**Scholars Journal of Medical Case Reports**
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

**Neonatology**

# Fetal-Placental Hydrops on Syndromic Abnormality: Salla's Disease: A Case Report

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**DOI:** https://doi.org/10.36347/sjmcr.2024.v12i08.006 | **Received:** 18.06.2024 | **Accepted:** 23.07.2024 | **Published:** 02.08.2024

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**Abstract** **Case Report**

Salla's disease is a rare and very pathogenic lysosomal disease, due to a transport defect through the lysosomal membrane of N-acetylneuraminic acid or scialic acid. Salla's disease has two clinical forms, a less severe that begins between 3 and 12 months of age but evolves very slowly over several decades, and a much more serious form beginning at birth and having a mortal evolution in the first years of life.

**Keywords:** Salla's disease, foeto-placental hydrops, scialidosis.



## INTRODUCTION

Hydrops fetalis is the abnormal accumulation of fluid in the tissues and serosal cavities of a fetus. There are two types: immune hydrops or maternal erythrocyte all immunization; and non-immune hydrops, which includes all other pathologies not linked to all immunization, i.e. the absence of anti-erythrocyte antibodies. With advances in medicine, and in particular the systematic use of immunoprophylaxis to prevent all immunization, this non-immune hydrops represents around 87% of observed fetal hydrops, of which 15 to 25% remain without etiology [1].

In this article, we'll look at a case of non-immune hydrops of the fetus based on a syndromic anomaly: a lysosomal disease known as Salla disease.

## CASE REPORT

This was a female newborn from 2nd degree consanguineous parents, admitted to hospital 30 minutes after birth for respiratory distress associated with a dysmorphic syndrome.

As regards her history, she was the product of a well-monitored pregnancy, carried out at 36 weeks' gestation, vaginal delivery, facial presentation with good adaptation to extra uterine life, birth weight 3430g. The mother was 25 years old, with no notable previous history, primiparous, blood group AB+. This pregnancy was marked by the discovery on 2nd trimester ultrasound of a peritoneal effusion and an occipital cyst, the serological profile was negative. The father, aged 40, had no notable antecedents, and his blood group was BRh+. No similar cases in the family.

The onset of the disease dates back to birth with the onset of immediate respiratory distress with a Silverman score of 3/10 associated with a malformative syndrome, motivating its transfer to our intensive care unit for management.

General examination revealed a conscious, pink, tonic and reactive newborn with a weak sucking reflex, hemodynamically stable, a respiratory rate of 60 cycles/minute, SpO2 at 92% in room air. glycemia= 1.22 g/l, temperature 36.5°C. Weight = 3430g (normal for age), height = 48 cm (normal for age), PC = 35 cm (normal for age).

Morphologically, we observed a dysmorphic syndrome with a puffy face, bilateral orbital oedema, stretched anterior fontanel, atypical ear morphology, silver-colored hair, pinched and pointed nose, hypertrophied neck, and bilateral equinus varus feet. Abdominal examination revealed moderate ascites with herniation of the linea alba and hepatosplenomegaly (Figure 1). The rest of the examination was unremarkable.

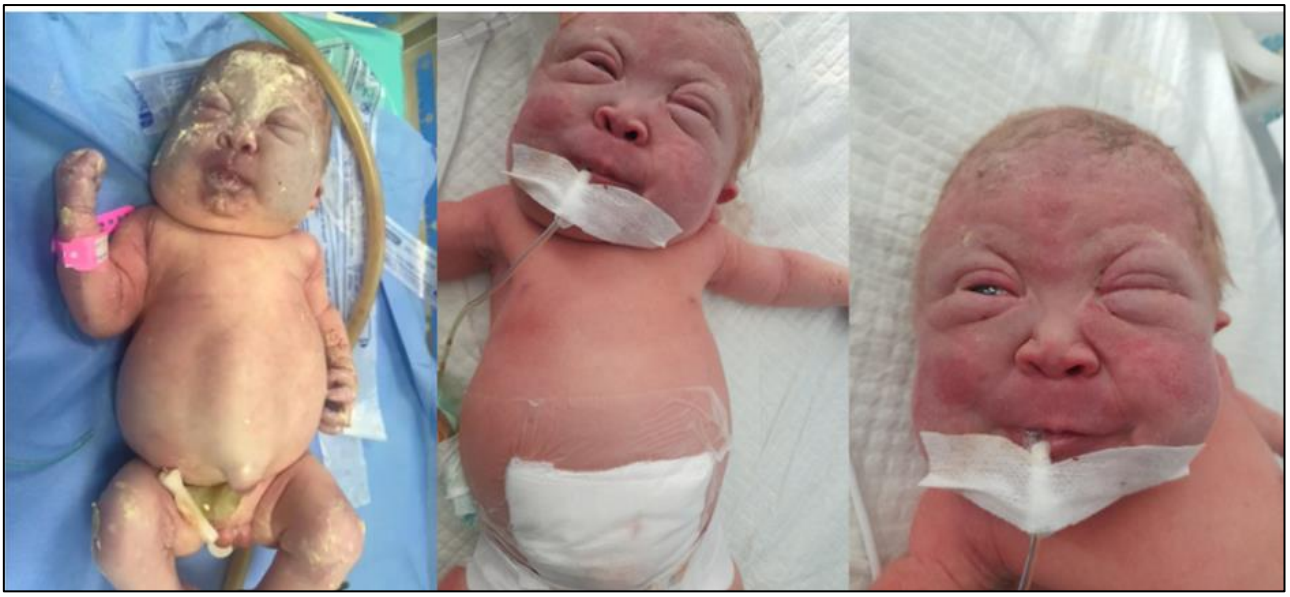

**Figure 1: Facial dysmorphia, white line and umbilical hernia, abdominal distension**

The patient was admitted to hospital and placed on ventilator support in the neonatal intensive care unit. A malformative work-up was performed: echocardiography showed a patent ductus arteriosus; transfontanellar ultrasound was unremarkable; abdominal ultrasound and CT showed hepatomegaly with moderate abdominal effusion. Brain MRI was unremarkable.

