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CASE REPORT

A case of Barber-Say syndrome in a male Japanese newborn

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Key Clinical Message

We reported a case of Barber-Say syndrome (BSS) in a Japanese newborn. Distinctive features of BSS were found; macrostomia, gingival dysplasia, cup-shaped low-set ears, wrinkling redundant skin, and hypertrichosis. Fundus showed subretinal drusenoid deposits, a novel finding of BSS. Genetic analysis is underway using next-generation genome sequencing and microarray analysis.

Keywords

Barber-Say syndrome, cutis laxa, macrostomia, subretinal drusenoid deposit.

Introduction

Barber-Say syndrome (BSS) is a very rare congenital disorder characterized by severe hypertrichosis, redundant skin, and facial dysmorphism (including macrostomia, ocular telecanthus, abnormal low-set ears, and bulbous nasal tip) [1]. In 1986, Say and Barber et al. [2] first described two brothers with unique congenital malformations, including macrostomia, cutis laxa, and transient hypogammaglobulinemia. As far as we know, only 13 cases of BSS have been reported worldwide since that time (clinical presentation shown in Table 1), and this is the first report involving a Japanese patient with BSS.

Case Report

Written informed consent was obtained from the patient's parents regarding publication of this case report and its accompanying images. The patient was born via vacuum extraction at term to a 28-year-old G1P0 mother and 29-year-old father. The pregnancy was uncomplicated. No abnormalities were detected by fetal ultrasonography. The parents were unrelated, healthy, and ethnically Japanese. Apgar scores were 9 and 9 at 1 and 5 min after birth, respectively. Family history was unremarkable. Because the initial physical examination revealed a markedly dysmorphic male, he was transferred to our neonatal intensive care unit by ambulance from the local obstetric hospital.

His birth weight was 3390 g (81st percentile), length 50.4 cm (71st percentile), and head circumference 31.8 cm (11th percentile). He breathed irregularly and sometimes had episodes of apnea. Significant physical findings included macrostomia with a wide angle of the mouth, canthus dissociation, a broad nose root, low-set cup-shaped ears, and dark brown dry skin with redundant folds and severe hypertrichosis (Fig. 1). Gingival hyperplasia and a high-arched palate were also observed, but rudimentary nipples were not. He was found to have ambiguous genitalia, including a micropenis bent to the scrotum, hypospadias, and a defect of the glans foreskin. Serum examination showed no abnormalities. G-banded chromosome analysis revealed a 46,XY karyotype. Chest and abdominal X-ray were normal, and ultrasonography of the brain, heart, and abdomen revealed no remarkable findings. Oral feeding was difficult because the bilateral corners of the mouth remained open, therefore, tube feeding and peripheral infusion were started.

He passed the automated auditory brainstem response test on both sides. Funduscopic examination revealed

Table 1. Summary of clinical presentation of Barber-Say syndrome in the literature.

Case	Clinical presentation
1–2 Say et al. [2]	Two brothers hypertrichosis, atrophic skin, ectropion, growth retardation
3 Cesarino et al. [12]	Ablepharon, macrostomia, hypertrichosis, redundant skin. Psychomotor retardation
4 David et al. [13]	Ectropion, macrostomia, redundant skin, hypoplastic nipples, abnormal ears, hypertelorism
5 Matinez et al. [10]	A child born to a consanguineous parents hypertrichosis, macrostomia, ectropion, and atrophic skin.
6 Sod et al. [4]	Macrostomia, hypertelorism, redundant skin, heypertrichosis without ectropion
7 Mazzanti et al. [6]	Redundant skin, ectropion, bulbous nose, macrostomia, absence of mammary glands
8–9 Dinulos et al. [9]	Mother to son transmission of Barber-Say syndrome hypertrichosis, redundant skin, small ears hearing loss
10 Haensel et al. [5]	Hypertrichosis, telecanthus, cup-shaped ears microblepharon, hearing impairment, mental retardation, redundant skin
11–12 Roche et al. [1]	Father and daughter: hypertrichosis, low-set ears, ectropion, macrostomia, redundant skin
13 Martins et al. [8]	Macrostomia gingival fibromatosis, hypoplastic nipples, hypertrichosis, ectropion, and redundant skin

bilateral subretinal yellowish-white plaques similar in appearance to drusen (Fig. 2). The plaques were not seen in and around the macula region. Erosions with leachate to areas of friction between the wrinkles of the skin were found in the groin and axilla. These skin lesions were improved by the treatment with wound protection dressing for the erosion and oil spray for water-repellent. Bottle feeding was eventually successful using nipples designed for patients with a cleft palate and by holding the corners of the mouth by hand. Electrical encephalogram on day of life 9 was normal. Brain magnetic resonance imaging (MRI) on day of life 13 revealed mild dilatation of the bilateral lateral ventricles. He was discharged on day of life 15.

At 3 months of age, his weight gain was good, and serum immunoglobulin remained normal.

