

The Diagnosis of Morquio Disease Correlating the Clinical, Radiological and Biochemical Findings: A Case Series

KAMLESH PALANDURKAR, SUMIT THAKUR, UDIT AGRAWAL, MADHUR M. GOYAL, ANJAN BASAK

ABSTRACT

Background: Mucopolysaccharidoses (MPS) are a group of genetic diseases and its diagnosis is a challenging task due to multiple differential diagnosis.

Materials and Methods: We had conglomerated clinical findings, radiological and Ophthalmological features. Biochemical test for urine glycosaminoglycans (GAG) was done for confirmation of diagnosis in two pediatric patients.

Case Summary: Both the cases of Morquio disease were characterized by short-trunk, dwarfism, fine corneal deposits,

a skeletal dysplasia that was distinct from other MPS and their intelligence were normal. Radiological features were suggestive of Morquio syndrome and urine GAG test for MPS was positive in both the cases.

Discussion and Conclusion: With the clinical features we had multiple differential diagnoses. The radiological investigations minimized the list and the biochemical test confirmed GAG in urine. Combination of clinical, radiological and biochemical findings confirmed the diagnosis of Morquio syndrome in these two cases.

Key Words: Morquio disease, Diagnosis, Clinical, Radiological, Biochemical

INTRODUCTION

Mucopolysaccharidoses (MPS) are a group of inherited storage diseases which are caused due to the deficiency of lysosomal enzymes which are needed to degrade glycosaminoglycans (GAGs). GAGs are the polymers of a disaccharide unit which are composed generally of uronic acid and sulphated amino or N-acetylated monosaccharides. GAGs are linked to proteins to form proteoglycans, which are the major constituents of the connective tissue as well as the nuclear membranes. The degradation of the proteoglycans starts with the proteolytic removal of the proteins, followed by the stepwise degradation of the GAG moiety. The failure to degrade due to an absent or a grossly reduced activity of the mutated lysosomal enzymes results in the intra-lysosomal accumulation of GAG. The distended lysosomes accumulate in the cell and interfere with the cellular functions. This leads to a characteristic pattern of clinical, radiological and biochemical abnormalities.

The Morquio disease (MPS IV) is caused by a deficiency of N-acetyl galactosamine-6-sulfatase or β -galactosidase. Both results in the defective degradation of keratan sulfate which is abundant in the cornea as well as in the loose connective tissue. Keratan sulfate plays a critical role in the corneal transparency[1].

CASE SERIES

We obtained the Institutional Ethical Committee's clearance before the start of the study. We also obtained the informed consent from the parents of the study subjects and permission from the patient's parents for the publication of the pictures and the radiographs.

In the last 10 month period, two cases of Morquio disease were diagnosed at our rural hospital. Case I (05years/F) reported to the Paediatric and the Case II (07years/F) to the Orthopaedic Department of our hospital with similar complaints of multiple deformities in both the upper and lower limbs, a protruding anterior chest and growth retardation.

There was no history of (h/o) constipation, diarrhoea, vomiting, bleeding, jaundice, seizures, weight loss, loss of appetite or consciousness in both the cases. Also, their bladder and bowel habits were normal.

The developmental milestones were normal as per their age. Both are well immunized as per their age according to the immunization program of the Indian Association of Paediatrics.

There were no past h/o tuberculosis, diabetes mellitus, asthma or any chronic respiratory or gastrointestinal disorder.

The family h/o both the cases did not show any similar complaints.

On examination, both the cases were found to have bossing of the head, pigeon's chest, Harrison's sulcus, ulnar deviation of both the forearms, knock knees, bowing of the legs, kyphosis and short trunks.

Case I also had a depressed nasal bridge and a pot belly appearance of the abdomen, with a normal umbilicus. On palpation, her abdomen was found to be soft and non-tender. The liver was just palpable below the right costal margin, in the mid-clavicular line and she had no other organomegaly. Case II did not have any organomegaly at all.

In both the cases, on auscultation, no murmur was heard with the normal first and second heart sounds. No accessory sound was auscultated.

Neurologically, both the females were normal, except that they had a waddling gait. The intelligence was normal in both these cases.

To differentiate these cases from other neurodegenerative and dwarfing conditions, their pathological, ophthalmologic as well as radiological examinations were done and the findings were as follows:

X-ray findings

The findings which were common to both the cases were -

- a) Chest: Ribs over ribs appearance [Table/Fig-1 and 2], b) Bilateral limbs: irregular epiphysial ends with osteopaenia [Table/Fig.-3 and 4], c) Vertebra: bullet vertebra (anterior beaking of the vertebra) [Table/Fig.-5 and 6], d) Hands: irregular epiphysial plates with anterior spiking of the proximal ends of the metaphysis [Table/Fig.-7 and 8], e) Hip: narrowed sciatic notch with flattening of the acetabulum roof [Table/Fig 9 and 10], f) Both knees: genu vulgus deformity [Table/Fig11 and 12].

