Skeletal and Brain Abnormalities in Fucosidosis, a Rare Lysosomal Storage Disorder

Camille Malatt1*, Jeffrey L. Koning2, John Naheedy2,3

1. University of California San Diego School of Medicine, La Jolla, California, USA
2. University of California San Diego, Department of Radiology, San Diego, California, USA
3. Rady Children’s Hospital, Department of Radiology, San Diego, California, USA

* Correspondence: Camille Malatt, UCSD School of Medicine, 9500 Gilman Drive San Diego, CA 92093, USA (cmalatt@ucsd.edu)

ABSTRACT

Fucosidosis is a rare genetic lysosomal storage disorder caused by a deficiency in alpha-L-fucosidase. We present a case of a 4-year, 11-month-old girl with developmental delay, as well as skeletal and brain abnormalities as shown on X-ray and MRI. Her spinal X-rays demonstrated lumbar kyphosis and anterior beaking of lumbar vertebral bodies. Lower iliac segment constriction, increased angulation of the acetabular roof, and widening of the ribs were apparent on abdominal X-ray. Her brain MRI illustrated symmetric T1 hyperintensity and T2 hypointensity of the bilateral globi pallidi. The case report highlights clinical and imaging findings of this rare disease.

CASE REPORT

A 4-year, 11-month-old girl presented to the neurology clinic in July 2013 with a history of developmental delay, and abnormal spinal and brain imaging from years prior. She had not been speaking, and did not seem interested in socially interacting with other children. Her mother, as well as other physicians that had seen her previously, thought that she might not be hearing normally. Her mother also noticed that she was falling quite frequently. On physical exam she had a slightly coarse facial appearance. Additionally she had poor language output and comprehension, which demonstrated her delayed language development. She had mildly increased lower extremity tone with hyperreflexia in the lower extremities. Her gait appeared mildly spastic with plantar flexion and intoeing, and she was prone to stumbling.

Imaging Findings

Previously she had been seen by the orthopedic clinic in February 2010 for a lumbar spine deformity, and a spinal X-ray revealed focal kyphosis at L1 and anterior beaking of the vertebral bodies at L1 through L4 (fig 1a). A spinal MRI in April 2010 showed similar findings (fig 1b). She was also diagnosed with bilateral conductive hearing loss and chronic serous otitis media in May 2011.

Furthermore, she had a brain MRI in January 2012 ordered by the neurology clinic to investigate her hypotonia and developmental delay. The MRI showed symmetric T1 hyperintensity (fig 2a) and T2 hypointensity (fig 2b, 3a, and 3b) of the bilateral globi pallidi with delayed myelination and at least a mild to moderate decrease in cerebral white matter volume. There were no inner ear abnormalities on imaging.

In response to her visit in July 2013, an X-ray performed in August 2013 additionally noted progressive anterior beaking and gibbus deformity at the level of L1, with hypoplasia of the anterior aspect of the superior endplate (fig 4a and 4b). In the pelvis, the lower iliac segment was constricted and there was a steep acetabular roof, with an
alpha angle of approximately 55 bilaterally (fig 5). There was mild proximal pointing of the metacarpals, and carpal ossification centers were delayed, small, and slightly irregular (fig 6).

**Management & Follow-up**

She returned for follow up in November 2013. Her mother stated that she was "walking crookedly" and continued not to speak any words; however, she did show communicative intent, including points and jabbars. Her comprehension was still minimal, and overall there was minimal improvement if at all in her development. Her physical exam demonstrated similar findings to the previous visit, with hyperreflexia now in her upper extremities as well, downgoing toes, and an increasingly spastic gait with stiffness, circumduction, and intoeing. Her mother observed noisy breathing and snoring. In addition, her short stature was noted with weight and height within the bottom 10th percentile, as well as asymmetric mild-moderate sensorineural hearing loss and Eustachian tube dysfunction. Kyphosis or gibbus was seen centered at the thoracolumbar junction with anterior beaking of several lumbar vertebrae.

