WHAT WOULD YOU SUSPECT?

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MORQUIO A: HIDING IN PLAIN SIGHT

Morquio A can progress to serious complications regardless of phenotype[1]

Morquio A is a multisystemic disorder, and patients may present with different subsets of symptoms. However, all patients are at risk for progressive organ damage due to N-acetylgalactosamine-6-sulfatase (GALNS) enzyme deficiency.[2-5]

EAR, NOSE, THROAT[6]

- Conductive and neurosensory hearing loss, airway obstruction

NEUROLOGICAL[7]

- Odontoid dysplasia, cervical myelopathy, cervical spine instability, cervical spine compression

GASTROINTESTINAL[4,5]

- Mild hepatosplenomegaly, hernias, loose stools, diarrhea, constipation, abdominal pain

MUSCULOSKELETAL[1,2,4-7,10,11]

- Classical phenotype: Bone deformity, short stature, abnormal gait, joint laxity, contractures and subluxation, dysostosis multiplex
- Nonclassical phenotype: Less overt skeletal involvement, with stature that may appear normal; hip stiffness and pain

OPHTHALMOLOGICAL[5,7,8]

- Diffuse corneal clouding, cataracts, reduction in visual acuity

DENTAL[5,9]

- Dentinogenesis imperfecta, hypodontia, pointed cusps, spade-shaped incisors, thin enamel, abnormal buccal surfaces

CARDIAC[3]

- Mitral and aortic valve stenosis and regurgitation, tricuspid regurgitation, hypertrophy

PULMONARY[5]

- Obstructive sleep apnea, respiratory infections

MORQUIO A: RAISE YOUR SUSPICION

The diverse presentations of Morquio A complicate patient identification

- High degree of genetic heterogeneity may be responsible for wide spectrum of phenotypic presentations[1]
  - Over 277 mutations have been identified encoding the *GALNS* gene[12]
- Patients of nonclassical phenotype may lack pronounced musculoskeletal manifestations, and either phenotype may present with a variety of symptoms[1]
- Unlike most other mucopolysaccharidosis (MPS) disorders, cognitive impairment is not associated with Morquio A[5]

WHEN TO SUSPECT MORQUIO A?

NONCLASSICAL PHENOTYPE
musculoskeletal presentations may include[1,4,5,11]:

- Hip stiffness and pain
- Stature that may be more than 140 cm
- A lack of overt skeletal manifestations

CLASSICAL PHENOTYPE
musculoskeletal presentations may include[5,7]:

- Short stature (< 120 cm)
- Spinal and skeletal abnormalities
- Joint laxity
- Genu valgum
- Abnormal gait
- Chest abnormalities
- Coarse facial features

Nonskeletal manifestations regardless of phenotype may include[2,5]:

- Respiratory manifestations
- Cardiovascular abnormalities
- Muscular impairment
- Hearing loss
- Oral health challenges
- Visual impairment

CONFIRM YOUR SUSPICION:
CONDUCT AN ENZYME PANEL ONCE MORQUIO A IS SUSPECTED

Enzyme testing provides a definitive diagnosis

ENZYME ACTIVITY ANALYSIS[2]

- Measure multiple enzymes to reduce risk of misdiagnosis
  - GALNS may be low in patients with multiple sulfatase deficiency or mucolipidosis type II or III
  - ß-Galactosidase analysis should be conducted to exclude MPS IVB

Molecular analysis: optional, but necessary for prenatal and carrier testing[2]

- Sequencing methods followed by quantitative methods if necessary and feasible
- Two mutations will not always be detectable

MPS IVA diagnosis

GLYCOSAMINOGLYCAN (GAG) TESTING ALONE MAY LEAD TO MISSED DIAGNOSIS[1,2]

- Patients with nonclassical phenotype may not have elevated keratan sulfate levels, putting them at risk for missed diagnosis
- Urinary keratan sulfate levels can be present without elevating total GAG, which may lead to false negatives
  - Most MPS IVA patients excrete keratan sulfate, but some do not excrete enough to elevate total GAG levels above the range for unaffected individuals

SUSPECT MORQUIO A AND CONFIRM WITH ENZYME TESTING

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