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Type 2 Sialidosis: A Rare Autosomal Recessive Condition in a 13-Year-Old Male: A Case Report

Kundan Kumar Yadav[1] | Milan Pokhrel[1] | Geeta Bashyal[2] | Shankar Pokharel[3] | Santoshi Pokharel Kunwar[4]

[1]Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Kathmandu, Nepal | [2]Department of Pediatrics, Maharajgunj Medical Campus, Institute of Medicine, Tribhuvan University, Kirtipur, Nepal | [3]Kathmandu Medical College and Teaching Hospital, Kathmandu, Nepal | [4]Nepal Army Institute of Health Sciences-College of Medicine, Kathmandu, Nepal

Correspondence: Milan Pokhrel (pokhrelmilan511@gmail.com)

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ABSTRACT

This report presents a 13-year-old male with abnormal body movements, generalized body weakness, and developmental regression who was further evaluated to conclude type 2 Sialidosis as the diagnosis. Genetic testing is key in diagnosing such rare conditions, and management is difficult, particularly in resource-limited settings.

1 | Introduction

Sialidosis, also known as mucolipidosis (ML1) is a rare autosomal recessive condition. The incidence of this disease is reported to be 0.04 in 100,000 [1] It results from insufficient α-n-acetyl-neuraminidase (NEU1) activity due to a defect in the NEU1 gene, also known as the Sialidase gene, which is located inside the locus of the major histocompatibility complex (6p21.3). Although different variations may be present, Missense mutations are the most common disease mechanism in patients with sialidoses. The deficiency of sialidase causes disruption in catabolic pathways for the degradation of sialylated glycoconjugates [2].Thus the disease is characterized by the progressive storage of sialylated glycopeptides and oligosaccharides in lysosomes [1–3].

Sialidosis is divided into two main groups: type I (nonmorphic) and Type II (dysmorphic). Type I Sialidosis is the nonneuropathic form of the disease, also known as cherry-red spot myoclonus syndrome. Symptoms appear in the second or third decades of life. The most common presentation is myoclonus with decreased visual acuity and bilateral macular cherry-red spots. Patients have no obvious defects, with normal or slightly impaired intelligence. Type II Sialidosis is classified as congenital, infantile, and juvenile. The clinical presentation of type II Sialidosis includes the typical presentation of storage disorders such as coarse facies and hepatomegaly, developmental delay, dysostosis multiplex, myoclonus, macular cherry-redspots, nystagmus, hearing loss, inguinal hernia, and vertebral deformities [1, 4, 5]. In this case report, We present a case of type 2 Sialidosis in a 13-year-old male patient.

2 | Case History/Examination

A 13 years male who is born of a non-consanguineous marriage presented with clinical indication of seizure with bicuspid aortic valve, abnormal body movement, and generalized

body weakness for 2.5 years, tremors, difficulty in fine movement, contracture, developmental regression of gross motor and fine motor domains since 5 years of age, difficulty in climbing stairs, and difficulty in writing. On examination, a thin build from head to toe, coarse facies, bushy eyelashes, possibly hypertelorism, short neck, pectus carinatum, and difficulty in extending upper and lower limbs were noted (Figure 1A–D). Eye examination revealed cherry-red spots and lenticular opacities, suggestive of mucopolysaccharidosis (Figure 2).

3 | Methods

X-ray reports showed features of skeletal dysplasia (Figure 3A–D). With this presentation, he was suspected to be affected by a lysosomal storage disorder and was evaluated for pathogenic variations as shown below. Management of this patient was mainly focused on counseling regarding the nature, progression, and outcome of the disease as well as counseling of parents regarding further pregnancy planning. Gene therapy, due to its unavailability in Nepal, was not considered for the treatment of our patient.

Gene (transcript)	Location	Variant	Zygosity	Disease (OMIM)	Inheritance	Classification
NEU1(–) (ENST00000375631.5)	Exon 4	c.679G>A (p. Gly227Arg)	Homozygous	Sialidosis type 1 (OMIM no. 256550)/ sialidosis type2 (OMIM no. 256550)	Autosomal recessive	Pathogenic (PS3, PM2, PP1, PP3, PP5)

