Imaging of Dentate Nucleus Pathologies: A Case Series

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Abstract

The dentate nucleus is the largest cerebellar nucleus, and it controls cognition and voluntary movement. It is found in each cerebellar hemisphere medially and posterolateral to the lateral ventricle. Pathologies of the dentate nucleus can be detected using computed tomography and magnetic resonance imaging of the brain. Here, we present a case series of seven different dentate nucleus diseases and their neuroimaging findings recovered from archives of our institution.

Keywords

► computed tomography
► dentate nucleus
► magnetic resonance imaging

Introduction

The largest and the most lateral of the four deep cerebellar nuclei is the dentate nucleus, located next to the vermis and posterolateral to the fourth ventricle.1 The dentate nucleus is a component of the cerebro-cerebellar circuitry, which relays information to the cortical and subcortical structures.1 It has domains for both motor and non-motor functions and is involved in motor movement planning and execution, cognition, and visuospatial sensory processing.1 The dentate nucleus can be affected by a variety of pathologies. Its involvement in imaging can be isolated or associated with lesions in other supra and/or infratentorial structures; thus, imaging aids in the formulation of differential diagnoses. Furthermore, lesions in the dentate nucleus may determine hypertrophic olivary degeneration and other transtaxial degenerations.2 This article reviews several possible causes of dentate nucleus lesions based on the neuroimaging studies recovered from the archives of our institution.

Cases’ Presentations

Case 1

Clinical Picture

A 54-year-old man was on regular peritoneal dialysis for end-stage renal disease (ESRD). He was diagnosed to have pulmonary tuberculosis (PTB) and was started on a four-drug antitubercular medication regimen that included isoniazid, rifampicin, pyrazinamide, and ethambutol. After 2 weeks, he developed symptoms of confusion, dysarthria, and gait imbalance as well as signs of bilateral horizontal gaze-evoked nystagmus, dysmetria and past-pointing in all limbs, and ataxic gait.

Imaging Findings

In magnetic resonance imaging (MRI) of the brain, T2-weighted imaging (WI) revealed symmetric hyperintensity involving the cerebellum’s bilateral dentate nuclei (►Fig. 1A). There was no diffusion restriction on diffusion-
weighted imaging (DWI)/apparent diffusion coefficient (ADC) mapping and there was no blooming on susceptibility weighted imaging (SWI) (image not shown). The rest of the brain parenchyma, including the midbrain and thalamus, was normal (►Table 1). After a provisional diagnosis of isoniazid (INH) toxicity, the drug was discontinued.

Discussion
After 4 weeks, the patient’s symptoms typically resolved. INH toxicity is caused by a lack of energy and a deficiency of vitamin B complex. Pyridoxal 5-phosphate synthesis is reduced, which is required for gamma-aminobutyric acid (GABA) neurotransmission. GABA is an inhibitory neurotransmitter that induces cerebellar symptoms when it is in the central nervous system.\(^3\)

Diagnosis
Isoniazid-induced encephalopathy and cerebellitis in a patient with ESRD and PTB manifested as symmetrical dentate nuclei hyperintensities on both sides, which resolved once the drug was stopped.

Case 2
Clinical Picture
A 28-year-old man underwent surgical hemorrhoidectomy. Since then, he has been taking ornidazole on a daily basis. After 3 months, he experienced new-onset symptoms of confusion, vertigo, and gait imbalance. He did not have seizures or peripheral neuropathy. His vitals and systemic examination were normal. The Glasgow Coma Scale (GCS) score was 13/15 (eye 3, motor 6, and verbal 4). Neurological examination revealed dysarthria, bilateral horizontal gaze-evoked nystagmus, impaired finger–nose test in all limbs, and ataxic gait.

Imaging Findings
MRI brain T2 WI showed symmetric hyperintensity involving bilateral dentate nuclei (►Fig. 1B). There was no diffusion restriction on DWI and ADC mapping and there was no blooming on SWI imaging (image not shown). The rest of the brain parenchyma including the supratentorial white matter, corpus callosum, and midbrain, was normal. (►Table 1). Ornidazole was withdrawn, and the patient showed typical clinical improvement and resolution of lesions on MRI.

