CASE REPORT

Nicolaides–Baraitser syndrome

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ABSTRACT

Nicolaides–Baraitser is a very rare clinical condition characterized by short stature, mental retardation, absent or limited speech, seizures, sparse hair, peculiar facial appearance, short metacarpals, and interphalangeal swelling. In this paper, we report a case of a 5-year-old female child belonging to the ethnic Kashmiri population with clinical features suggestive of Nicolaides–Baraitser syndrome. Clinical rarity of this condition prompted this communication.

Key words: Mental retardation, Nicolaides–Baraitser syndrome, seizures, short stature

INTRODUCTION

In 1993, Nicolaides and Baraitser reported a new clinical condition consisting of short stature, mental retardation, seizures, sparse hair and brachydactyly. It is a rare condition, which has been reported in only 24 cases worldwide. It is a distinct clinical condition with well-recognizable symptoms and has probably been under-diagnosed until now.[1]

Main clinical features of this rare syndrome are short stature, mental retardation, absent or limited speech, seizures, sparse hair, typical facial appearance, brachydactyly and prominent finger joints with broad distal phalanges.

Other clinical features include umbilical hernias, inguinal hernias, cryptorchidism, and cardiac defects.

The etiology of this rare disorder is not known. For diagnosing this condition, an integrated approach involving a dermatologist, clinical geneticist and a radiologist is required.

CASE REPORT

A 5-year-old female child, born of a consanguineous marriage, was brought by her parents to the out-patient Department of Dermatology, STD and Leprosy of our institute with chief complaints of sparse scalp hair associated with increased facial hair since infancy. As per her parents, the patient had a normal hair at birth after which the sparse hair replaced the normal hair over the scalp gradually over a period of 2-year. Despite several treatments, her scalp hair did not grow beyond a particular length. There was also a history of growth retardation and mental impairment. On further enquiry, the parents revealed that she had a febrile convulsion at 2-year of her age and thereafter started to have regular episodic seizures. The patient was put on anti-convulsant treatment and was continuing the same at the time of presentation. Motor milestones were achieved normally, but there was a significant delay in speech. At the time of presentation (5-year of age), she had mental impairment, absent speech, poor concentration and short attention span. Except for her seizures, her general health was good.

The child was totally dependent for her basic cares and was not toilet trained. The parents described the child as being happy and friendly and there were no bouts or periods of aggression.

The child was born at term after an uneventful pregnancy with normal growth parameters. She was fourth in birth order with no similar history in the

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parents or other sibs. Both of her parents enjoyed good health and were of normal height and weight.

Examination of the patient revealed short stature (height < 3rd percentile), microcephaly and absent speech. The facial appearance was peculiar with a characteristic triangular contour [Figure 1]. Palpabral fissures had normal width with slight downward slanting. There was mild wrinkling of the skin at the cheeks, especially when the child used to smile. Examination of the limbs and joints revealed broad distal phalanges with prominent interphalangeal joints [Figure 2]. During examination, it was found that the patient had an umbilical hernia [Figure 3].

Cutaneous examination revealed a very fine and sparse scalp hair [Figure 4], facial hypertrichosis particularly over the forehead and temples, dense eyebrows and eyelashes [Figure 5]. Facial skin was coarse and wrinkled. Examination of the mucosa and nails revealed no abnormality. Ophthalmological, Dental, ENT (Eye, Nose and Throat) examination was normal.

Mental assessment of the child was done by a trained clinical psychologist, and it revealed that the child had mental retardation with global deficits in adoptive functions. The child was found to be hyperactive, hyperkinetic, inattentive, most of the type happy and hyper sociable, being able to go away with complete strangers. The child's Intelligence Quotient as per "Stanford Binnet Test of Intelligence" was found to be 61, while as the 'Vineland's Social Maturity Scale' score was 30.