In case I, the radiograph of skull showed a 'J' shaped sella tursica, which was an unusual presentation (Figure-13).

Pathological findings

In both the cases, there were no abnormalities in the peripheral smear, except for mildly hypochromic RBCs. Their urine reports were normal.

Ophthalmologic findings

In case I, there was no corneal clouding or any other significant changes. But in case II, there was a bilateral corneal haze which was detected by slit lamp examination [2], [3].

With the help of all these features and findings, we could successfully distinguish the dysostosis multiplex from other conditions. The biochemistry was diagnostic and it helped in distinguishing MPS from other dysostosis multiplex conditions.

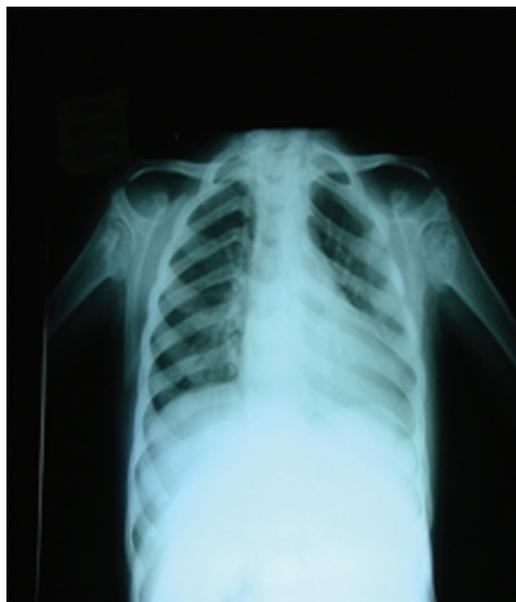
Biochemical findings

Her blood biochemistry was normal. The phosphate, calcium, vitamin D and the parathromone levels were normal.

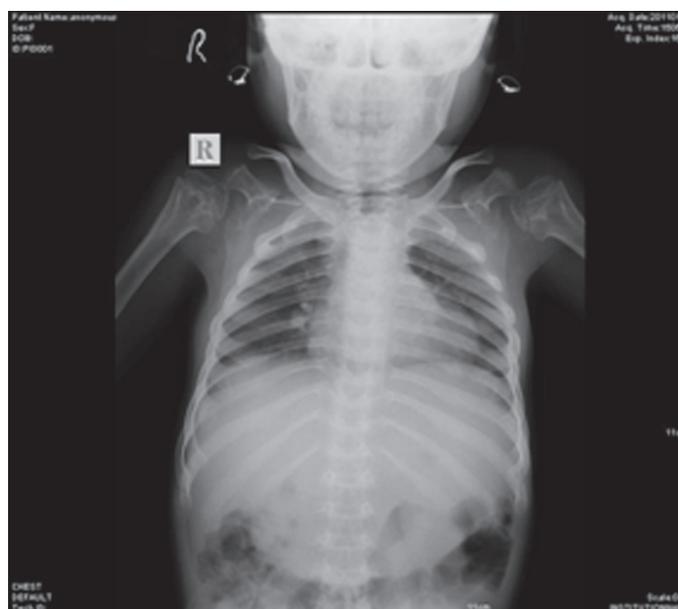
The Cetylpyridinium Chloride (CPC) test for Mucopolysaccharid-osis (urinary GAG fragments) was positive in the urines of these patients [4].

Principle of the test

Interaction between the cationic, quaternary ammonium compound, Cetylpyridinium Chloride and polyanionic glycosaminoglycans results in turbidity in the test (T), which can be compared with the standard (S) (chondroitin sulphate). Appearance of turbidity in the test as in the standard suggests the presence of a significant amount of GAG in the urine.



