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TEST YOURSELF: ANSWER

# 4-year-old boy referring for diffuse joint stiffness and progressive bilateral visual impairment

Vinh Dat-Minh Le[1] · Paolo Simoni[1]

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## Answer

**Diagnosis**: Mucopolysaccharidosis VI

## Discussion

Mucopolysaccharidosis VI (MPS VI also known as Maroteaux–Lamy syndrome) is a rare autosomal recessive inherited disease [1]. The reported incidence ranges from 1/238,095 to 1/1,300,000 newborns without ethnical prevalence [2]. Males and females are equally affected [1]. MPS VI is due to a complete or partial deficiency of arylsulfatase B enzyme (ARSB), also known as *N*-acetylgalactosamine-4-sulfatase. ARSB is involved in the glycosaminoglycans (GAGs) catabolism [1].

A deficiency of ARSB leads to the accumulation of GAGs into the lysosome of multiple organs, including central nervous system, arterial walls, blood, bone marrow, skeleton, eyes, joints, ears, skin, teeth but also respiratory system, liver, spleen. This lysosomal storage disease leads to progressive cellular damage, organ dysfunction, and death in the majority of patients before the third decade of life [1].

Patients with MPS VI do not display any features at birth. In the most severe or rapidly progressive form of MPS VI, the first symptoms occur during the second year of life, including reduced joint stiffness, neurological impairment due to cervical spine compression, and reduced respiratory function [3].

The case presentation can be found at https://doi.org/10.1007/s00256-018-3076-4

✉ Paolo Simoni
paoloemiliosimoni@gmail.com

[1] "Reine Fabiola" Children's University Hospital, Université Libre de Bruxelles, 15, Avenue Jean Joseph Crocq, 1020 Brussels, Belgium

Hypoacusia, visual impairment, skeletal and cardiopulmonary systems, skin, liver, spleen and brain are usually observed at the later stage of the disease. The clinical features along with a number of others systemic symptoms linked to GAGs accumulation are quite variable as regards the age of onset and the severity of the MPS VI [4, 5].

At clinical examination, typical features may include macrocephaly, short stature, hepatosplenomegaly, umbilical hernia, hirsutism, gingival hypertrophy, dental malocclusion, macroglossia, and corneal opacification [6].

Although the final diagnosis of MPS VI relies on laboratory tests, multiple typical features can be observed on imaging, especially in patients before the diagnosis.

In patients suffering from MPS VI, a skeletal X-ray workup of the skeleton system reveal multiples joint and bone abnormalities also refer under the umbrella term of dysostosis multiplex [6].

As the presented case, the skull of patients with MPS is enlarged and it may show a "J-shaped" sella turcica and a thickened diploic space (Fig. 3 in the Question part).

Spinal disorders are due to abnormal development of vertebral bodies and result in thoracolumbar kyphosis and gibbus deformity. Patients with MPS VI have an increased incidence of hypoplasia of the odontoid process that predisposes them to atlanto-axial instability. Spinal stenosis may occur as a result of atlanto-axial subluxation or/and GAGs deposition in the surrounding tissues, ligaments, and dura mater.

Chest deformities consist of pectus carinatum, paddle-shaped ribs which are widened anteriorly and tapered posteriorly. Clavicles appear short and thickened (Fig. 2 in the Question part).

The hip bone of MPS patients is often slightly rounded and shaped like iliac wings. Acetabulum dysplasia is common and frequently associated with coxa valga and underdevelopment of the femoral head due to the development of femoral head osteonecrosis and collapse.

As in our case, femoral head abnormalities can be responsible of joint stiffness that can be related to hypoplastic femoral head osteonecrosis and collapse (Fig. 1 in the Question part). This abnormal appearance of the ribs and the "J Shape" of sella turcica along with clinical symptoms suggest MPS disease to rule out by a clinical evaluation and genetic tests.

Morphological changes of the appendicular bones are frequent. The femoral neck can be narrow and abnormally long, and the ulna can be hypoplastic in the distal part. In addition, diaphyses can appear thickened and short; short metacarpal bones are usually short and triangular in shape with proximal thin cortex. Tarsal bones can be irregular and hypoplastic [6].

The diagnosis of MPS VI disease relies on clinical symptoms and imaging features but requires genetic tests to be confirmed. An elevated level of urinary GAG suggests a spectrum of mucopolysaccharidosis disorder. The increase of dermatan sulfate at chromatography or electrophoresis confirms the diagnosis of a MPS. With laboratory tests, the differential diagnosis between MPS VI, other MPSs, and mucolipidoses require the measurement of ARSB enzyme activity less than 10% of the lower limit of normal in cultured fibroblasts or isolated leukocytes suggest MPS VI [4].

Life expectancy of patients affected by MPS VI depends on the severity of the disease and the efficacy of the supportive care, if specific treatment is currently available. In most severe cases, this disease can be lethal during the first years of age.

A minority of patients with a less severe form of MPS VI can survive until adulthood, although their life expectancy is consistently reduced.

Recently, enzyme replacement therapy using genetically engineered human enzyme manufactured by recombinant DNA technology has been tested as a substitute for the deficient enzyme.

As supportive care, physical therapy may improve joint stiffness [2, 4].

## Compliance with ethical standards

**Conflict of interest** The authors declare no conflicts of interest.

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