Routine laboratory investigations including a complete hemogram, blood sugar, blood urea, serum creatinine, liver function, kidney function, thyroid function, serum calcium and routine urine tests were all within normal limits. Skeletal survey of hands and feet revealed short metacarpals and metatarsals. Abdominal ultrasonography as well as computed tomography brain were both normal. The patient had an abnormal electroencephalogram pattern with a left fronto-parietal temporal spike and slow wave activity. Echocardiography of the patient was also done revealing no abnormality.

In view of the constellation of clinical features, a diagnosis of Nicolaides–Baraitser syndrome (NBS) was made in this patient.

DISCUSSION

Nicolaides–Baraitser syndrome is named after Paola Nicolaides, a Pediatric Neurologist and Michael Baraitser, a clinical geneticist. Both of them worked in Ormond Street Hospital for children in London. They saw a 16-year-old girl with an unusual combination of signs and symptoms and thought this to be a recognizable entity. They published this in a medical journal in 1993.[2] Other authors later suggested naming the entity after the two authors that described this entity first.[3] Until date, about 24 cases of , NBS have been reported.

Etiology of NBS is still unknown. It has been seen to occur in patients with different ethnic backgrounds. There is no significant gender difference in the occurrence and frequency of this syndrome. No familial cases have been known so far, and parental consanguinity has not been reported. Chromosomal analysis of these patients has revealed a normal karyotype. One of the probable explanations regarding the etiology of this syndrome is that it is caused by a heterogeneous dominant *de novo* mutation in a single gene.

Major clinical features of NBS include:

- Short stature
- Developmental delay
- Severely impaired speech
- Seizures
- Microcephaly
- Sparse hair
- Progressive skin is wrinkling
- Long and broad filtrum
- Progressive prominence of distal phalanges
- Progressive prominence of inter-phalangeal joints
- Short metacarpals and metatarsals.

As a result of prenatal and postnatal growth retardation, most of these patients have a short stature. The facial features are characteristic with a typical triangular contour. Palpebral fissures have a normal width and may show downward slanting. Eyelashes and eyebrows may be dense and prominent. The nose has a narrow bridge. The filtrum is broad and usually long with a wide mouth. There can be wrinkling of skin at the cheeks especially during smiling. Some patients may show wrinkling of skin at the neck as well.

Sparseness of scalp hair is regarded as one of the major features of NBS. Sparse scalp hair is usually noted in the neonatal period and is usually progressive. The patients are noted to have facial hypertrichosis, especially over the forehead and the temples. Eyelashes are usually prominent and dense.

Another typical feature is the development of prominent inter-phalangeal joint swellings and broader distal