Subsequent lysosomal enzyme testing revealed results consistent with fucosidosis, and the parent samples showed carrier status. She likely has type II due to onset in early childhood. She was referred to the metabolic clinic, and her family was referred to a genetic counselor to discuss future family planning. Her only treatment was to continue thoracolumbosacral orthosis with a full-time brace.

---

**DISCUSSION**

**Etiology & Epidemiology**

Fucosidosis is a rare lysosomal storage disorder caused by a deficiency in alpha-L-fucosidase. This results in an accumulation of fucose-rich glycoproteins, glycolipids, and mucopolysaccharides within lysosomes in organs such as the liver, spleen, kidney, heart, brain, peripheral nerves, and skin [1]. There have been fewer than 100 cases reported worldwide [2]. However, there is a comparatively high incidence in people of Italian descent and in the Mexican-Indian populations of New Mexico and Colorado. Family history is the only known risk factor. The disease is autosomal recessive and mutations in the alpha-L-fucosidase gene, FUC1, have been identified, but specific mutations have not been found to be associated with any particular phenotype. Despite its pattern of inheritance, a review of 77 reported patients had a male:female ratio of 1.75:1 [3].

**Clinical & Imaging Findings**

The clinical presentation includes progressive mental and motor deterioration, coarse, dysmorphic facies, growth retardation, recurrent infections, dysostosis multiplex, angiokeratoma corporis diffusum, visceralmegaly, seizures, and hearing loss [3]. Although there is a spectrum of disease presentation, fucosidosis has typically been categorized into two main types. Type I presents initially in early infancy, and there is a rapid progression of neurologic deterioration that leads to a decerebrate state and early death. Type II has a later onset in infancy, and survival is longer. [1,3].

Neuropathological studies show prominent neuronal loss in gray matter structures, particularly in the thalamus, hypothalamus, cerebellar cortex, Purkinje cells, and dentate nucleus. Nerve cell bodies are distended with unusual lamellated fibrogranular intracellular inclusion bodies as a result of glycolipid accumulation. There is also prominent white matter demyelination [1].

Radiological studies show dysostosis multiplex, especially affecting the spine, pelvis, epiphyses of long tubular bones, metacarpals, and skull. There is flattening and anterior beaking of the lower thoracic and lumbar vertebrae, and there also may be kyphosis or scoliosis. In addition, the diaphysis of long bones are widened, scalloped, and sclerotic; iliac bones show acetabular widening and flare. There may be skull thickening and poorly developed sinuses as well. Overall, patients display delayed skeletal maturation and osteoporosis [1,3,4].

Cranial imaging with CT demonstrates diffuse and severe atrophy of the cerebrum and cerebellum. There are bilateral low-attenuation regions localized in the corona radiata, globi pallidi, and internal medullary laminae of the thalami, reaching up to the subcortical white matter [1,5]. MRI shows prominent and progressive changes in white matter signal intensity, including corpus medullare, periventricular, lobar, and subcortical supratentorial areas, internal and external capsules, internal medullary laminae of the thalami, putamina, and both hypothalami. The globi pallidi and substantia nigra have high signal intensity on T1 and low signal intensity on T2 and FLAIR [5, 6].

**Treatment & Prognosis**

Patients with Type I typically progress quickly to death by 5 years of age. Two-thirds of patients with Type II survive into the 2nd decade, and rarely survive past 30 years of age [1,3]. There is currently no effective treatment [1,3].

**Differential Diagnoses**

The differential diagnosis should include other lysosomal storage diseases: alpha and beta-mannosidosis, aspartylglucosaminuria, mucopolysaccharidoses I and II, Fabry syndrome, and neuronal ceroid lipofuscinosis.

Radiograph findings in alpha-mannosidosis include mild- to-moderate dysostosis multiplex, thickened calvarium, ovoid configuration, flattening, and hook-shaped deformity of the vertebral bodies, hypoplasia of the inferior portions of the ilia, mild expansion of short tubular bones of the hands, and genu valgum. On MRI, sagittal T1 and axial T2 weighted images show a partially empty sella turcica, cerebellar atrophy, white matter signal modifications, brachycephaly, thick calvarium, and poor pneumatization of the sphenoid sinus [7]. Findings on MRI in beta-mannosidosis are limited to brain atrophy without white matter changes [8].

