Infections of the Cerebellum

Amy A. Pruitt, MD

KEYWORDS

- Autoimmune cerebellitis • CLIPPERS • Creutzfeldt-Jakob disease
- Epstein-Barr virus • Influenza • JC virus granule cell neuronopathy
- *Listeria* rhombencephalitis • Progressive multifocal leukoencephalopathy

KEY POINTS

- Infectious pathogens that frequently or preferentially affect the cerebellum include *Listeria monocytogenes*, varicella-zoster virus, JC virus, and Creutzfeldt-Jakob disease. Fever, headache, and brainstem signs and symptoms may accompany cerebellar signs. Magnetic resonance imaging (MRI) may show leptomeningeal enhancement and swelling.
- Acute postinfectious cerebellitis is more common in children and young adults. It is a pure cerebellar syndrome often with normal MRI at onset. Reported antecedent infections include Epstein-Barr virus, influenza A and B, mumps, varicella-zoster, Coxsackie virus, rotavirus, echovirus, *Mycoplasma*, and immunization.
- Acute ataxia caused by cerebellar disease must be distinguished from other anatomic sites whose dysfunction causes imbalance, including vestibular nuclei, and peripheral neuropathies, such as Guillain-Barré syndrome and Miller Fisher syndrome.
- Acute cerebellitis can result in significant cerebellar edema, and the resulting obstructive hydrocephalus can require surgical decompression.
- Some patients with acute postinfectious cerebellitis may benefit from immunologic modification with intravenous immunoglobulin or plasmapheresis.

INTRODUCTION: SUSPECTING AN INFECTIOUS CEREBELLITIS

Definitions and Terms

Acute cerebellitis (AC) can be caused by either primary infection or postinfectious immune-mediated processes. In this article, the term *acute* is defined as symptoms evolving over a few hours to 2 days. *AC* denotes an infection that directly affects the cerebellum often with abnormal magnetic resonance imaging (MRI) and with symptoms and signs beyond a pure cerebellar syndrome. AC may be unilateral or bilateral. The term *acute postinfectious cerebellar ataxia* (APCA) designates a postinfectious (mostly viral) cerebellitis that is usually a pure pan-cerebellar syndrome

Disclosures: The author has no relevant disclosures.
University of Pennsylvania, 3400 Spruce Street, Philadelphia, PA 19104, USA
E-mail address: pruitt@mail.med.upenn.edu

Neurol Clin 32 (2014) 1117–1131
http://dx.doi.org/10.1016/j.ncl.2014.07.009 **neurologic.theclinics.com**
0733-8619/14/$ – see front matter

without other signs of central nervous system (CNS) infection often with an initially normal MRI scan. Although the 2 entities may represent a spectrum, the presentation, outcome, and therapeutic implications are often different.

Laboratory Investigations

Because the differential diagnosis of cerebellar infection is broad (**Box 1**), the clinician must consider concurrent drugs, patient immune status, and a limited range of distinguishing radiographic characteristics. Cerebrospinal fluid (CSF) may show a nonspecific lymphocytic pleocytosis of multiple possible causes. **Table 1** summarizes additional special studies. MRI, particularly diffusion-weighted imaging (DWI), can be helpful but often is nonspecific or normal in APCA. Transient cerebellar cortical swelling leptomeningeal enhancement, limited involvement of deep cerebellar nuclei, middle cerebellar peduncles, other brainstem structures, and splenial lesions can aid differential diagnostic considerations. Cerebellar atrophy may develop after the acute cerebellar infectious or parainfectious insult. Succinate peaks on MR spectroscopy (MRS) raise suspicion of infection.

Physical Examination

Article reviews cerebellar signs and symptoms. In the setting of acute presentations suggestive of infection, the examination should also be directed at sensory or vestibular dysfunction that can cause ataxia.[1] In most infections, motor dysfunction will predominant; but when dentate nuclei are preferentially involved, the cognitive-affective syndrome may color the clinical presentation.[2]

DIFFERENTIAL DIAGNOSIS: NONINFECTIOUS MIMES

Neoplasms

The cerebellum and its coverings can be sites of parenchymal metastatic disease, primary brain tumors, or leptomeningeal dissemination usually in the context of known malignancy. However, one recently described syndrome is predominantly seen in the posterior fossa and has diagnostic and therapeutic implications. The recently described definable disorder of chronic lymphocytic inflammation with pontine perivascular enhancement responsive to steroids (CLIPPERS) was reported in 2010 and could be confused with infection (**Fig. 1**).[5] Concern that it may not be a benign steroid-responsive condition but rather a sentinel lesion of primary CNS lymphoma has since arisen. Use of MRS may suggest the correct diagnosis with rising Cho:NAA ratios as well as lipid and lactate resonances.[6] CLIPPERS also may represent a form of immune reconstitution inflammatory syndrome in patients who have been withdrawn from natalizumab.[7]

Paraneoplastic Syndromes

Acute cerebellar symptoms evolving over hours to a few days can raise the possibility of antibody-associated disorders as an alternative to infection. The paraneoplastic disorders most likely to present with a predominantly cerebellar syndrome include the onconeural antibodies, such as anti-Hu, anti-Ri, anti-Tr, and anti-Yo. Nonparaneoplastic cerebellitis associated with antibodies can be seen with glutamic acid decarboxylase, metabotropic glutamate receptor type I,[8] and contactin-associated protein 2.[9] Homer 3 antibodies have been described in 2 adult patients without neoplasm who presented with a subacute pancerebellar syndrome.[10,11] The onset of paraneoplastic cerebellar degeneration can be extremely acute and accompanied by significant pleocytosis, thus, mimicking acute postinfectious cerebellitis.[12]