Prenatal Diagnosis of Binder Phenotype and their outcomes - Insights from a case series

Brinda Sabu, Dhanya R Shenoy, Vidyalekshmy R, Department of Maternal Fetal Medicine, KIMSHEALTH, Trivandrum, India

INTRODUCTION

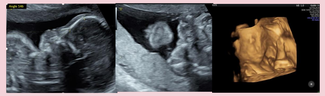
- Binder facies or Maxillo-Nasal Dysostosis is a a rare congenital malformation of the anterior part of the maxilla and nasal complex.
- In 1962, Binder described the condition maxillo-nasal dysostosis (defective ossification of nasomaxillary complex) characterized by a short nose with flat bridge, a short columella, an acute nasolabial angle, perialar flatness, a convex upper lip, and "reverse overbite" (or class III malocclusion). Today, Binder facies is considered to be a heterogeneous phenotype with multifactorial origin rather than a single nosologic entity.
- Due to its rarity, only few case reports exist which outlines the prenatal diagnosis, management and prognosis of fetuses with Binder facies and controversy still exists whether to define it as syndrome or phenotype.
- Here we present 5 cases of Binders phenotype detected antenatally, their management and outcome which ended in healthy outcomes with normal neurodevelopment in 4 babies and termination of one pregnancy

OBJECTIVES & METHODOLOGY

- To provide an insight into the management and outcome of prenatally diagnosed Binder phenotype
- The Ultrasound features of Binder phenotype are midfacial hypoplasia with verticalized nasal bones, short columella with flattened tip and alar wings, and the naso-frontal angle(NFA) measuring >140 degrees. These Ultrasound measurements in 2D and 3D were done on the 5 fetuses with Binder profile, and were compared with postnatal phenotype.

CASE REPORTS

Case 1- 38 yr-old third gravida with unremarkable obstetric and past history other than intractable vcomiting, diagnosed to have isolated Binder phenotype at 23 weeks. Her pregnancy went onto term with no complications and she delivered female baby 2600g by Cesarean section. Currently the child is 1.5 years old and is doing well.

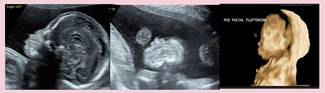


Antenatal 2D USS with flattened midfacial profile (Fig 1), short columella(Fig 2), 3D USS showing face view from front(Fig 3)

Postnatal- Immediate neonatal appearance (Fig 4), Appearance at 1.5 yrs age(Fig 5)

Images & photos shared with informed consent

Case 2- 27 yr-old second gravida with low HCG and Gestational diabetes, diagnosed to have Isolated Binder ohenotype at 18weeks, and fetal growth restriction at 33weeks, closely followed till delivery & delivered female baby 2710g. Postnatally Binder's facies was confirmed, there was no associated abnormalities and currently the child is 1 yr old with normal neurodevelopment.



Antenatal 2D USS with flattened midfacial profile (Fig 6), short columella(Fig 7), 3D USS showing face view from front(Fig 8)

Postnatal- Immediate neonatal appearance (Fig 9), Appearance at 1.5 yrs age(Fig 10)

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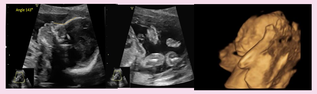
Case 3- 28 year old second gravida, a known case of connective tissue disorder, ANA positive, anti Sm Ab strong positive was diagnosed to have Binder phenotype for the fetus at 19 weeks. With close surveillance she progressed to 36weeks and delivered a female baby of weight 2310g. Postnatally, the baby had subtle features of isolated Binder phenotype and is currently 1 year old and doing well.



Antenatal 2D USS with flattened midfacial profile (Fig 11), short columella(Fig 12), 3D USS showing face view from front(Fig 13)

Postnatal- Immediate neonatal appearance (Fig 14), Appearance at 1.5 yrs age(Fig 15)

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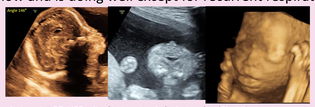
Case 4- 24 y- old primi, a known case of Overlap syndrome, on Tacrolimus diagnosed to have Binder phenotype for the fetus at 18weeks with hydrops, underwent Medical termination of pregnancy in view of active connective tissue disease & hydrops. Genetic Chromosomal microarray was done which was normal.

