Generic Contrast Agents

Our portfolio is growing to serve you better. Now you have a *choice*.



Bruton-type (congenital X-linked) agammaglobulinemia: MR imaging of unusual intracranial complications.

\$

FRESENIUS KABI

VIEW CATALOG

E J Lerner and L T Bilaniuk

AJNR Am J Neuroradiol 1992, 13 (3) 976-980 http://www.ajnr.org/content/13/3/976

This information is current as of May 10, 2025.

Bruton-Type (Congenital X-Linked) Agammaglobulinemia: MR Imaging of Unusual Intracranial Complications

Elliot J. Lerner¹ and Larissa T. Bilaniuk²

Summary: The authors describe two patients with Bruton-type agammaglobulinemia, their purpose being to indicate the spectrum of findings, clinical and imaging. MR in one patient revealed diffuse leptomeningeal enhancement in the brain and spine; in the second patient, a heterogeneous mass was seen that had broken through the basiocciput and displaced a cerebellar hemisphere. Awareness of the common and unusual CNS manifestations of this disease can impact clinical management.

Index terms: Brain, infection; Meningoencephalitis; Immune deficiency

Bruton-type (congenital X-linked) agammaglobulinemia (XLA) represents a congenital defect in B-cell development, resulting in a severe paucity of mature B cells and hence profoundly decreased serum immunoglobulin levels (1). The diagnosis is usually reached between the ages of 2 and 4 years on the basis of recurrent, often serious bacterial infections that commonly begin during the first 2 years of life (2). The pathogens most frequently implicated are the common encapsulated organisms such as Haemophilus influenzae and Streptococcus pneumoniae (1, 2). The inability of patients with XLA to handle common infections may lead to a wide spectrum of complications in the head and neck region. Chronic enteroviral infection has also been noted in patients with XLA, one manifestation of which is chronic enteroviral meningoencephalitis (CEME) (3-5). While the syndrome of CEME has been well delineated, the magnetic resonance (MR) appearance warrants description and documentation. We also present the clinical and MR findings in a patient with a chronic desmoplastic, space-occupying neck mass that developed following multiple tympanomastoidectomies and

that extended intracranially. Though no pathogen could ever be demonstrated, we believe that this represents an incomplete host response to a chronic infectious process. These cases are presented to make radiologists and clinicians aware of the wide spectrum of complications associated with XLA that potentially involve the central nervous system (CNS).

Case Reports

Case 1

A 27-year-old man, who carries the diagnosis of XLA, was evaluated in the spring of 1990 for unsteady gait and decreased hearing acuity.

At the age of 18 months, the patient developed recurrent staphylococcal skin infections. At 36 months, he developed a persistent non-bloody diarrhea with vomiting and arthralgias. He was then found to have decreased immunoglobulin levels (IgG level 100 mg/dL (normal range 650–1900 mg/dL); no IgM or IgA) and absent lymphoid tissue (lack of palpable lymph nodes and absent retropharyngeal lymphoid tissue on lateral neck radiographs). At this time, the patient was diagnosed as having XLA and he was treated with oral antibiotics and monthly intramuscular gammaglobulin.

Over the ensuing two decades, the patient had numerous infections, some control over which was achieved with continued intramuscular gammaglobulin.

In mid-February 1990, the patient presented to our institution complaining of several weeks of a gradual onset of imbalance, headaches, and greenish-yellow nasal discharge. An audiogram demonstrated bilateral central sensorineural hearing loss. The patient's gait was unsteady and wide-based. His serum IgG was 419 mg/dL (2 weeks after intravenous therapy). Sinus computed tomography

Received July 3, 1991; accepted and revision requested August 21; revision received December 31.

¹ Neuroradiology Fellow, Department of Radiology, Hospital of the University of Pennsylvania, Philadelphia, PA 19104. Present address: Radiology Associates of Ridgewood, 20 Franklin Turnpike, Walwick, NJ 07463.

² Address reprint requests to Larissa T. Bilaniuk, MD, The Children's Hospital of Philadelphia, 34th Street & Civic Center Boulevard, Philadelphia, PA 19104.

AJNR 13:976-980, May/June 1992 0195-6108/92/1303-0976 © American Society of Neuroradiology



A





B

Fig. 1. Case 1: Enteroviral meningitis demonstrated on brain and spinal T1weighted MR images (600/20/1) following intravenous gadopentatate dimeglumine (0.1 mmol/kg).

C

A, Diffuse meningeal thickening and enhancement.

B, At level of posterior fossa, enhancement is seen in left internal auditory canal (*arrow*) as well as around the temporal lobes and cerebellum.

C, Same region as B, 17 minutes later, shows leakage of gadopentetate into basilar cisterns.

