Pediatric Neurology 72 (2017) 65–69

Contents lists available at ScienceDirect

Pediatric Neurology

journal homepage: www.elsevier.com/locate/pnu

Clinical Observations

Opsoclonus-Myoclonus Syndrome: A New Era of Improved Prognosis?

Armine Galstyan MD, Colin Wilbur MD, FRCPC, Kathryn Selby MBChB, FRCPC, Juliette Hukin MBBS, FRCPC *

Division of Neurology, Department of Pediatrics, University of British Columbia and BC Children's Hospital, Vancouver, British Columbia, Canada

ABSTRACT

BACKGROUND: Opsoclonus-myoclonus syndrome is an autoimmune neurological disorder characterized by opsoclonus, myoclonus, ataxia, and behavioral changes. Although long-term outcomes have historically been poor, including motor and cognitive disabilities, the advent of new and more aggressive immunotherapy regimens may be improving prognosis in opsoclonus-myoclonus syndrome. **METHODS:** We retrospectively reviewed the records of all children diagnosed with opsoclonus-myoclonus syndrome at BC Children's Hospital from 2000 to 2010. Neurological outcomes were compared with those previously reported in the literature. **RESULTS:** Twelve children with opsoclonus-myoclonus syndrome were identified, four of whom had an associated neuroblastoma. Two thirds of patients received initial treatment with a combination of corticosteroids, intravenous immunoglobulin (IVIG), and an additional immunosuppressant agent. After a median follow-up of three years from diagnosis, ten patients had no or minimal neurological abnormalities. Two patients had poor outcome with significant cognitive impairment. **CONCLUSIONS:** Most patients in this series were treated with early multimodal immunotherapy, and neurological outcomes were better than those in most historical reports. This finding is consistent with recent studies that suggest multimodal immunotherapy regimens may be improving the prognosis in this challenging disease. However, some individuals did well with less aggressive treatment, and further studies are required to determine optimal treatment approach.

Keywords: Opsoclonus-myoclonus syndrome, neuroblastoma, ataxia, immunotherapy

Pediatr Neurol 2017; 72: 65-69

Background

Opsoclonus-myoclonus syndrome (OMS) is a rare autoimmune neurological disorder that has a median childhood age of onset of 18 months.[1] The disease is characterized by acute or subacute onset of ataxia, opsoclonus, myoclonic jerks, irritability, sleep disturbance, and other behavioral changes.[2] Because all classic features may not be present initially, the diagnosis can be delayed by weeks or months from the first onset of symptoms. About half of affected children have an underlying neuroblastoma (NB), and OMS occurs as a paraneoplastic syndrome in 2% to 3% of all children with NB.[3] The remaining patients, often classified as having idiopathic OMS, may have a parainfectious autoimmune process following a variety of antecedent infections.

Although OMS symptoms typically improve with treatment, a relapsing course is common and long-term neurological sequelae are reported in up to 80% of patients.[4] Deficits may include motor, cognitive, language, and behavioral impairment. The mainstay of treatment has traditionally been corticosteroids. A variety of other immunosuppressive treatments have been used, typically in combination with corticosteroids, such as intravenous immunoglobulin (IVIG), cyclophosphamide, cyclosporine, azathioprine, or plasmapheresis.[5] Rituximab, a monoclonal antibody to CD20, has more recently shown efficacy as an add-on therapy to corticotropin (ACTH) and/or IVIG in one uncontrolled study.[6] There is early evidence that more

Conflicts of Interest: The authors have no conflicts of interest to declare in relation to this work.

Article History:
Received November 21, 2016; Accepted in final form March 18, 2017

* Communications should be addressed to: Dr. Hukin; Division of Pediatric Neurology and Oncology; British Columbia Children's Hospital; 4480 Oak Street; Room K3-147; Vancouver, BC V6H 3V4, Canada.
E-mail address: jhukin@cw.bc.ca

0887-8994/$ – see front matter © 2017 Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.pediatrneurol.2017.03.011

aggressive therapy with a combination of agents, including newer treatments such as rituximab, may result in improved outcome compared with historical control subjects.[7]

To help further clarify the optimal treatment approach to children with OMS, this study evaluates the response to therapy and long-term outcome of a cohort of patients diagnosed with OMS between 2000 and 2010. This period corresponds to a shift to more aggressive initial immunotherapy at our institution.