Refused sharing ultrasound images of the fetus

Case 5- 32 yr-old second gravida with history of subclinical hypothyroidism, migraine and bronchial asthma, with low HCG, diagnosed with Binder phenotype at 19weeks with mild hypertelorism, polyhydramnios went on to deliver a term male baby of weight 2890g. Postnatally confirmed Binder phenotype. The baby is 2 years old now and is doing well except for recurrent respiratory infections.



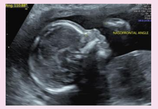
Antenatal 2D USS with flattened midfacial profile (Fig 11), short columella(Fig 12), 3D USS showing face view from front(Fig 13)

Postnatal- Immediate neonatal appearance (Fig 14), Appearance at 1.5 yrs age(Fig 15)

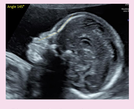
Images & photo shared with informed consent

DISCUSSION

- Binder phenotype is a developmental disorder of the anterior part of the maxilla and nasal complex.
- It is a rare congenital malformation with multifactorial origin, but the true etiology is unclear
- It is caused by a growth disturbance in the prosencephalic induction centre
- Among all fetuses with Binder phenotype, the diagnosis was physiognomy (I fetus), probable Vit K deficiency (1 fetus) and connective tissue disorder (2 fetuses) and unexplained in 1 pregnancy, thus demonstrating the heterogenic etiology of Binder phenotype.
- One pregnancy underwent termination as the parents were anxious and the mother's connective disease status was active with intake of multiple medications.
- Among those who continued pregnancy, postnatally no associated abnormalities were found and currently the age of the children ranges between 1 to 3 years with normal neurodevelopment.



Normal facial profile view <140 degrees



Binder's facies with abnormal frontonasal angle >140 degrees

Etiology of Binder's facies

- **Isolated Binder's facies**
- **Associated with Chondrodysplasia Punctata**
- Chromosomal abnormalities eg.Trisomy 21
- Metabolic abnormalities like Zellweger syndrome
- Autoimmune maternal disorders such as SLE
- Abnormal Vit K metabolism
  - a) Inherited causes eg. Xp22.3
  - b) Extrinsic factors
    - -Prenatal exposure to phenytoin, alcohol, coumarin derivatives
    - -Maternal chronic diseases with vitamin K deficiency eg. untreated Coeliac disease, Secondary Short Bowel Syndrome or digestive malabsorption or intractable vomiting of early pregnancy

MANAGEMENT

- Once the diagnosis of Binder's phenotype is made in the midsagittal and coronal views of the fetal face, a detailed and meticulous evaluation of the fetus is done with a special focus on the heart and the skeletal system.
- 3D imaging complements the 2-dimensional imaging findings.
- MRI imaging can provide added information if skeletal defects are suspected.
- A comprehensive review of antenatal and pre-conception history such as comorbidities like hepatic disease, chronic malabsorption syndromes and connective tissue disorders , intractable vomiting, intake of teratogens like alcohol, warfarin etc should be embarked.
- Physiognomy which is the normal familial appearance should be considered before concluding whether the observed feature is normal or pathological.
- Invasive testing (Amniocentesis for Chromosomal microarray) is advised as it identifies common chromosomal abnormalities and microdeletion
- Additional blood tests for hepatic conditions, Vit K deficiency and drug assays for chronic conditions are recommended as a normal result gives solace to the parents.
- Counselling by a multi-disciplinary team consisting of the primary obstetrician, perinatologist, fetal medicine specialist, and neonatologist is pertinent and may need multiple sessions to reduce the anxiety of the parents and family.
- Serial USG to monitor, growth/liquor and any evolving pathologies should be done.
- Delivery should be planned in a tertiary care centre as the neonate may experience immediate respiratory compromise. Mode of delivery is based on Obstetric indication.
- A detailed postnatal evaluation and liaison with an orthodontist/ oromaxillary surgeon is advised.

To Summarise

- ➢Diagnosis of Binder's phenotype & other facial dysmorphism bring a lot of apprehension & agony in the parents
- ➢Once diagnosed, a detailed evaluation of the fetus is warranted with focus on the heart & skeletal system.
- ➢Isolated Binder's phenotype carries a favourable outcome.
- ➢Physiognomy (normal familial appearance) to be considered.
  ➢Amniocentesis is advisable.
- Accurate diagnosis, adequate testing & dedicated counselling will help prevent needless termination of pregnancies