Discussion
Ornidazole toxicity is primarily caused by mitochondrial dysfunction, free-radical damage, and impairment of GABAergic neurotransmission in the cerebellum and brainstem, which results in cytotoxic edema and localized axonal swelling.\(^4\)

Diagnosis
Ornidazole toxicity manifested itself as encephalopathy, cerebellitis, and bilateral dentate nucleus hyperintensities, all of which disappeared once the drug was stopped.

Case 3
Clinical Picture
A 39-year-old woman had a short-duration fever 15 days ago and recovered spontaneously. She had not received any vaccines and had not experienced any infections requiring treatment recently. She had abrupt onset drowsiness and was unable to stand or walk on her own. Her vitals and systemic examination findings were normal. The GCS score was 13/15 (eye 3, motor 5, and verbal 4). On neurological evaluation, she was disoriented to time, place, and person. She also had dysarthria and horizontal nystagmus and was uncooperative for the rest of the examination.

Imaging Findings
MRI brain fluid-attenuated inversion recovery (FLAIR) sequence revealed hyperintensity in the bilateral dentate nuclei, cerebellum, middle cerebellar peduncles, pons (►Fig. 1C), and supratentorial white matter (bilateral corona radiata, centrum semiovale, sub-cortical white matter of bilateral frontal, and temporal lobes). However, there was no diffusion restriction, blooming, or post-contrast enhancement in the corresponding areas. Bilateral thalami and the rest of the brain were normal (images not shown) (►Table 1).
<table>
<thead>
<tr>
<th>Case</th>
<th>Diagnosis</th>
<th>Presentation</th>
<th>Dentate/cerebellum</th>
<th>Medulla</th>
<th>Other areas $^a$</th>
<th>Midbrain/Thalamus</th>
<th>WM</th>
<th>DR</th>
<th>SWI</th>
<th>MRI resolution</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Isoniazid toxicity</td>
<td>Encephalopathy and ataxia</td>
<td>Y</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>4 wk</td>
</tr>
<tr>
<td>2</td>
<td>Ornidazole toxicity</td>
<td>Encephalopathy and ataxia</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>4 wk</td>
</tr>
<tr>
<td>3</td>
<td>ADEM</td>
<td>Acute disseminated encephalomyelitis</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>12 wk</td>
</tr>
<tr>
<td>4</td>
<td>CTX</td>
<td>Childhood cerebral Xanthomatosis</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>Data not available</td>
</tr>
<tr>
<td>5</td>
<td>NF1</td>
<td>Neurofibromatosis Type 1</td>
<td>Y</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>12 wk</td>
</tr>
<tr>
<td>6</td>
<td>Primary hypothyroidism</td>
<td>Seizures</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>No resolution</td>
</tr>
<tr>
<td>7</td>
<td>CLIPPERS</td>
<td>Headache, vomiting, dysequilibrium, and ataxia</td>
<td>Y</td>
<td>Y</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>–</td>
<td>No resolution</td>
</tr>
</tbody>
</table>

Abbreviations: ADEM, acute disseminated encephalomyelitis; BG, basal ganglia; CC, corpus callosum; CTX, cerebroside Xanthomatosis; CLIPPERS, chronic lymphocytic inflammation with pontine perivascular enhancement sensitive to steroids; CSO, centrum semiovale; DR, diffusion restriction; IC, internal capsule; MCP, middle cerebellar peduncle; MRI, magnetic resonance imaging; NF1, neurofibromatosis type 1; SWI, susceptibility weighted imaging; WM, white matter. $^a$: Other areas likely involved in each disease.
Discussion
Acute disseminated encephalomyelitis (ADEM) was the pre-
liminary diagnosis. She was treated with a 1 g/day dose of
methylprednisolone for 5 days and was switched to oral
prednisolone, 40 mg/day, which was slowly tapered over a
period of 3 months and discontinued. After 3 months, the
patient’s symptoms improved significantly, and the lesions
resolved on MRI. Okumura et al reported a case study of two
patients with ADEM and severe brain involvement, including
dentate nuclei.5

Diagnosis
Diffuse brain including bilateral dentate nuclei hyperinten-
sities in a patient with ADEM.