D, Midsagittal image demonstrates thick circumferential contrast enhancement around thoracic cord.

(CT) scans demonstrated bilateral maxillary sinusitis with air-fluid levels. The patient was begun on cetrimoxazole.

MR examination of the spine and brain demonstrated extensive, diffuse leptomeningeal enhancement with evi-

dence of leakage of gadolinium into the subarachnoid spaces on delayed sequences (Fig. 1). Lumbar puncture demonstrated a markedly elevated protein (2867 mg/dL (normal range 16–46 mg/dL)) as well as pleocytosis (white

count $843,000/\mu$ L with 87% polymorphonuclear neutrophils and 11% monocytes). Culture was ultimately positive for enterovirus, identified by the Centers for Disease Control as ECHO-18.

Following intraventricular shunt placement with Ommaya reservoir, gammaglobulin was administered into the ventricular system via the shunt catheter monthly and intravenous gammaglobulin was also administered biweekly.

Case 2

A 26-year-old man had an early childhood characterized by multiple episodes of otitis, sinusitis, pneumonia, and conjunctivitis. At the age of 8 years, immunoelectrophoresis was performed that demonstrated a decreased gammaglobulin level (<100 mg/dL), confirming the clinically suspected diagnosis of XLA. Soon thereafter, the patient was begun on gammaglobulin therapy and there was a resultant decrease in the patient's symptoms, as well as number and severity of infections. However, beginning at age 11, his ear infections became more difficult to treat and required multiple surgical procedures. He eventually developed a left neck mass that periodically would drain "cheesy" white material that was culture negative. By age 19 he had had seven surgical procedures, including opening of multiple fistulous tracts in the neck and a radical left neck dissection which revealed an "abscess" cavity that extended from the base of the mastoid around the carotid artery. All cultures were negative. As the left-sided ear and neck inflammation subsided, the patient began to have intermittent drainage from a 2×2 cm pink, hard nodule behind his right ear. The right neck inflammation became more extensive over the years, despite antibiotic therapy and surgical drainage. Multiple CT and MR scans showed progression of a collection of ring-enhancing right neck masses. Eventually one of the masses was noted to extend through the skull base into the posterior fossa indenting the cerebellum (Fig. 2). All cultures were negative including specialized ones for mycoplasma. Surgery on the right neck at age 24 revealed deep cervical granulations with irregular fragments of cyst tissue. On microscopic exam, there was bland sclerotic fibrous tissue infiltrating the muscle and involving suture material with traumatic neuromas. The skin was heavily infiltrated by mixed inflammatory cells, excluding plasma cells. Whether this represented a bizarre reaction to previous surgery or a primary process could not be determined. The diagnosis was "fibromatosis, soft tissues of the neck" including a "muscle desmoid." The skin was noted to have chronic inflammation. Although the patient has done relatively well clinically since the surgery, he still has evidence of an intracranial lesion on numerous MR scans that have been subsequently performed. The patient also has received several courses of isotretinoin which seems to have decreased the amount of inflammation that he develops.

Of incidental note, the family history was positive in this patient in three generations for six affected male relatives who died of infection in the first 2–3 years of life.

Discussion

In addition to frequent, often serious bacterial infections, patients with XLA, particularly those receiving gammaglobulin prophylaxis, are also prone to develop certain viral infections, most notably those associated with enteroviruses (3-5). While the primary role of cell-mediated immunity against viral infections is generally recognized, the most important antagonist to the enteroviruses (including polioviruses, echoviruses, and Coxsackieviruses A and B) appears to be a neutralizing antibody (4). Hence, patients with XLA, as well as other persons with antibody deficiencies, are particularly prone to develop severe enteroviral infections, such as vaccineassociated paralytic poliomyelitis, as well as CEME.

CEME represents prolonged enteroviral infection of the CNS and is most frequently caused by echoviruses. Patients with CEME typically present with a slowly progressive neurologic syndrome, symptoms of which may include ataxia, headache, decreased cognition, and paresthesias (4). Patients may also have a more acute presentation, with seizures and perhaps fever. Treatment is with exogenous antibodies, though many patients will relapse despite initial improvement (6). Since 1985, the therapy of choice has been intraventricular administration of gammaglobulin, usually via a reservoir (6–9).

The MR appearance in patients with CEME has not been previously reported. As might be expected, there was extensive leptomeningeal enhancement about the convexity and, most prominently, the basilar cisterns extending into the internal auditory canals. In fact, the initial examinations demonstrated actual enhancement of the cerebrospinal fluid spaces themselves on delayed images, suggesting that there was leakage of gadopentetate into the subarachnoid spaces, presumably secondary to the markedly abnormal blood-cerebrospinal fluid barrier. On subsequent imaging studies following placement of an intraventricular (Ommaya) reservoir with intraventricular gammaglobulin therapy, there was some resolution of the meningeal enhance-



ment as well as improvement in the patient's clinical status.