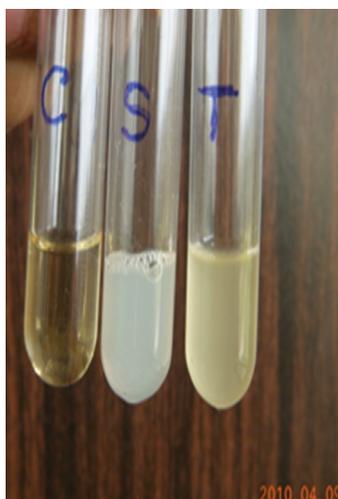
[Table/Fig-1]: Ribs over ribs appearance in Case I



[Table/Fig-2]: Ribs over ribs appearance in Case II



[Table/Fig-3]: irregular epiphysial ends with osteopenia in Case I



Cetylpyridinium Chloride (CPC) test: Case-I (C-control, S-standard, T-test)



Cetylpyridinium Chloride (CPC) test: Case-II (C-control, S-standard, T-test)



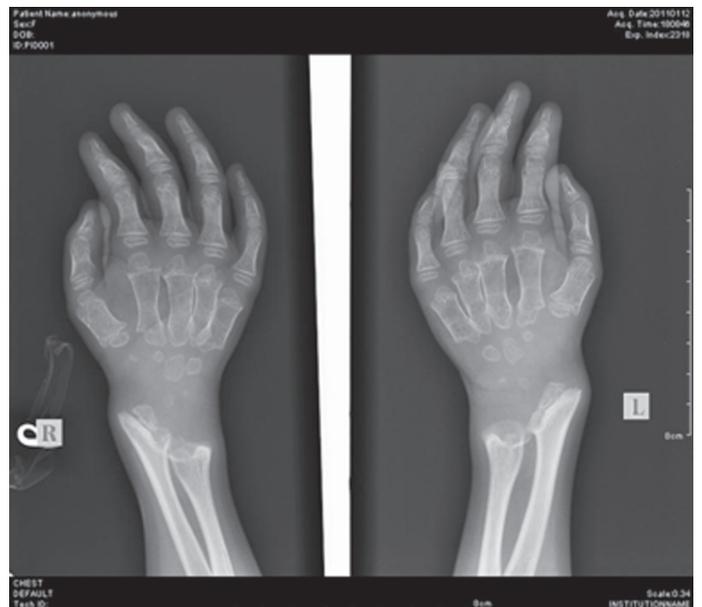
[Table/Fig-4]: irregular epiphysal ends with osteopenia in Case II



[Table/Fig-7]: irregular epiphysal plates with anterior spiking of proximal ends of metaphysis in Case I.



[Table/Fig-5]: Bullet vertebra -anterior beaking of vertebra in Case I



[Table/Fig-8]: irregular epiphysal plates with anterior spiking of proximal ends of metaphysis in Case II.



[Table/Fig-6]: Bullet vertebra -anterior beaking of vertebra in Case II



[Table/Fig-9]: Narrowed sciatic notch with flattening of acetabulum roof in Case I.



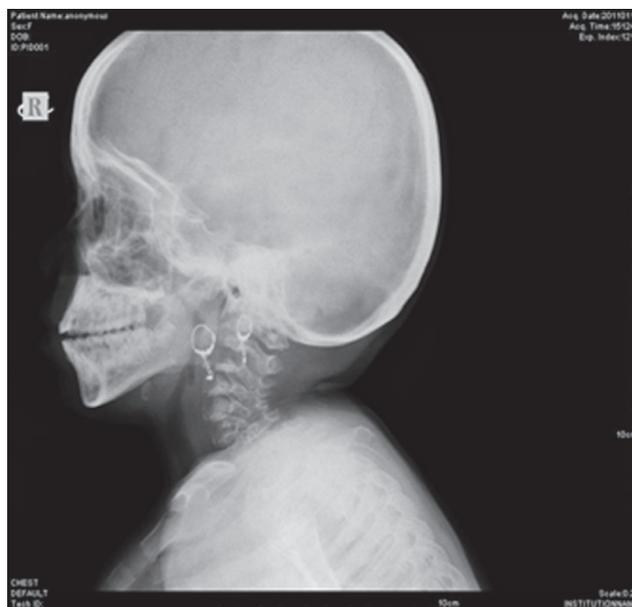
[Table/Fig-10]: Narrowed sciatic notch with flattening of acetabulum roof in Case II.