Discussion

The key symptoms in this case (macrostomia, cutis laxa, hypertrichosis, etc.) were distinctive, therefore, the diagnosis of BSS was rapidly made by searching both the Pub-Med database (http://www.ncbi.nlm.nih.gov/pubmed) and the University of Ryukyu Database for Malformation Syndromes (http://becomerich.lab.u-ryukyu.ac.jp/). Of note, Ablepharon-Macrostomia Syndrome (AMS) is similar to BSS. AMS is also characterized by distinctive malformations, including ablepharon or microblepharon, "fish-like" mouth (macrostomia), abnormal ears, rudi-

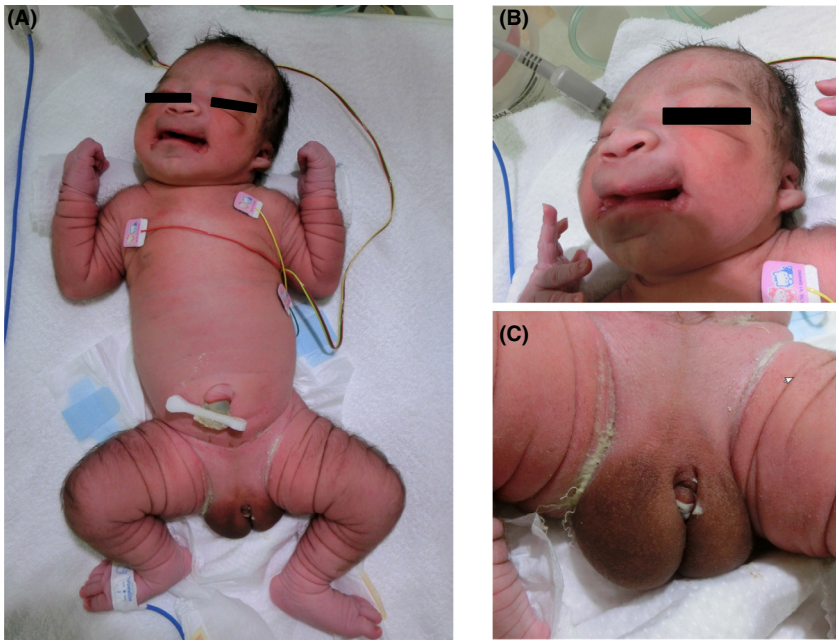

Figure 1. Clinical photographs at birth, published with parental permission. (A) Wrinkling of the skin is marked in the limbs; (B) macrostomia with unfused lateral commissures and broad ala of the nose are notable; (C) micropenis is buried in the scrotum.

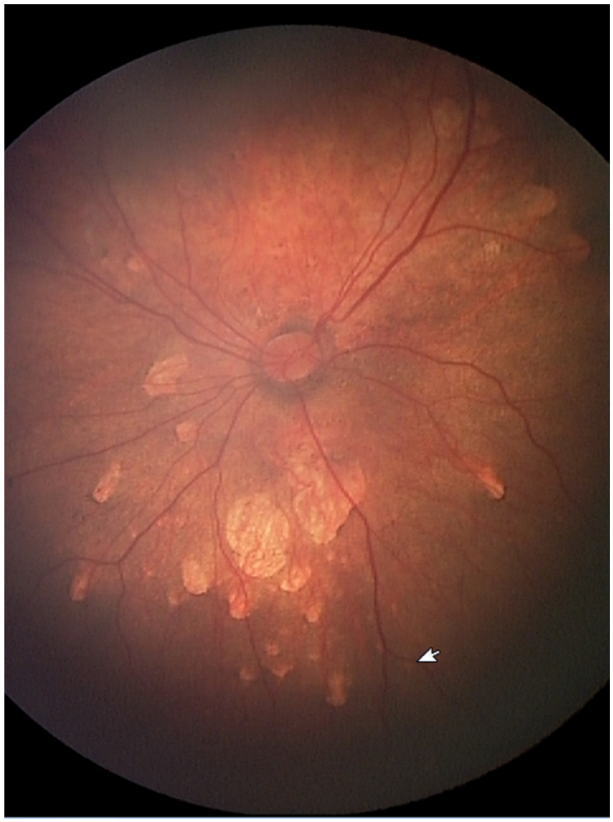

Figure 2. The fundus shows many yellow-white plaques in the subretinal region.

mentary nipples, redundant dry skin, and ambiguous genitalia [3]. AMS is also very rare, and fewer than 20 patients have been reported to date. Hypertrichosis is often seen in BSS, and a lack of lanugo is seen in AMS. As another clinical differential point, ectropion of the eyelids is a hallmark of BSS, whereas ablepharon or microblepharon is a hallmark of AMS. However, a BSS patient without ectropion (as with the present patient) has been previously reported [4]. Furthermore, a BSS patient with microblepharon has also been described [5]. Therefore, it is possible that BSS and AMS may derive from defective regulation of the same or similar genes [6].

Post-discharge, this patient has been followed by specialists, including an oral surgeon, a dermatologist, an ophthalmologist, and a plastic surgeon. He requires permanent skin care for eczema and erosions between the redundant skin folds. The corners of his mouth require plastic surgery, and the gingival dysplasia will require treatment from an orthodontist in the future. Psychomotor retardation is common with BSS [1, 2], and careful neurological follow-up is required due to the small head circumference and the dilatation of the bilateral lateral ventricles seen on MRI.

The subretinal drusenoid deposits are a unique feature in this case. These findings are different from those in retinitis pimentosa, and likely to be fatty deposits, such as those found in Coats' Disease [7]. The pathological significance of these lesions remains uncertain, and ophthalmology has been consulted concerning this finding.

Unfortunately, the etiology of BSS remains unclear. Histological analyses of the skin and gingival tissue revealed a lack of elastic fibers, supporting the suggestion that BSS is related to ectodermal dysplasia [8]. Some reports of familial BSS have indicated an autosomal dominant inheritance [1, 9]. On the other hand, one case has been reported in which the parents of child with BSS were consanguineous, suggesting autosomal recessive inheritance [10]. The causative gene or chromosome of BSS remains unknown. Only one case of AMS in a patient with chromosome 18q abnormalities has been reported, but that study was not conclusive [11]. In the present patient, gene analysis by microarray and next-generation sequencing is planned, partly due to the desire of his parents to conceive another child.

In conclusion, a new case of BSS was reported. A close follow-up for his various complications is ongoing. Further genetic analysis is necessary in order to better understand the incidence of this disease, to aid in the interdisciplinary treatment approach, and to counsel his parents regarding future childbearing.

Conflict of Interest

None declared.

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