

# Rhombencephalitis Caused by Adenovirus: MR Imaging Appearance

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**Summary:** Encephalitis is a rare manifestation of adenovirus infection. We report the MR imaging findings of a patient with rhombencephalitis caused by adenovirus. Imaging findings included T2 signal abnormalities in the brain stem and cerebellum with mild patchy enhancement and mass effect.

Rhombencephalitis is a potentially fatal inflammatory process involving the brain stem and cerebellum in which bacteria and viruses are the most common offending agents. We describe the clinical course and MR imaging appearance of a case of rhombencephalitis caused by adenovirus infection.

## Case Report

A 53-year-old woman presented with nausea, headache, weakness, and double vision of approximately 3 weeks' duration. Her medical history was significant for acute myelogenous leukemia, which had been diagnosed 7 years previously and treated with daunorubicin and cytarabine induction, followed by high-dose cytarabine intensification chemotherapy. She remained in complete remission for a year after her diagnosis, but then relapsed. Remission was again achieved with high-dose cytarabine therapy. Her course was complicated by a cutaneous herpes zoster infection with posttherapeutic neuralgia. She underwent autologous bone marrow transplantation with busulfan and cyclophosphamide preparation, and cyclosporine-A autologous graft-versus-host disease induction. This was complicated by pulmonary and cutaneous aspergillosis, which was successfully treated. After transplantation, she remained free of leukemia and had returned to her normal level of function; however, she had persistent pancytopenia, along with slowly resolving elevated liver transaminases, and she had occasional upper respiratory tract infections.

Findings at physical examination were normal except for left lateral gaze nystagmus, mild left finger-to-nose and heel-knee-shin dysmetria, mild dysidiadochokinesia, and ataxia. Results of laboratory tests showed a lymphocytic pleocytosis of the CSF with 52 white blood cells (95% lymphocytes, 3% monocytes, and 1% polymorphonuclear leukocytes), a protein level of 62 mg/dL, glucose of 73 mg/dL, and no evidence of leukemic cells. A cytospin preparation of CSF was very cellular with ependymal cells seen. CSF VDRL, cryptococcal antigen, varicella zoster virus antigen, toxoplasma IgG antibodies, and antinuclear antibodies were all negative. Bacterial, fungal, and mycobacterial cultures of CSF and blood showed no growth. Peripheral blood cytomegalovirus (CMV) culture, Epstein-Barr virus

IgM antibodies, and hepatitis C virus RNA detection by polymerase chain reaction were all negative. The CSF IgG index was elevated (0.90%; normal range, 0.30–0.70%), and oligoclonal gamma globulin bands were detected by CSF electrophoresis. Serum levels of IgG were depressed (502 mg/dL; normal range, 694–1618 mg/dL). MR imaging studies showed abnormal signal intensity and enhancement within the brain stem and cerebellum (Fig 1A–E). Primary differential diagnostic considerations for rhombencephalitis included viral and bacterial infections, particularly herpes simplex, varicella, and CMV; and *Listeria monocytogenes*.

The patient was initially treated with both intravenous acyclovir until serology and cultures ruled out a herpes viral infection, and an infusion of immunoglobulin 400 mg/kg of body weight. Viral cultures of the CSF subsequently grew adenovirus, confirming the diagnosis of viral rhombencephalitis. The patient's symptoms improved during the first week of therapy and almost completely resolved by 14 months, except for mild residual fatigue and ataxia.

## Discussion

Rhombencephalitis is a form of brain stem and cerebellar inflammation that may be life-threatening. It is often difficult to diagnose on the basis of clinical and laboratory findings. The cause is frequently not identified, although viral agents are commonly suspected. *Listeria monocytogenes* and herpes simplex virus are two known causes of rhombencephalitis requiring early treatment to avoid permanent neurologic sequelae (1, 2). Influenza A virus, arbovirus, and herpes zoster encephalitis may also involve the brain stem (3, 4), although any viral encephalitis could result in rhombencephalitis. Bacterial agents such as *Mycobacterium*, *Rickettsia*, *Borrelia burgdorferi*, *Salmonella typhi*, *Legionella bozemanii*, and *Mycoplasma pneumoniae* rarely cause encephalitis but can involve the brain stem (4–7).