Materials and Methods

This study was approved by the Children's and Women's Health Centre of British Columbia Ethics Board. Patients diagnosed with OMS from 2000 to 2010 were identified through British Columbia Children's Hospital health records. Retrospective chart review was performed to extract clinical data including demographics, presence of NB, antecedent infection, treatment, response to treatment, and neurocognitive outcome. For comparison purposes, the degree of gross motor impairment at presentation was classified as follows: abnormal examination findings, but ambulates independently (mild); sits independently, but cannot ambulate independently (moderate), neither sits nor ambulates independently (severe). Periods of OMS remission were defined as a symptom-free interval lasting at least one month. Neurological outcome was determined by the clinical assessment of the treating pediatric neurologist, neuropsychology evaluation (Patient 10), and documented developmental and/or school performance history. Because of the small study size, analysis is primarily descriptive.

Results

Patient characteristics

Twelve patients were diagnosed with OMS during the study period and included for analysis (Table 1). Median age

TABLE 1.
Summary of Patients

Patient	Age at Diagnosis, Sex	Presumed OMS Trigger	Time From Symptom Onset to Diagnosis	Gross Motor Impairment at Presentation*	First-Line Treatment	Second-Line Treatment†	Time From Diagnosis to Initial OMS Symptom Remission	Number of Relapses	Age at Last Follow-Up, Neurological Outcome
1	18 months, Female	Postinfectious (URTI, no virus identified)	10 days	Moderate	ACTH IVIG azathioprine		3 months	1	4 years, Normal
2	15 months, Male	NB	42 days	Severe	Resection of NB prednisone IVIG cyclophosphamide	Rituximab ACTH	24 months	0	6 years, Normal
3	8 months, Male	NB	14 days	Severe	Resection of NB ACTH prednisone IVIG cyclophosphamide		4 months	0	6 years, Mild coordination difficulties
4	39 months, Male	Postinfectious (varicella)	56 days	Mild	ACTH prednisone IVIG azathioprine		2 months	1	6 years, Intellectual disability
5	38 months, Male	Postinfectious (enterovirus)	1 day	Moderate	ACTH IVIG azathioprine		1 month	0	5 years, Poor enunciation, otherwise normal
6	21 months, Male	None identified	56 days	Moderate	ACTH IVIG azathioprine		2 months	2	4 years, Normal
7	15 months, Male	Post-Infectious (metapneumovirus)	28 days	Moderate	ACTH IVIG azathioprine		2 months	0	3 years, Normal
8	25 months, Male	None identified	2 days	Severe	ACTH IVIG rituximab		2 months	3	6 years, Normal
9	15 months, Female	Postinfectious (URTI, no virus identified)	2 days	Moderate	None (spontaneous resolution)		3 days	2	5 years, Normal
10	17 months, Female	NB	140 days	Severe	Resection of NB ACTH prednisone		8 months	Chronic, relapsing course	12 years, Intellectual disability
11	35 months, Female	None identified	21 days	Mild	ACTH		1 month	0	5 years, Normal
12	18 months, Female	NB	84 days	Mild	Resection of NB		16 days	0	2 years, Normal

Abbreviations:
ACTH = Add-on therapy to corticotropin
IVIG = Intravenous immunoglobulin
NB = Neuroblastoma
OMS = Opsoclonus-myoclonus syndrome
URTI = Upper respiratory tract infection

* Mild = abnormal signs but independent ambulation; Moderate = sits but does not walk independently; Severe = unable to sit or walk independently.
† Treatment initiated after inadequate response to 6 months of first-line therapy.