A case of adult-onset poststreptococcal opsoclonus-myoclonus syndrome

Authors: Borislav Radic, Ivana Cajic, Zeljka Petelin Gadze, Vlatko Sulentic, Sibila Nankovic

Department of Neurology, University Hospital Centre Zagreb, School of Medicine, University of Zagreb, Referral Centre of the Ministry of Health of the Republic of Croatia for Epilepsy, Kispaticeva 12, Zagreb 10000, Croatia

Corresponding author:

Ivana Cajic, M.D.

Department of Neurology, University Hospital Center Zagreb, School of Medicine, University of Zagreb, Referral Centre of the Ministry of Health of the Republic of Croatia for Epilepsy, Kispaticeva 12, Zagreb 10000, Croatia

Office phone: +385 1 2388 344

Mobile phone: +385 98 309 094

E-mail: ivana345@gmail.com

Keywords: opsoclonus-myoclonus syndrome, streptococcus, immunoglobulin, penicillin.

Dear Editor,

Opsoclonus-myoclonus syndrome (OMS) is a rare neuroinflammatory disease of paraneoplastic, parainfectious or idiopathic origin, characterized by opsoclonus, myoclonus, ataxia, as well as behavioral and sleep disorders. OMS is a rare disorder that appears in 1 in a million individuals worldwide. It usually affects infants and young children. In approximately 50 percent of affected children, a tumor of embryonic nerve cells (neuroblastoma) is responsible for the symptoms associated with OMS. In other cases, the disorder has been designated „idiopathic“ or attributed to various mostly viral infections (Coxsackie virus B3 or St. Louis encephalitis virus) or bacterial infections (Streptococcus) [1, 2]. We present a case of a 22-year old girl that was admitted to our hospital due to opsoclonus with rapid, involuntary, horizontal and vertical, conjugate fast eye movements, mild myoclonic jerks of eyelids, upper and lower limbs, and mild ataxia. Extensive diagnostic evaluation was performed. Her routine investigations of laboratory tests, including thyroid hormones were normal. Erythrocyte sedimentation rate, C-reactive protein and other immunological tests (antinuclear antibody, antineutrophil cytoplasmic antibodies, anti-dsDNA antibodies, C3 and C4-complement, serum immunoelectrophoresis) were negative, as well as oncomarkers, paraneoplastic and antiganglioside antiboidies. Swab of the posterior pharynx revealed Streptococcus pyogenes (group A). Patient did not have signs of pharyngitis. Antistreptolysin O (ASO) titer was 653 IU/ml. Tests for detection of viral markers for cytomegalovirus, Epstein-Barr virus, herpes simplex viruses type 1 and 2, varicella-zoster virus, human immunodeficiency virus, hepatitis

B and C virus were negative. Molecular-genetic analysis for spinocerebellar ataxia type 1, 2, 3, 6, and 7, MELAS (mitochondrial myopathy, encephalopathy lactic acidosis, and stroke-like) syndrome, myoclonic epilepsy with ragged red fibers, Unverricht-Lundborg disease (EPM1) and Lafora disease (EPM2A or EPM2B) was normal. Anti-neuroleukin antibodies, urinary vanillymandelic acid and homovanillic acid were not determined in our patient. Anti-Ri and anti-Hu antibodies were negative. Cerebrospinal fluid analysis was within normal limits. Electroencephalogram showed right tempoparietal lateralisation and left focal abnormalities with occasional generalized spike-and-wave discharges. Brain magnetic resonance imaging 3-Tesla was normal. Positron emission tomography showed increased glucose metabolism in the tonsils and sublingual glands. Electromyoneurography found a mild sensory polyneuropathy. Following diagnostic evaluation, we have made the diagnosis of poststreptococcal OMS and administered intravenous immunoglobulin (IVIG) at doses of 0.4 *g*/kg given on 5 consecutive days, with oral penicillin V for 10 days and then intramuscular benzathine penicillin G, which resulted in clinical improvement and gradual normalization of neurological status. We have also started antiepileptic therapy with levetiracetam and clonazepam. The treatment of IVIG continued till today once a month, with remission of the disease. Intramuscular benzathine penicillin G was introduced every month for a year. Two years since the beginning of the treatment, the ASO titer decreased (304 IU/ml). Five years since the beginnig of the treatment, the disease is still in remission.

The immunopathogenesis of OMS is poorly understood. There appears to be humoral and cell-mediated immune mechanisms involved both in paraneoplastic and idiopathic syndromes [3]. In many cases the symptoms are reversible after treatment with immunotherapy [3, 4]. Our patient presented with poststreptococcal OMS, with high ASO titer, but without signs of bacterial inflammation of the pharynx. She was much older than the typical patient with pediatric paraneoplastic OMS and much younger than the typical adult patient with paraneoplastic OMS. First two similar case reports of post-streptococcal OMS were presented 2006 by Candler *et al*, and they were associated with CSF anti-neuroleukin (NLK) antibodies. The antigen was identified as human neuroleukin (glucose-6-phosphate isomerase, GPI). GPI is present on the cell surface of streptococcus making the protein a candidate target for molecular mimicry. We suppose anti-neuroleukin antibodies were responsible for the immunopathogenesis of OMS in our patient. The role of streptococcus in OMS and the frequency with which anti-NLK responses occur should be investigated further [5].

Compliance with ethical standards

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: This article does not contain research including human participants or animals performed by any of the authors.

Informed consent: Informed consent was obtained from the patient included in the study.

Acknowledgements: Authors are very grateful to Prof. Sanja Hajnsek, M.D., Ph.D. for her important contribution in treating patient presented in this paper.

References

1. Baets J, Pals P, Bergmans B, Foncke E, Smets K, Hauman H, Vanderwegen L, Cras P. Opsoclonus-myoclonus syndrome: a clinicopathological confrontation. Acta Neurol Belg. 2006 Sep;106(3):142-6.
2. Deconinck N, Scaillon M, Segers V, Groswasser JJ, Dan B. Opsoclonus-myoclonus associated with celiac disease. Pediatr Neurol. 2006 Apr;34(4):312-4. doi: 10.1016/j.pediatrneurol.2005.08.034.
3. Wong A. An update on opsoclonus. Curr Opin Neurol. 2007 Feb;20(1):25-31. Review. doi: 10.1097/WCO.0b013e3280126b51.
4. Groiss SJ, Siebler M, Schnitzler A. Full recovery of adult onset opsoclonus myoclonus syndrome after early immunotherapy: a case report. Mov Disord. 2011 Aug 15;26(10):1805-7. doi: 10.1002/mds.23854.
5. Candler PM, Dale RC, Griffin S, Church AJ, Wait R, Chapman MD, Keir G,Giovannoni G, Rees JH. Post-streptococcal opsoclonus-myoclonus syndrome associated with anti-neuroleukin antibodies. J Neurol Neurosurg Psychiatry. 2006 Apr;77(4):507-12. doi: 10.1136/jnnp.2005.078105.