Adenoviruses are commonly encountered pathogens, causing respiratory infections, conjunctivitis, pharyngitis, and gastroenteritis in immunocompetent hosts, especially children (8). Some cases of meningoencephalitis have been described. The onset of illness is typically acute and the evolution is usually benign, although severe sequelae and fatalities have been reported. Observations in immunocompetent

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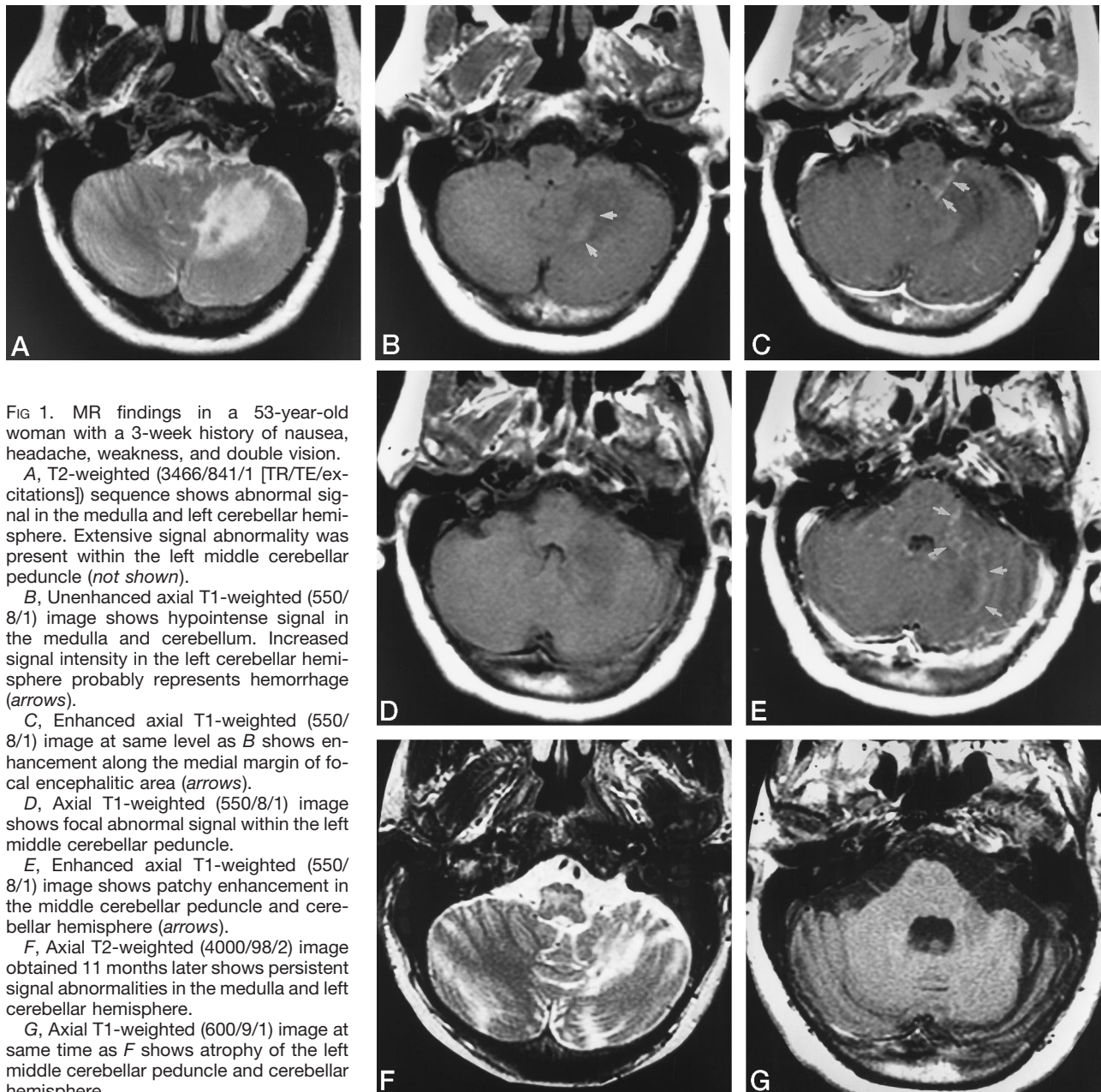


FIG 1. MR findings in a 53-year-old woman with a 3-week history of nausea, headache, weakness, and double vision.

A, T2-weighted (3466/841/1 [TR/TE/excitations]) sequence shows abnormal signal in the medulla and left cerebellar hemisphere. Extensive signal abnormality was present within the left middle cerebellar peduncle (not shown).

B, Unenhanced axial T1-weighted (550/8/1) image shows hypointense signal in the medulla and cerebellum. Increased signal intensity in the left cerebellar hemisphere probably represents hemorrhage (arrows).

C, Enhanced axial T1-weighted (550/8/1) image at same level as B shows enhancement along the medial margin of focal encephalitic area (arrows).

D, Axial T1-weighted (550/8/1) image shows focal abnormal signal within the left middle cerebellar peduncle.

E, Enhanced axial T1-weighted (550/8/1) image shows patchy enhancement in the middle cerebellar peduncle and cerebellar hemisphere (arrows).

F, Axial T2-weighted (4000/98/2) image obtained 11 months later shows persistent signal abnormalities in the medulla and left cerebellar hemisphere.

