CASE REPORT

Bosma Arhinia Microphthalmia Syndrome [BAMS] : A Case Report

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ABSTRACT :

Bosma Arhinia Micropthalmia Syndrome [BAMS] is an extremely rare genetic syndrome with characteristic major features of complete absence or hypoplastic nose, eye defect and absent sexual maturation. BAMS is usually caused by mutations in the SMCHD1 Gene. Fewer than 50 cases of BAMS have been reported in the literature.

Herein we report a case of BAMS in newborn with classical features of underdeveloped nose, bilateral choanal atresia, bilateral coloboma, cleft palate, undescended testis and micropenis.

Keywords : Hypoplastic nose, Micropenis, Coloboma, choanal atresia

INTRODUCTION :

Bosma Arhinia Micropthalmia Syndrome [BAMS] is an extremely rare and striking genetic disorder with fewer than 50 case reports and series. Bosma arhinia microphthalmia syndrome (Bosma) describes an extremely rare constellation of findings characterized by congenital arhinia associated with microphthamia, colobomas, hypogonadism but normal brain structure and intact intellect. Brasseur et al.[1] tabulated the clinical findings from 14 reported BAMS patients and suggested that the criteria for BAMS should include arhinia, midface hypoplasia (hypoplastic maxilla), and normal cognition, as well as hypogonadotropic hypogonadism in males. Microphthalmia with or without coloboma, high-arched palate, anosmia, absent paranasal sinuses, and absent olfactory bulbs would also be important findings.

Bosma et al.[2] delineated a syndrome affecting two unrelated males with congenital arihinia or severe hypoplasia of the nose, eyes defects, palatal abnormalities, deficient taste and smell, micropenis with cryptorchidism, and normal intelligence. During embryonic development, the nasal placodes form 28 days after conception shortly after the optic vesicles makes contact with the overlying surface ectoderm at 26–27 days, and both layers invaginate to form the eyes between34 and 44 days. Mice with homozygous mutations of Pax6, manifest underdevelopment of ocular and nasal structures, and a network of developmentally regulated genes function downstream of Pax6 to form nasal, ocular, and pituitary structures. These genes represent candidate genes for this disorder, and familial recurrence of Bosma syndrome has been reported to occur.

BAMS is caused by mutations in Structural maintenance of chromosomes flexible hinge domain-containing 1 (SMCHD1) gene that occur in the egg or sperm so that it is not inherited from parents. Changes in this gene may lead to abnormal development of face and head and because of abnormal nasal development may affect gonadotropic releasing hormone { Gn RH} which could explain hypogonadotropic hypogonadism in BAMS patients[3].

Gordon et al[4]. performed whole exome sequencing and/or Sanger sequencing in 14 probands with arhinia. They identified mutations in the

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SMCHD1 gene in all 14 probands. The mutations were shown to have occurred de novo in the 11 families for which DNA was available from the parents; all occurred at highly conserved residues within the ATPase domain and none was found in public variant databases. Functional analysis by Gordon et al. (2017) was consistent with gain-of-function or neomorphic activity by the BAMS-associated missense variants.

In BAMS, Arhinia can be diagnosed prenatally. Diagnosis of BAMS should need a team of a medical geneticist, pediatrician, or other pediatric subspecialist. Molecular genetic testing to specific confirmation changes in the SMCHD1 gene is available at specialized laboratories[4]. Herein we report a case of BAMS with classical features of this syndrome.

CASE HISTORY :

A 23 year old female, non-consanguineous marriage, primigravida, came to the obstetric department of Gangori hospital attached to SMS Medical College, Jaipur for routine antenatal check-up. No previous history of fever, rash or teratogenic drug consumption during pregnancy and had attended antenatal check-ups regularly. TORCH screen, HIV and hepatitis B surface antigen (HBs Ag) test results were negative. Ultrasound was done as a routine, no abnormalities have been detected. Later on a spontaneous vaginal delivery occurred at 33th week gestation yielded a malformed newborn 1.200kg weight with severe hypoplastic nose and respiratory distress.

On external examination small head size [head circumference: 26cm], Bilateral choanal atresia with hypoplastic nose with cleft palate with right sided undescended testis with small penis [extended length: 1.2cm] [Figure 1,2,3], abdomen was distended but soft. Due to respiratory failure, baby was to put on ventilator. As the newborn was not stable vitally so it was difficult to operate for bilateral choanal atresia.