Biological: Standard workup (complete blood count, ionogram, renal function; phosphocalcium, liver function, CRP) was unremarkable. A Rh+ blood grouping and direct coombs test were negative. The TORSCH and Parvo B19 profiles were negative. Urinary glycosaminoglycan (GAG) test was normal. Measurement of β-glucocerebrosidase and acid sphingomyelinase enzyme activity returned normal, thus ruling out the diagnosis of Gaucher disease and Niemann Pic A/B. The standard karyotype was female (46 XX).

A urinary oligosaccharide test was performed. Strong elevation of sialic acid (1387µmol/mmol creatinine for a normal value of less than 99.5µmol/mmol). The diagnosis of hydrops fetoplacental on syndromic anomaly related to Salla disease was therefore retained.

The patient was admitted to intensive care for 5 days, during which time the evolution was initially favorable, marked by an improvement in respiratory function under ventilatory support for 24 hours, then progressive and definitive weaning with good pulmonary aeration on standard radiography. Cardiovascularly, she was put on Lasilix and iburofen following the discovery of a large ductus arteriosus. In metabolic terms, jaundice appeared at 2 days of age, requiring intensive phototherapy with a good outcome. In terms of infection, digestion and neurology, she presented no problems.

Given the absence of curative treatment for Salla disease, the evolution was fatal at home at the age of 2 months.

## DISCUSSION

Salla disease is an autosomal recessive lysosomal storage disease characterized by early physical impairment and intellectual disability. It was first described in 1979, after Salla, a municipality in Finnish Lapland. Salla disease is one of 40 Finnish heritage diseases and affects approximately 130 individuals, mainly from Finland and Sweden.

Salla disease comprises two clinical forms, the classic and the severe infantile form, which are due to an abnormality in the transport of free sialic acid across the lysosomal membrane [2]. The abnormal gene responsible for this disease is located at 6p [3]. In both Salla disease and sialuria, there is an exaggerated urinary elimination of free sialic acid, which is very useful for diagnosis.

In the severe infantile form, Salla disease is clinically evident from the neonatal period: the hypotonic newborn presents with hepatosplenomegaly, sometimes anasarca with ascites, and a face with coarse features resembling early GM1 gangliosidosis. The course is severe, with very severe motor impairment in the form of spastic tetraplegia and massive mental retardation. Epileptic seizures, often including myoclonus, are frequent in this form. Bone abnormalities include punctiform calcifications, widening of the diaphyses of the long bones and vertebral anomalies. Cerebral MRI shows extensive leukodystrophy. Death occurs within the first three years, often due to respiratory disorders. Ascites, hepatosplenomegaly and coarse features have been reported in several antenatal cases. The differential diagnosis of this severe form of

Salla disease is with early-onset GM1 gangliosidosis or Landing's disease, sialidosis and galactosialidosis [4].

In the classic form, on the other hand, the first symptoms begin 3 to 12 months after birth with hypotonia, soon followed by ataxia of the head and trunk. Very often, these children also develop nystagmus in the first few months of life, which subsequently disappears. The psychomotor development of these children is slowed down. Thirty percent of children will never be able to walk. There is severe mental retardation. Many have an IQ below 50, with severe language difficulties. In almost 20% of cases, epileptic seizures begin in childhood. Dysmorphic signs, somewhat resembling those of Hurler's disease, do not become evident until adulthood. There is often a marked worsening of the disease between the ages of 20 and 30. Patients who have been walking become increasingly ataxic and dystonic. These patients have a very long life expectancy.

Both forms are diagnosed on the basis of clinical signs, a massive increase in urinary sialic acid excretion and the presence of dilated lysosomes, particularly in fibroblasts [5]. Patients with the classic form of Salla disease are mostly of Finnish origin, whereas the severe infantile form has been reported in several countries around the world, particularly France.

Antenatal diagnosis of Salla disease is made possible by electron microscopy showing the accumulation of intra-lysosomal sialic acid in amniocytes and chorionic villi [6]. There is also a marked increase in free sialic acid in amniotic fluid, particularly in the severe form of Salla disease [6]. Now that the gene for these two diseases has been located and cloned, the identification of mutations in the affected individual enables antenatal diagnosis by molecular biology in the event of a new pregnancy [3, 7].

Treatment is symptomatic only. It relies on specialized educational care for these children due to their mental deficiency, and the prevention and treatment of neurological (epilepsy), respiratory, digestive and orthopedic complications, which are inevitable in progressive neurological diseases. There is currently no specific treatment for Salla disease.

## CONCLUSION

Salla disease is a rare lysosomal disorder with very specific pathogenic features. Several studies have been carried out, sometimes showing the difficulties of obtaining a precise diagnosis of this pathology. There is currently no curative treatment.

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