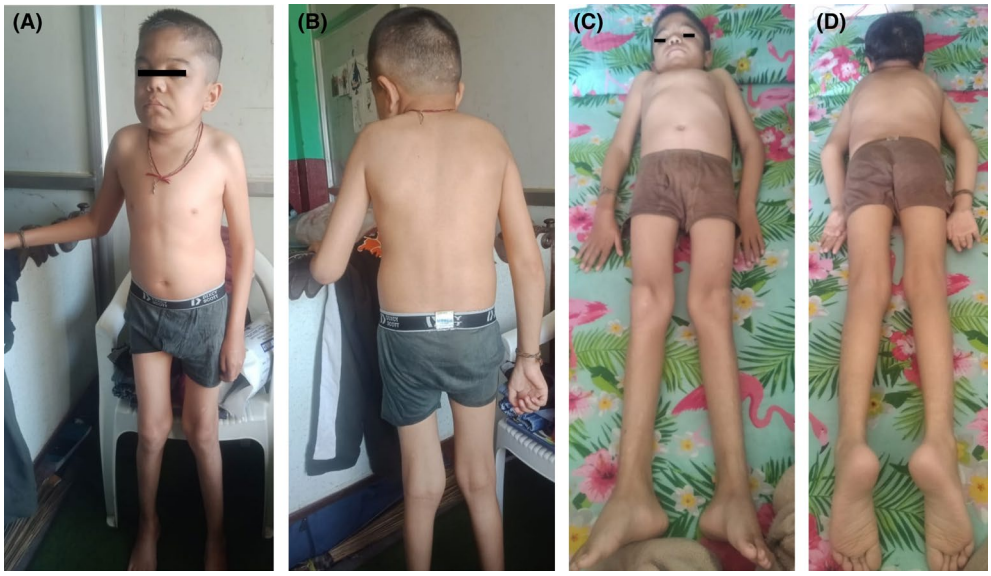

FIGURE 1 | (A) Child with sialidosis in ventral view. (B) Sialidosis in dorsal view. (C) Child with sialidosis in supine position. (D) Child with sialidosis in prone position.

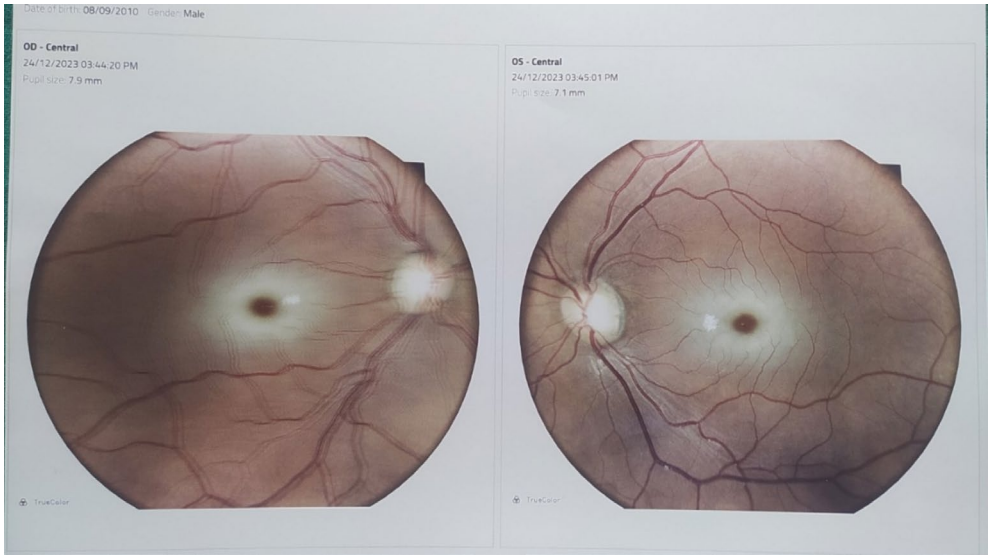

FIGURE 2 | Fundoscopic view showing bilateral cherry red spot.

4 | Conclusion

Sialidosis is a rare autosomal recessive disorder and can be confused with other diagnoses. Genetic testing is key for diagnosing the condition, and the management of this condition in resource-poor settings is limited to prenatal counseling and treatment of symptoms.

5 | Discussion

Sialidosis was first described by Lowden and O'Brian in 1979 and included two forms of the disease: Mucolipidosis and the cherry red spot-myoclonus syndrome [6]. Sialidosis is divided into type 1 and type 2 based on phenotype; however, both have autosomal recessive inheritance and are caused by a mutation of the NEU1 gene located on chromosome 6p21.3. As the gene is responsible for encoding lysosomal sialidase, the mutation causes a complete absence of sialidase in Type2 and some residual activity is present in Type 1 sialidosis. Sialidase removes terminal sialic acid molecules from oligosaccharides and glycoproteins; thus, its deficiency causes sialic acid-rich macromolecular storage and urinary sialyl-oligosaccharide secretion [7].

Sialidosis type 2 is further divided into 3 subtypes: (i) Congenital/hydropic (in utero) (ii) infantile (0–12 months) (iii) juvenile (2–20 years). The congenital type is characterized by ascites and hydrops fetalis, hepatomegaly, and stillbirth or death at an early age. Coarse facies, visceromegaly, dysostosis multiplex, vertebral deformities, and mental retardation are the defining features of the infantile and juvenile types. Other features such as Myoclonic seizures and cherry red spots are present in type 1 as well. [8, 9] Our patient had presented with features very similar to the abovementioned features, thus suggestive of type 2 Sialidosis.

