Published in final edited form as:
Mov Disord. 2011 August 1; 26(9): 1768–1769. doi:10.1002/mds.23626.

Opsoclonus-myoclonus syndrome and exaggerated startle response associated with small-cell lung cancer

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Key words/terms

Opsoclonus; myoclonus; paraneoplastic; startle; oscillopsia

Opsoclonus-myoclonus syndrome (OMS) is a rare neurological disorder that is usually seen in conjunction with tumors (most commonly breast, lung and gynecological), infections or toxic-metabolic processes. In addition to opsoclonus and/or myoclonus, the clinical features of OMS may include ataxia and encephalopathy.[1, 2] We describe a patient who presented with OMS and a strikingly exaggerated startle response, prompting an evaluation for an underlying malignancy which led to diagnosis of a small-cell lung carcinoma.

A 64-year-old woman presented with a three month history of dizziness and unsteadiness. Her symptoms began suddenly with an attack of dizziness and unsteadiness that lasted only a few seconds. The dizziness was described as a light-headed feeling without vertigo. Over the next few weeks, she had similar episodes, lasting longer and occurring more frequently and eventually her symptoms became constant. Then, two weeks prior to her presentation, she developed “jumping” vision. The patient also had lost approximately 15 pounds over the past few months. She had a remote history of tobacco use. Before our evaluation she had a normal brain MRI.

On examination, the patient had bursts of back-to-back, multi-directional saccades, with variable amplitude (i.e., opsoclonus), that were exacerbated during pursuit. The saccadic oscillations were also visible under closed eyelids.(video 1) She had occasional spontaneous

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Financial Disclosure/Conflicts:
We report no disclosures related to the currently submitted manuscript.

Author Roles
ES Sotirchos: Project organization and execution; Writing of the first draft;
ER Dorsey: Project conception, organization and execution; Manuscript review and critique;
IL Tan: Project organization and execution; Manuscript review and critique;
DS Zee: Project conception, organization and execution; Manuscript review and critique;

Full Financial Disclosures of all Authors for the Past Year
ES Sotirchos reports no financial disclosures.
ER Dorsey has received research support from industry (Amarin and Medivation, Inc.), the federal government (NIH) and foundations (American Parkinson Disease Association, CHDI Foundation, Inc., National Parkinson's Foundation, and the Robert Wood Johnson Foundation). Dr. Dorsey has consulted and served on advisory boards for Lundbeck, Inc. consulted for Medtronic, and holds stock options in Avid Radiopharmaceuticals, Inc.
IL Tan reports no financial disclosures.
DS Zee has research support from the National Institutes of Health.

myoclonic jerks of her head, and a strikingly exaggerated startle response to sound and light, that could be elicited even with expected stimuli.(video 2) Eye movements were otherwise remarkably intact A subtle intention and postural tremor of her hands was present, as well as a slight dysmetria on finger-to-nose and heel-to-shin testing, more on the left side. Her gait was wide-based and mildly unsteady and she could not walk in tandem unassisted. The remainder of her examination was normal.

Routine blood studies showed no abnormalities. Cerebrospinal fluid analysis was normal. Viral PCRs including West Nile Virus were negative. An EEG was within normal limits and when she was startled there was no EEG correlate to her myoclonic jerk apart from muscle artifact. A comprehensive serum paraneoplastic antibody panel (including, among others, anti-Ri, amphiphysin, Yo, CV2 and Hu) was negative. A CT of the chest-abdomen-pelvis, mammograms, transvaginal ultrasound and FDG-PET/CT were performed and a 4.2cm lung mass was found in the left lower lobe with involvement of one lymph node. Lung biopsy showed this to be a small-cell lung carcinoma. PET also revealed physiologically increased uptake in the cerebrum and in the cerebellar hemispheres, though more so in the latter. Treatment for the malignancy was initiated with combination chemotherapy and radiation therapy. Over the course of several months her tumor shrunk, her ocular oscillations markedly improved and her startle myoclonus disappeared.

Paraneoplastic neurological syndromes are considered to arise from an autoimmune response directed against neuronal antigens ectopically expressed by tumor cells.[3] Specific auto-antibodies have been associated with OMS, especially anti-Ri and anti-amphiphysin, but most patients with OMS are seronegative for all known anti-neuronal antibodies, suggesting that cell-mediated immunity plays an important role.[2-4] Alternatively, there may be associated novel autoantibodies that are yet to be identified.

Localization of the lesion in OMS remains controversial with evidence supporting two predominant theories. One hypothesis states that cerebellar dysfunction leads to disinhibition of the fastigial nucleus by the Purkinje cells, resulting in OMS.[4] In our case, this hypothesis correlates well with the relative hypermetabolism of the cerebellar cortex revealed on PET and the beneficial action of clonazepam, but does not provide a plausible explanation of the augmented startle response. Another view is that the culprit is the caudal pontine reticular formation and represents either dysfunction of pause neurons that inhibit the burst neurons that drive saccades, or primary hyperexcitability of the burst neurons themselves.[5, 6] The exaggerated startle response of our patient is consonant with the second hypothesis, since the nucleus reticularis pontis caudalis plays an important role in the startle reflex, and therefore hyperexcitability of neurons here would account for her response.[6] Finally, a caveat. An exaggerated startle response must be distinguished from reflex reticular myoclonus, a response that also originates in the caudal brainstem[7]. Unfortunately, we could not perform tests to make this distinction at at ime when our patient was symptomatic.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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