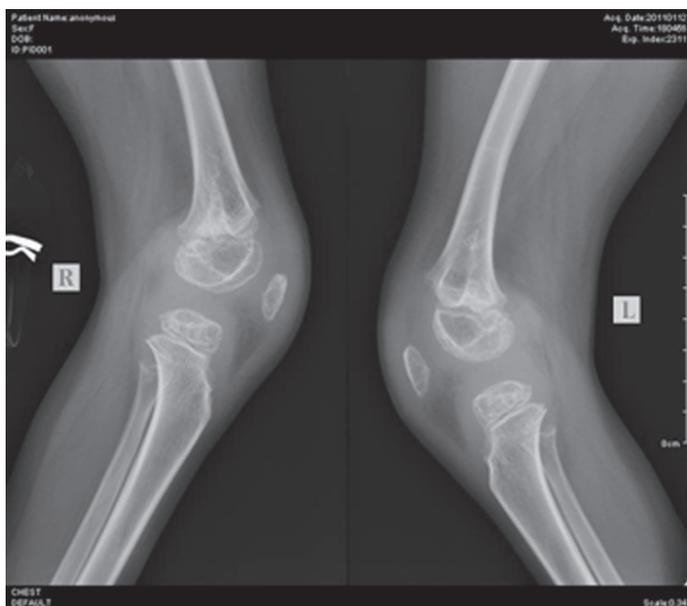
[Table/Fig-13]: 'J' shaped sella tursica in Case I.



[Table/Fig-11]: Genu valgus deformity in Case I.



[Table/Fig-14]: 'J' shaped sella tursica in Case II.



[Table/Fig-12]: Genu valgus deformity in Case II.

Unfortunately, we could not perform the enzyme assay due to lack of the facility for it in our hospital.

We made the diagnosis of Morquio disease on the basis of the clinical, pathological, ophthalmological, radiological and biochemical examinations of the patients.

DISCUSSION

MPS is a group of inherited diseases which is characterized by defective lysosomal enzymes which are responsible for the degradation of mucopolysaccharides, which leads to the accumulation of incompletely degraded mucopolysaccharides in the lysosomes that affect various organs of the human body.

The incidence of MPS is between 3.5 to 4.5/100,000[5]. The most common subtype is MPS III [5].

We have reported these cases of MPS as it is a rare disease and also Morquio is not the common presentation among the MPS.

Morquio disease (MPS IV) is caused by the deficiency of N-acetylgalactosamine-6-sulfatase (MPS IV-A) or β -galactosidase

(MPS IV-B). Both the types of Morquio disease are characterized by short-trunks, dwarfism, fine corneal deposits, skeletal dysplasia that are distinct from other MPS, and the preservation of intelligence [5], [6], [7], [8].

Both our patients were females and they had almost similar presentations with some unusual findings. In Morquio disease, the cornea is usually involved but case I had a normal cornea. The cardiac anomalies which are found usually are atrial regurgitation and mitral regurgitation or coronary artery diseases. But both these cases didn't have any cardiac involvement. Radiologically, there was no 'J' shaped sella in the MPS IV case [9]. Case I had this unusual feature in her skull radiograph [9], [10],[11]. Usually, in Morquio disease, the diagnosis is missed by the CPC test [5], but in both these cases we got positive results.

These cases mimicked other dwarfing conditions on clinical presentation. Radiologically, we could differentiate the dysostosis multiplex from the other conditions. But for the diagnosis of MPS, biochemical tests are the definitive diagnostic tools [6].

The urinary detection of GAG to distinguish MPS from the other dysostosis multiplex by the CPC test not only helps in making the correct diagnosis, but it is also rapid and inexpensive. Also, there is no need of any costly equipment to do the test. This rapid and cost-effective test is effective for the diagnosis of MPS at rural hospitals.

CONCLUSION

We could successfully diagnose the atypical presentations of two cases of Morquio disease by the simple, rapid and inexpensive Cetylpyridinium Chloride test.

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AUTHOR(S):

1. Dr. Kamlesh Palandurkar
2. Dr. Sumit Thakur
3. Dr. Udit Agrawal
4. Dr. Madhur M. Goyal
5. Dr. Anjan Basak

PARTICULARS OF CONTRIBUTORS:

1. Department of Biochemistry, Jawaharlal Nehru Medical College, D.M.I.M.S. (D.U.), Wardha-442004.India.
2. Department of Biochemistry and Paediatrics, Jawaharlal Nehru Medical College, D.M.I.M.S. (D.U.), Wardha-442004.India.
3. Department of Biochemistry, Jawaharlal Nehru Medical College, D.M.I.M.S. (D.U.), Wardha-442004.India.
4. Department of Biochemistry, Jawaharlal Nehru Medical College, D.M.I.M.S. (D.U.), Wardha-442004.India.
5. Department of Biochemistry, Jawaharlal Nehru Medical College, D.M.I.M.S. (D.U.), Wardha-442004.India.

NAME, ADDRESS, TELEPHONE, E-MAIL ID OF THE CORRESPONDING AUTHOR:

Dr. Anjan Basak
Department of Biochemistry,
Jawaharlal Nehru Medical College, D.M.I.M.S. (D.U.),
Wardha-442004.India.
E-mail: drabasak1@yahoo.com

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