In aspartylglucosaminuria, T2 weighted images show increased signal intensity of white matter, with many focal areas of very high signal intensity in the subcortical white
mature, and poor differentiation between gray and white matter [9].

Radiograph findings in mucopolysaccharidosis I are dysostosis multiplex, thoracolumbar gibbus, oar-shaped ribs, thickened clavicles, coxa valga, J-shaped sella turcica, genu valgum, abnormal dens, and atlantoaxial subluxation. On MRI, T2 images show brain atrophy, thickened meninges, patchy white matter changes, multiple perivascular spaces, hydrocephalus, and cervical cord compression [10]. CT shows low-attenuation white matter areas, ventricular and subarachnoid space dilation [11].

Mucopolysaccharidosis II has similar findings [10].

Fabry syndrome demonstrates nonspecific asymmetric, widespread deep white-matter nodules that are hyperintense on T2 and FLAIR, sometimes with equal proportion of grey and white matter involvement, hyperintensity of deep gray nuclei, especially the lateral pulvinar on T1, left ventricular hypertrophy, renal cysts, and decreased corticomedullary differentiation in the kidney. CT reveals structural cardiac valve abnormalities and renal cysts [12].

CT and MRI in neuronal ceroid lipofuscinosis demonstrate diffuse atrophy of both grey and white matter without a disorder of myelination. There is a hypointense signal of grey matter and hyperintense signal of white matter on T2 weighted images [13].

TEACHING POINT

Fucosidosis is a rare genetic lysosomal storage disorder caused by a deficiency in alpha-L-fucosidase, resulting in skeletal abnormalities and progressive neurological deterioration. Imaging findings include dysostosis multiplex and flattening and anterior beaking of the lower thoracolumbar vertebrae on radiograph, cerebral and cerebellar atrophy and low-attenuation regions (such as the corona radiata and globi pallidi) on CT, and globi pallidi and substantia nigra with high signal intensity on T1-MRI and low signal intensity on T2-MRI.

REFERENCES


Figure 1: 1 year 6 months old female with new kyphosis on physical exam, and fucosidosis subsequently confirmed by laboratory testing. FINDINGS: 1a - Lateral radiograph of the spine demonstrates anterior beaking and focal kyphosis at L1 (white arrow) also with anterior beaking of L2-4. 1b - Sagittal T2 MRI of the lumbar spine for comparison, with anterior beaking of L1 (white arrow). TECHNIQUE: Radiography, Sagittal 1.5T T2W MRI (TR 4717 TE 107)
Figure 2: 3 year old female with global developmental delay, and fucosidosis subsequently confirmed by laboratory testing. FINDINGS: 2a - Axial T1 weighted MR of the brain demonstrating symmetric hyperintensity in the globi pallidi (white arrows). 2b - Axial T2 weighted MR of the brain demonstrating symmetric hypointensity in the bilateral globi pallidi with streak hyperintensity delineating the medial and lateral pallidal segments. TECHNIQUE: Axial 1.5T T1W MRI (TR 350 TE 12), Axial T2W MRI (TR 4778 TE 103)

Figure 3: 3 year old female with global developmental delay, and fucosidosis subsequently confirmed by laboratory testing. FINDINGS: 3a - Axial FLAIR MR of the brain demonstrating symmetric hypointensity in the globi pallidi (white arrows). 3b - Coronal FLAIR MR of the brain demonstrating symmetric hypointensity in the bilateral globi pallidi with streak hyperintensity delineating the medial and lateral pallidal segments. TECHNIQUE: Axial and Coronal FLAIR MRI (TR 6200 TE 128)
Figure 4: Follow up kyphosis at 4 years 5 months old, and fucosidosis subsequently confirmed by laboratory testing.