Treatment of Type 2 Sialidosis is challenging because of early onset, systemic involvement, and a fulminant course. Carrier detection, prenatal molecular diagnosis, and proper genetic counseling may be suitable management approaches. Different therapeutic options are being explored such as the use of an immunosuppressant (celastrol) along with a proteasomal inhibitor (MG132) as well as chaperone-mediated gene therapy but with

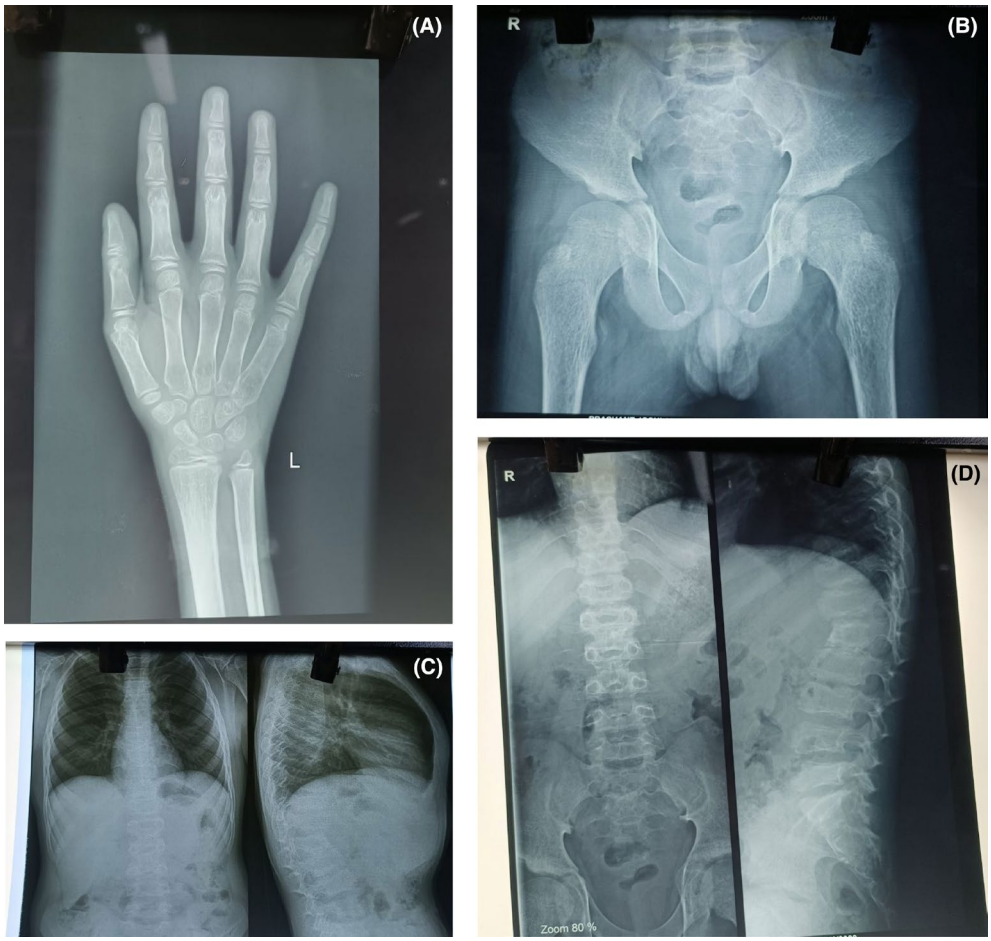

FIGURE 3 | (A) X-rays of the wrist show a widening of the metaphysis of the distal radius, ulna, and metacarpal. There is a triangular-shaped epiphysis of both the radius and ulna distal epiphysis. (B) X-rays of the pelvis in AP view show widening of bilateral iliac wings with small pelvic inlet giving champagne glass apperance. (C) Chest x-rays PA view shows narrowing of the posterior part of the rib at the costovertebral junction and flaring of ribs rest of the posterior aspects of ribs give paddle-shaped ribs. (D) X-rays of spine AP and lateral view show flattening of dorsal and lumbar vertebral bodies. The end plate appears irregular with decreased intervertebral disc space. There decrese AP dimension of L1 vertebra. Diffuse osteopenia of vertebral bodies is seen.

limited success [8]. Extensive research is required to explore effective therapy for this condition.

Author Contributions

Kundan Kumar Yadav: conceptualization, writing – original draft, writing – review and editing. **Milan Pokhrel:** conceptualization, writing – original draft, writing – review and editing. **Geeta Bashyal:** resources, writing – review and editing. **Santoshi Pokharel Kunwar:** writing – review and editing. **Shankar Pokharel:** writing – review and editing.

Consent

Written informed consent to publish this report is in accordance with the journal's patient consent policy.

Conflicts of Interest

The authors declare no conflicts of interest.

Data Availability Statement

Data sharing not applicable-no new data generated.

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