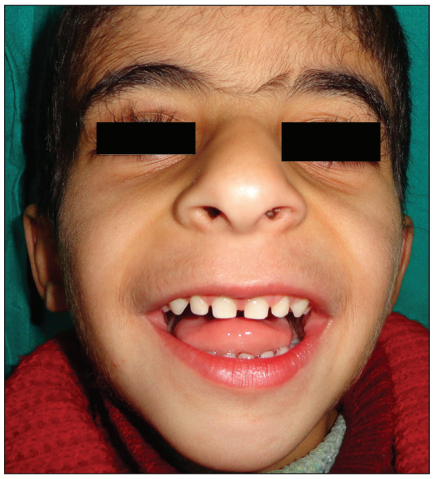

Figure 1: Triangular facial contour

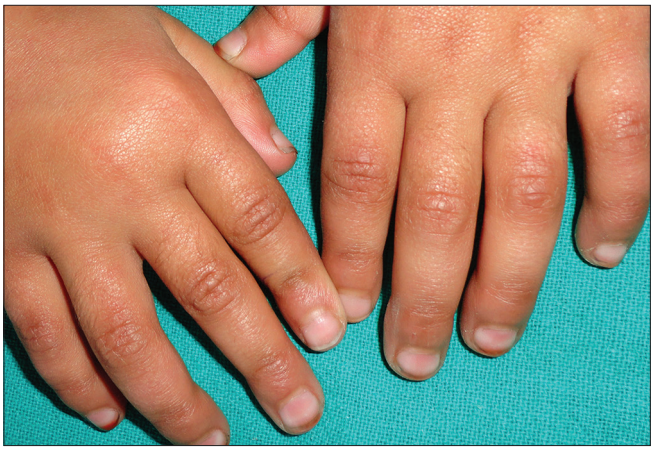

Figure 2: Broad distal phallanges

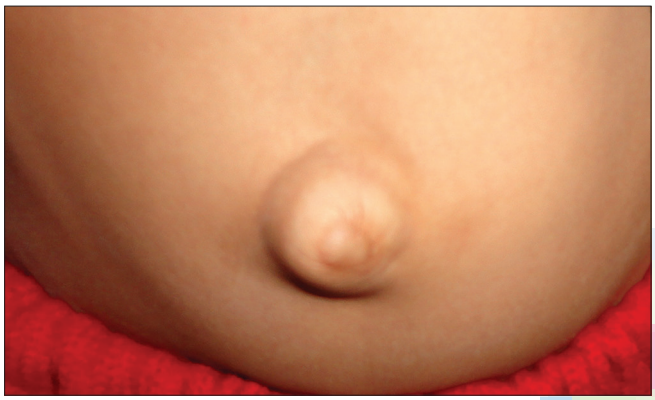

Figure 3: Umblical hernia

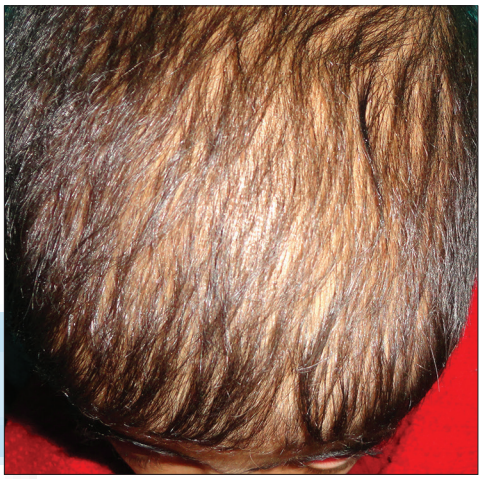

Figure 4: Fine scalp hair

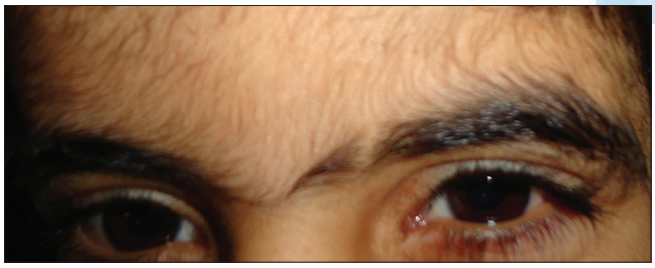

Figure 5: Facial hypertrichosis with dense eyebrows

phalanges. Short phalanges, metacarpals or metatarsals are frequent. Scoliosis is present in a few patients.

Major motor milestones are usually attained normally, but there is usually a severe impairment of language. Several patients never develop any speech. These patients usually have a short attention span. Some patients present with autistic features.

Majority of these patients are epileptic. Seizures start at around 1–2 years of age and are usually progressive and resistant to medical treatment, usually requiring multiple anti-epileptic drugs.

Other features that have been described in these patients include:

- Umbilical hernias
- Inguinal hernias
- Cardiac defects (mitral valve regurgitation, double aortic arch)
- Vesico-ureteric reflux
- Cryptorchidism
- Mild dyslipidemias.

In patients with atypical phenotypes, several other conditions should be considered.[4] Coffin–Siris syndrome should be considered in the differential diagnosis.[5,6] It is characterized by mental retardation, sparse hair, coarse facial features, growth restriction and epilepsy, thus resembling NBS. Coffin–Siris Syndrome differs in the presence of severely hypoplastic or absent fifth nails with or without hypoplastic terminal phalanges. Furthermore, short metacarpals, broad terminal phalanges and prominent interphalangeal joints are not seen.

An integrated approach involving the dermatologist, clinical geneticist and radiologist is crucial for diagnostic definition of this rare condition.

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