G, Axial T1-weighted (600/9/1) image at same time as F shows atrophy of the left middle cerebellar peduncle and cerebellar hemisphere.

adults are rare because the adenovirus is common and most adults are immunized. In six well-documented cases of adenovirus meningoencephalitis in immunocompetent adults ranging in age from 19 to 50 years, all but one recovered fully (8, 9). Symptoms included headache, myalgia, anorexia, somnolence, mental alteration, and seizures. The duration of symptoms was 2 to 14 days. In immunosuppressed patients, particularly those having had bone-marrow transplantation, adenovirus infection can be devastating, causing lethal pneumonia, hepatitis, renal failure, and diffuse encephalitis (10). Our literature search uncovered several isolated case reports of meningoencephalitis caused by adenoviruses in normal and immunosuppressed patients (9–17). We found no documented cases of isolated rhombencephalitis caused by adenovirus.

The diagnosis of rhombencephalitis can be difficult to confirm on a clinical basis. A subset of this disease first described by Bickerstaff and Cloake (18) is characterized by ophthalmoplegia, ataxia, and areflexia. Cerebellar ataxia similar to that seen in our patient has been reported in encephalitis caused by adenovirus infection (11). CSF examination in patients with adenovirus encephalitis shows normal to slightly increased opening pressure, reactive pleocytosis, and elevated protein; CSF glucose levels are usually normal. The diagnosis can be confirmed by culturing the virus from CSF or brain tissue or by documenting a fourfold rise in serum-neutralizing antibody titres.

We have found three case reports documenting the pathologic findings in adenovirus. Nonspecific pathologic findings of edema, gliosis, chronic perivascular inflammation, and petechial hemorrhage may be

present (11). Grossly there may be inferomedial temporal and occipital degeneration and hemorrhage. Davis et al (13) reported a case of fatal necrotizing encephalitis involving the inferior colliculi, hypothalamic and several brain stem nuclei, and inferomedial temporal lobes in a bone marrow transplant patient. Anders et al (16) reported a case of encephalitis and widespread ependymitis in a child with AIDS, in whom sloughing of the ependymal lining of the entire ventricular system was found. The presence of ependymal cells in the CSF of our patient may have represented a manifestation of ependymitis, although MR imaging studies did not show abnormal signal or enhancement in the ependyma to suggest inflammation. Other viruses that have an affinity for ependymal surfaces include CMV and the mumps virus.

We found two descriptions of imaging abnormalities associated with adenovirus encephalitis in the literature. Hydrocephalus with periventricular radiolucency and multiple parenchymal hypodensities have been described on CT scans (17). Riikonen (19) reported a child with probable adenovirus encephalitis with necrotic changes resembling herpes encephalitis on CT scans.

The differential diagnosis for infections causing rhombencephalitis includes Legionnaire's disease, mycoplasma infection, Lyme disease, tuberculosis, and viral infections. Acute disseminated encephalomyelitis, multiple sclerosis, sarcoidosis, Behçet disease, and Whipple disease are additional inflammatory processes that can affect the brain stem. Differentiating the causes of rhombencephalitis on the basis of imaging studies can be difficult. When there is evidence of ependymitis on imaging or laboratory studies, adenovirus, CMV, and mumps are the primary diagnostic considerations. In herpes simplex rhombencephalitis, additional signal abnormalities in the frontal and temporal lobes are a common finding. In the absence of temporal and frontal lobe signal abnormalities, other causes of rhombencephalitis, particularly *Listeria monocytogenes*, need to be considered in the differential diagnosis. While a focal tectal mass demonstrating intense enhancement has been described in the literature as a manifestation of viral encephalitis, marked brain stem enlargement and exophytic mass effect are more suggestive of a neoplasm (20). Contrast-enhanced T1-weighted MR images may be helpful in the evaluation of rhombencephalitis. Leptomeningeal and gyriform enhancement can be seen in herpes simplex encephalitis. *Listeria monocytogenes* typically produces patchy enhancement in the pons, medulla, and midbrain (1). Focal abscesses may be seen. Although *Listeria monocytogenes* typically affects immunocompromised persons, it can cause fatal CNS infections in immunocompetent people with no underlying predisposing factors. This organism is difficult to isolate from CSF but is often readily cultured from blood. The CSF in listerial infection typically reveals an increased leukocyte count, usually with predominance of polymorphonuclear cells, increased protein, and normal glucose. Negative blood and CSF cultures in addition to

the presence of a CSF lymphocytic pleocytosis helped to exclude this organism as the offending agent in our patient. Listeriosis, sarcoidosis, Lyme disease, and tuberculosis often cause leptomeningeal enhancement, which may be a distinguishing feature.

## Conclusion

While meningoencephalitis is a rare manifestation of adenovirus infection, it needs to be considered in the differential diagnosis of persons presenting with abnormal CSF and focal neurologic deficits referable to the brain stem, especially those who are immunosuppressed or who have undergone bone marrow transplantation.

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