Our second patient presented with clinical and radiologic findings that were even more puzzling. The patient had had recurrent otitis media not responding to medical therapy and requiring surgical treatment that led to soft tissue inflammation in the neck, first on the left, finally requiring radical neck dissection, and then on the right. Following multiple surgical procedures on the middle ear cleft and mastoid sinus for treatment of chronic otitis on the right, the patient developed a chronic, indolent, space-occupying process that eventually extended intracranially into the extradural space of the posterior fossa. Thickened enhancing meninges separated the mass from the cerebellum. Pathologic specimens obtained from this mass on two separate occasions failed to demonstrate any infectious agent or significant histopathologic evidence of acute or chronic inflammation. Rather, the process was felt to be akin to fibromatosis. This entity has not been previously described in association with XLA, and may represent an unusual (deficient) response to a very indolent, low-grade infectious agent. Alternatively, it is possible that because of the multiple courses of antibiotics the patient

Fig. 2. Case 2: Infiltrative mass extending through skull base.

A, Sagittal T1-weighted gradient-echo MR image (330/9/1) demonstrates slightly heterogeneous mass (*arrows*) that has broken through basiocciput and displaces cerebellar hemisphere.

B, Coronal T2-weighted MR image (3000/80/2) shows multilobulated cystic and solid mass with low intensity thickened dura (*black arrow*) and high intensity thickened leptomeninges (*arrowheads*). Soft-tissue intensity material within right transverse sinus (*white arrow*) consistent with thrombosis.

C, Axial T1-weighted MR image (800/ 30/2) following gadopentetate shows enhancement of mass and adjacent leptomeninges (*arrow*). Subtle pial enhancement is present in cerebellum.

D, Axial T1-weighted MR image (800/ 30) following gadopentetate dimeglumine shows infiltrative enhancing upper cervical component of the mass (*arrows*) with central, more defined cavitary masses (*arrowheads*).

received, the infection was partially treated and, consequently, cultures remained negative. MR imaging in this patient was useful for surgical planning and to supplement clinical findings in follow-up evaluation.

Infections are the most common presenting feature of patients with XLA and the upper respiratory tract is the most frequent site. Otitis media is the most frequent infection, followed by sinusitis, conjunctivitis, and mastoiditis (1). The infection may be caused by unusual organisms, may spread into adjacent structures invading nerves and vessels, and may cause abscesses and meningitis. In a child that has severe chronic or recurrent ear infections that do not respond to conventional treatment and coexist with paranasal, pulmonary, and/or gastrointestinal infections, a diagnosis of XLA should be excluded.

Conclusion

XLA may have protean manifestations, some of which can involve the intracranial space. It behooves the radiologist to be aware both of the more common and unusual complications involving the CNS, as these may significantly impact upon the patient's clinical management.

References

- Lederman HM, Winkelstein JA. X-linked agammaglobulinemia: an analysis of 96 patients. *Medicine (Baltimore)* 1985;4:145–156
- Goddard EA, Beatty DW. X-linked agammaglobulinemia. S Afr Med J 1989;76:605–607
- Wilfert CM, Buckley RH, Mohammakumar T, et al. Persistent and fatal central nervous system echovirus infections in patients with agammaglobulinemia. N Engl J Med 1977;296:1485–1489
- McKinney RE Jr, Katz SL, Wilfert CM. Chronic enteroviral meningoencephalitis in agammaglobulinemic patients. *Rev Infect Dis* 1987;9:334–356
- 5. Prentice RL, Dalgleish AG, Gatenby PA, et al. Central nervous system echovirus infection in Bruton's X-linked hypogammaglobulinemia.

Aust N Z J Med 1985;15:443-445

- Robertson DM, Jack I, Joshi W, et al. Failure of intraventricular gammaglobulin and alpha interferon for persistent encephalitis in congenital hypogammaglobulinemia. *Arch Dis Child* 1988;63:948– 952
- Erlendsson K, Swartz T, Dwyer JM. Successful reversal of echovirus encephalitis in X-linked hypogammaglobulinemia by intraventricular administration of immunoglobulin. N Engl J Med 1985;312:351–353
- Hadfield MG, Seidlin M, Houff SA, et al. Echovirus meningomyeloencephalitis with administration of intrathecal immunoglobulin. J Neuropathol Exp Neurol 1985;44:520–529
- Dwyer JM, Erlendsson K. Intraventricular gammaglobulin for the management of enterovirus encephalitis. *Pediatr Infect Dis J* 1988;7:S30–S33