic testing for cytomegalovirus, Epstein-Barr virus, herpes simplex virus 1 and 2, Mycoplasma pneumoniae, Lyme disease and HIV were negative. Follow-up brain magnetic resonance imaging (MRI) six months later showed dissemination of the lesions in time and space. Her parents refused treatment with immunomodulatory therapy. To date, three years after initial presentation, tonic spasms did not reoccur and she has no other neurological symptoms.

1.2. Patient two

A 14-year-old boy was referred with a one week history of spontaneous, brief (15–30 s) tonic spasms, involving the left limbs and the left side of his face, occurring several times per day. All episodes were triggered by hyperventilation. Consciousness was preserved at all times. There was no headache, visual, sensory or mental disturbances associated with the presentation of TS. The neurological examination was otherwise normal. Past medical and family history were unremarkable. Routine laboratory tests were normal. The hyperventilation during EEG recording triggered a typical clinical episode of left sided tonic spasms accompanied by slow waves over the right hemisphere, without the presence of epileptic discharges or other abnormal finding. Tonic spasms spontaneously disappeared three weeks after the initial presentation and did not reoccur. Seven months after onset of the spasms, a MRI scan of the brain revealed areas of T2 abnormality in periventricular frontal white matter, right internal capsule and right corona radiata, none of which displayed gadolinium enhancement. Fourteen months later, he was admitted to our depart-

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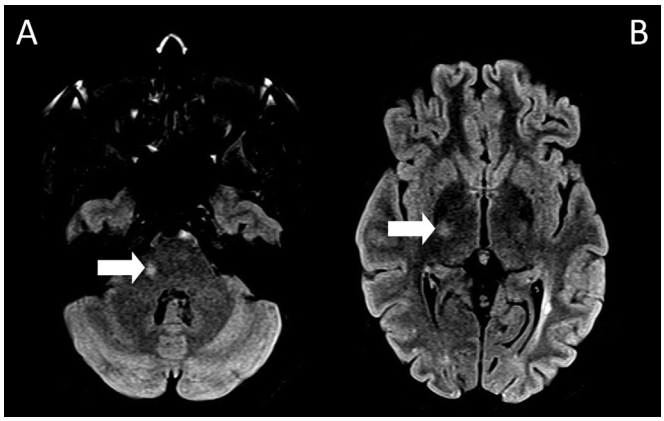

Fig. 1. Brain MR images with arrows pointing to two demyelinated lesions in the right cerebral peduncle (A) and right internal capsula (B).

ment again because of paresthesias of the left arm and the left side of his face. Expanded laboratory tests showed positive CSF oligoclonal bands, while all other tests were normal. Visual and brainstem auditory evoked potentials were within the normal limits. A control brain MRI showed new demyelinating lesions in the CNS and at this point, the diagnosis of a multiple sclerosis was made. His parents refused specific disease-modifying therapy and further follow-up MRI scans over the next 3 years revealed obvious signs of progression of MS.

2. Discussion

Tonic spasms in MS patients were initially described by Matthews (1958) in 1958 as brief involuntary movements with dystonic posturing, which could be frequent, painful, and often localized to one side of the body. Tonic spasms can occur in 3.8 to 17.0% of MS patients (Berger et al., 1984). Although well defined, they are often missed or even misdiagnosed by clinicians, (Tranchant et al., 1995; Waubant et al., 2001; Spissu et al., 1999a) leading to unnecessary investigations or a delay in the diagnosis of MS. It is therefore not surprising that only two cases of TS as the initial manifestation of MS were reported in pediatric population, one by Berger et al. (1984) and the other by Yilmaz et al. (2011). We report two additional cases. In our cohort of 57 sequential pediatric patients with MS treated at our tertiary hospital in the years from 1992 to 2016, only two (3,5%) had TS, which is at the lower end of the spectrum of what was reported in other studies (Berger et al., 1984). The estimated incidence of TS in pediatric MS patients in Slovenia is thus 35 per 1000 patients. However, the reported numbers are small and further prospective studies are needed to establish a more precise incidence.

Tonic spasms can occur as the only neurological symptom of MS, as was the case in one of our patients. Tonic spasms usually have a stereotypical course of presentation, with episodes between presentation lasting from several days to months (Spissu et al., 1999b). In our patients the main triggering factors were hyperventilation, strong emotions and sudden voluntary movements. Tonic spasms occurred in our patients for a period of three to four weeks, usually several times per day, although not necessarily every day, and resolved in up to two minutes. Tonic spasms are known to spontaneously disappear within a few weeks, while more resistant forms can be treated with steroids, antiepileptic drugs, botulinum toxin and others (Yilmaz et al., 2011; Deuschl, 2016; Restivo et al., 2003). In both of our cases TS spontaneously disappeared within three to four weeks.

Tonic spasms presumably result from axonal activation secondary to ephaptic cross-transmission in the demyelinated plaques (Osterman and Westerberg, 1975) along motor pathway, especially in sites where the motor fibers are close enough to allow radial spreading of the ectopic impulse. Preservation of the more distal motor tract presumably facilitates the pathologic discharge to reach the peripheral effectors and generate the spasm (Spissu et al., 1999a).

We report these two cases to raise the awareness of this underrecognized, transient neurological symptoms of MS, especially as TS could be the initial presentation of MS. Early recognition of MS could provide better treatment options for patients and potentially improve their outcome.

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