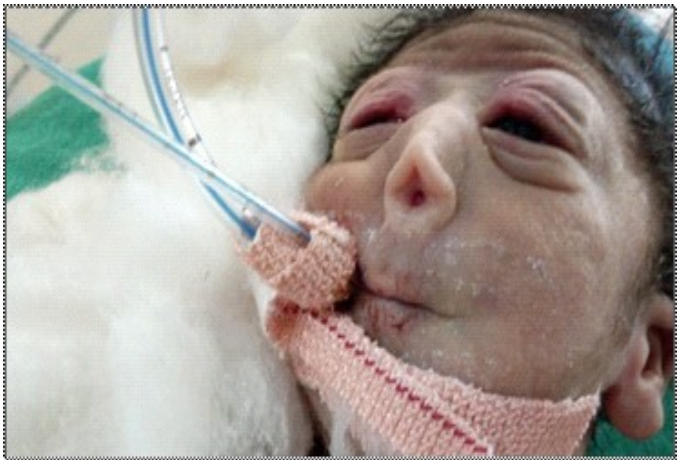

Figure 1 : Showing underdevelopment nose with coanal atresia

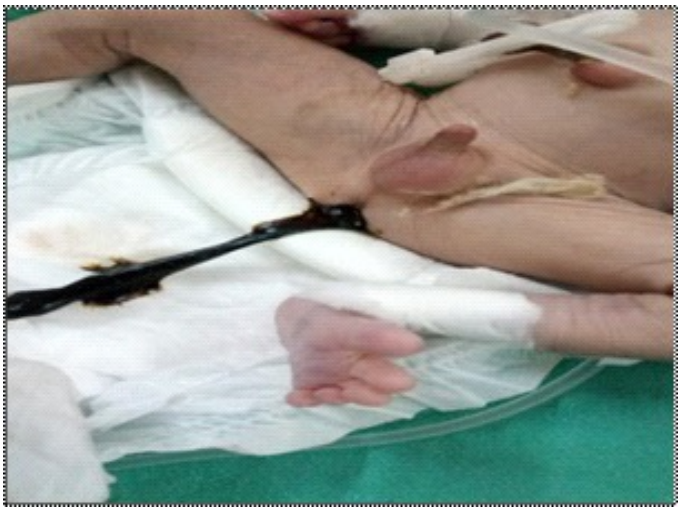

Figure 2 : Showing underdevelopment genitals

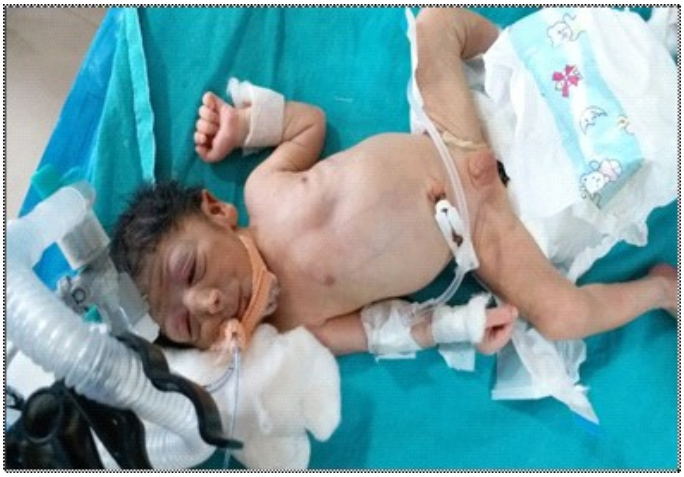

Figure 3 : Full image of baby

On ophthalmic examination bilateral coloboma was found. Ultrasonography of whole abdomen was done where right testis was not visualized and in brain ultrasound semilobar holoprosencephaly was found. TORCH profile was negative. Karyotyping was negative. Baby was expired on day 4 of life due to sepsis, disseminated intravascular coagulation, respiratory failure and shock.

DISCUSSION :

Bosma Arhinia Micropthmia Syndrome is a complex congenital extremely rare genetic disorder. Synonyms of Bosma Arhinia Microphthalmia Syndrome are Gifford-Bosma syndrome, Bosma syndrome, Ruprecht Majewski syndrome, Arhinia, choanal atresia, microphthalmia, and hypogonadotropic hypogonadism and BAM syndrome.

Shaw et al[5]. Summarized the clinical findings in 40 patients from 38 families with arhinia. All affected individuals had complete arhinia, accompanied in most cases by other craniofacial abnormalities, including high-arched or cleft palate, absent paranasal sinuses, hypoplastic maxilla, nasolacrimal duct stenosis or atresia, and choanal atresia. Ocular phenotypes included anophthalmia or microphthalmia (77%), uveal coloboma (79%) and cataract (53%), and 6 patients had normal eye anatomy and vision. Dysmorphic pinnae or low-set ears were seen in 41%. of 31 assessable subjects (22 male and 9 female), 97 % demonstrated hypogonadotropic hypogonadism (HH), and the 7 subjects for whom brain MRI data were available had no olfactory structures. SMCHD1 have an important role in epigenetic silencing and normal mammalian development. SMCHD 1 mutations cause facioscapulohumeral muscular dystrophy type 2 (FSHD2) lead to loss of function epigenetic mechanism. While missense mutations in the epigenetic regulator SMCHD1 mapping to the extended ATPase domain of the encoded protein cause BAMS also.

Prenatal diagnosis of nasal aplasia in a male with associated microphthalmia with microcornea was reported by Cusick et al[6]. [2000], and Olsen et al[7]. [2001] reported prenatal diagnosis of a female with nasal aplasia and bilateral iris colobomata with hypertelorism. Mc Glone[8] [2003] reported a male with arhinia, rightsided optic atrophy, single central incisor, hypogonadotropic hypogonadism, micropenis with cryptorchidism and described associated findings in 27 reported cases, and by 2005 there were 30 reported cases [Shino et al[9]., 2005].

In our case we found all major features of BAMS. These major features were facial and head abnormality including microcephaly, cleft palate, severe hypoplastic nose, bilateral choanal atresia and sex immaturityincludes hypogonadotropic hypogonadism, micropenis and undesendedtestis and in eyes abnormalities bilateral coloboma were present[2,3]. Karyotyping of baby was negative.

CONCLUSION :

BAMS is a rare genetic syndrome and arhinia can be diagnosed prenatally. We should also aware classical feature of underdeveloped nose, bilateral choanal atresia, bilateral coloboma, cleft palate, undescended testis and micropenis. Diagnosis of BAMS should need a team of a medical geneticist, pediatrician, or otherpediatric subspecialist. Parents should be counselled about the outcome of child.

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