Case 4
Clinical Picture
A 47-year-old woman experienced symptoms of progressive
unsteadiness and abnormal behavior over the past 9 years.
As a toddler, she had suffered from severe diarrhea and later
developed juvenile cataracts. During systemic and neuro-
logical evaluation, she was found to have multiple xan-
thomas, impaired cognition, horizontal gaze-evoked
nystagmus, dysmetria and past-pointing in all four limbs,
and ataxic gait. Her younger sister is afflicted with the same
condition.

Imaging Findings
An MRI brain T2 sequence revealed symmetric hyperinten-
sity in the bilateral dentate nucleus (►Fig. 1D), inferior olive,
cerebellar hemisphere, posterior limb of internal capsule,
and parieto-occipital deep white matter (images not shown).
Nonetheless, there was no diffusion restriction, blooming, or
contrast enhancement in these hyperintensities. The rest of
the brain including globus pallidus and substantia nigra was
normal (►Table 1). MRI orbit T1/T2 WI showed the presence
of a hypointense lesion in the lower eyelid, which was
suggestive of xanthoma.

Discussion
The presence of chronic diarrhea, juvenile cataracts, tendon
xanthomas, progressive cerebellar ataxia, and cognitive de-
cline suggested cerebrotendinous xanthomatosis (CTX). Pud-
hiavan et al. reported similar clinical and imaging
findings in CTX in his case report.6

Diagnosis
CTX

Case 5
Clinical Picture
A 5-year-old girl had multiple café-au-lait spots and a few
neurofibromas. She was diagnosed with neurofibromatosis
type 1 (NF1) based on its diagnostic criteria. Her neurological
evaluation was unremarkable.

Imaging Findings
MRI brain T2WI/FLAIR revealed hyperintensities in the bilat-
eral dentate nuclei and left middle cerebellar peduncle
without diffusion restriction. There was no blooming on SWI and there was no post-contrast enhance-
ment. The rest of the brain was normal (►Table 1). There
were no other NF1 features, either clinically or on
brain/whole spine imaging

Discussion
Takashi Itoh described a range of imaging abnormalities in
NF1. The lesions primarily affect the cerebellar hemisphere
and the dentate nucleus in the first decade and never after
the third decade.7

Diagnosis
Bilateral dentate nucleus hyperintensities were identified on
screening brain/spine MRI in a patient with NF1.

Case 6
Clinical Picture
A 36-year-old woman receiving regular treatment for pri-
mary hypoparathyroidism experienced hypocalcemia symp-
toms as well as multiple generalized tonic-clonic seizures.
Trousseau’s and Chvostek’s signs were both present. The
neurological exam was unremarkable.
Imaging Findings
The 36-year-old woman’s CT brain showed hyperdense signal in the bilateral dentate nuclei, cerebellar hemispheres (Fig. 2B), basal ganglia, and supratentorial white matter (Fig. 2C). These imaging findings were suggestive of calcification (Table 1).

Discussion
Primary hypoparathyroidism is a well-known cause of metabolic intracranial brain calcifications.

Diagnosis
A patient with primary hypoparathyroidism and seizure disorder had pathological intracranial calcification involving the diffuse brain parenchyma and including the bilateral dentate nuclei.

Case 7
Clinical Picture
A 23-year-old man had suffered from severe headache and vomiting for 4 weeks. He also experienced a slight unsteadiness while walking. Neurological evaluation revealed bilateral gaze-evoked nystagmus, pyramidal signs in the form of generalized spasticity, hyperreflexia, and bilateral extensor planter response and cerebellar signs in the form of dysmetria and past-pointing involving all the limbs and gait ataxia.

Imaging Findings
On MRI brain plain and post-contrast imaging, T2WI/FLAIR showed symmetric hyperintensity in the dentate nucleus, middle cerebellar peduncle, pons (Fig. 2D), and midbrain without any diffusion restriction on DWI/ADC mapping. Furthermore, the pons and midbrain showed diffuse punctate nodular enhancement. On SWI, there were multiple punctate areas of blooming in the pons (images not shown) (Table 1).

Discussion
The patient responded to intravenous methylprednisolone 1 g/day for 5 days. A follow-up MRI performed after 4 weeks showed near-complete resolution. He was diagnosed with chronic lymphocytic inflammation with pontine perivascular enhancement sensitive to steroids (CLIPPERS) based on imaging characteristics and steroid responsiveness.

Diagnosis
CLIPPERS.

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