FINDINGS: 4a - Lateral radiograph of the spine demonstrates progressive anterior beaking and focal kyphosis at L1 (white arrow), also with anterior beaking of L2-4 and hypoplasia of the anterior aspect of the superior endplate. 4b - Sagittal T2 MRI of the lumbar spine for comparison, with progressive anterior beaking of L1 compared to prior (white arrow). TECHNIQUE: Radiography, Sagittal 1.5T T2W MRI (TR 4717 TE 107)
Figure 5 (left): 5 year old female with history of hypotonia, and fucosidosis subsequently confirmed by laboratory testing. FINDINGS: Frontal radiograph of the pelvis demonstrates a constricted lower iliac segment and a steep acetabular roof, with an alpha angle of approximately 55 bilaterally (white arrows). TECHNIQUE: Radiography

Figure 6: 5 year old female with history of hypotonia, and fucosidosis subsequently confirmed by laboratory testing. FINDINGS: Frontal radiographs of both hands demonstrate mild proximal pointing of the metacarpals (white arrows). Carpal ossification centers are delayed, small, and slightly irregular (yellow arrows). TECHNIQUE: Radiography
### Table 1: Differential diagnosis table for fucosidosis.

<table>
<thead>
<tr>
<th>Lysosomal storage disease</th>
<th>Radiograph Findings</th>
<th>MRI Findings</th>
<th>CT Findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fucosidosis</td>
<td>- Dyostosis multiplex&lt;br&gt;- Flattening and anterior beaking of the lower thoracic and lumbar vertebrae&lt;br&gt;- Kyphosis or scoliosis&lt;br&gt;- The diaphysis of long bones are widened, scalloped, and sclerotic&lt;br&gt;- Iliac bones show acetabular widening and flaring&lt;br&gt;- Skull thickening and poorly developed sinuses&lt;br&gt;- Delayed skeletal maturation and osteoporosis</td>
<td>- Prominent and progressive changes in white matter signal intensity, including corpus medullare, periventricular, lobar, and subcortical supratentorial areas, internal and external capsules, and internal medullary laminae of the thalami&lt;br&gt;- The globi pallidi and substantia nigra have high signal intensity on T1 and low signal intensity on T2 and FLAIR</td>
<td>- Diffuse and severe atrophy of the cerebrum and cerebellum&lt;br&gt;- Bilateral low-attenuation regions focalized in the corona radiata, globi pallidi, and internal medullary laminae of the thalami, reaching up to the subcortical white matter</td>
</tr>
<tr>
<td>Alpha-mannosidosis</td>
<td>- Mild-to-moderate dyostosis multiplex&lt;br&gt;- Thickened calvarium&lt;br&gt;- Ovoid configuration, flattening, and hook-shaped deformity of the vertebral bodies&lt;br&gt;- Hypoplasia of the inferior portions of the ilia&lt;br&gt;- Mild expansion of short tubular bones of the hands&lt;br&gt;- Genu valgum</td>
<td>Sagittal T1 and axial T2 sections show:&lt;br&gt;- Partially empty sella turcica&lt;br&gt;- Cerebellar atrophy&lt;br&gt;- White matter signal modifications&lt;br&gt;- Brachycephaly&lt;br&gt;- Thick calvarium&lt;br&gt;- Poor pneumatization of the sphenoid body</td>
<td>- Brain atrophy&lt;br&gt;- without white matter changes has been described</td>
</tr>
<tr>
<td>Beta-mannosidosis</td>
<td>- Dyostosis multiplex&lt;br&gt;- Thoracolumbar gibbus&lt;br&gt;- Oar-shaped ribs&lt;br&gt;- Thickened clavicles&lt;br&gt;- Coxa valga&lt;br&gt;- J-shaped sella turcica&lt;br&gt;- Genu valgum&lt;br&gt;- Abnormal dens&lt;br&gt;- Atlantoaxial subluxation</td>
<td>T2 images show:&lt;br&gt;- Increased signal intensity of white matter, with many focal areas of very high signal intensity in the subcortical white matter&lt;br&gt;- Poor differentiation between gray and white matter</td>
<td>- Low-attenuation white matter areas&lt;br&gt;- Ventricular and subarachnoid space dilation</td>
</tr>
<tr>
<td>Mucopolysaccharidosis 1 (Hurler syndrome)</td>
<td>- Dyostosis multiplex&lt;br&gt;- Thoracolumbar gibbus&lt;br&gt;- Oar-shaped ribs&lt;br&gt;- Thickened clavicles&lt;br&gt;- Coxa valga&lt;br&gt;- J-shaped sella turcica&lt;br&gt;- Genu valgum&lt;br&gt;- Abnormal dens&lt;br&gt;- Atlantoaxial subluxation</td>
<td>T2 images show:&lt;br&gt;- Brain atrophy&lt;br&gt;- Thickened meninges&lt;br&gt;- Patchy white matter changes&lt;br&gt;- Multiple perivascular spaces&lt;br&gt;- Hydrocephalus&lt;br&gt;- Cervical cord compression</td>
<td>- Similar to MPS I&lt;br&gt;- Similar to MPS I</td>
</tr>
<tr>
<td>Mucopolysaccharidosis 2 (Hunter syndrome)</td>
<td>- Dyostosis&lt;br&gt;- multiplex, similar to MPS I</td>
<td>- Similar to MPS I</td>
<td></td>
</tr>
<tr>
<td>Fabry syndrome</td>
<td>- Nonspecific asymmetric, widespread deep white-matter nodules that are hyperintense on T2 and FLAIR&lt;br&gt;- Sometimes equal proportion of grey and white matter involvement&lt;br&gt;- Hyperintensity of deep gray nuclei, especially the lateral pulvinar on T1&lt;br&gt;- Left ventricular hypertrophy&lt;br&gt;- Renal cysts&lt;br&gt;- Decreased corticomedullary differentiation in the kidney</td>
<td>- Structural cardiac valve abnormalities&lt;br&gt;- Renal cysts</td>
<td></td>
</tr>
<tr>
<td>Neuronal ceroid lipofuscinosis</td>
<td>-</td>
<td>- Diffuse atrophy of both grey and white matter&lt;br&gt;- Hypointensity of grey matter and hyperintensity of white matter on T2</td>
<td>- Diffuse atrophy of both grey and white matter</td>
</tr>
</tbody>
</table>
Skeletal and Brain Abnormalities in Fucosidosis, a Rare Lysosomal Storage Disorder

**Table 2: Summary table of fucosidosis.**

<table>
<thead>
<tr>
<th>Findings on Imaging</th>
<th>Radiograph:</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>- Dysostosis multiplex</td>
</tr>
<tr>
<td></td>
<td>- Flattening and anterior beaking of the lower thoracic and lumbar vertebrae</td>
</tr>
<tr>
<td></td>
<td>- Kyphosis or scoliosis</td>
</tr>
<tr>
<td></td>
<td>- Diaphysis of long bones are widened, scalloped, and sclerotic</td>
</tr>
<tr>
<td></td>
<td>- Iliac bones show acetabular widening and flaring</td>
</tr>
<tr>
<td></td>
<td>- Skull thickening and poorly developed sinuses</td>
</tr>
<tr>
<td></td>
<td>- Delayed skeletal maturation and osteoporosis</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Craniol CT:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Diffuse and severe atrophy of the cerebrum and cerebellum</td>
</tr>
<tr>
<td>- Bilateral low-attenuation regions focalized in the corona radiata, globi pallidi, and internal medullary laminae of the thalami, reaching up to the subcortical white matter</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>MR:</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Prominent and progressive changes in white matter signal intensity, including corpus medullare, periventricular, lobar, and subcortical supratentorial areas, internal and external capsules, and internal medullary laminae of the thalami</td>
</tr>
<tr>
<td>- The globi pallidi and substantia nigra have high signal intensity on T1 and low signal intensity on T2 and FLAIR</td>
</tr>
</tbody>
</table>

**ABBREVIATIONS**

CT: computed tomography  
FLAIR: fluid attenuated inversion recovery  
MRI: magnetic resonance imaging

**KEYWORDS**

Fucosidosis; lysosomal storage disorder; radiography; skeletal; brain; CT; MRI

---

**Online access**  
This publication is online available at:  

**Peer discussion**  
Discuss this manuscript in our protected discussion forum at:  
www.radiolopolis.com/Forums/JRCR

**Interactivity**  
This publication is available as an interactive article with scroll, window/level, magnify and more features.  
Available online at www.RadiologyCases.com

Published by EduRad  
www.EduRad.org