

# Bohring-opitz syndrome - A case of a rare genetic disorder

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### SUMMARY

The diagnostic challenge of Bohrning-Opitz Syndrome, a rare genetic disorder has haunted clinicians for ages. Our patient was born at term via caesarean-section with a birth weight of 1.95 kilograms. She had mild laryngomalacia, gastroesophageal reflux disease and seizures. Physical signs included microcephaly, hemangioma, low set ears, cleft palate, micrognathia and the typical BOS posture. Chromosomal analysis showed 46 xx -Bohrning-Opitz Syndrome overlapped with C- syndrome. Goal-directed holistic care with integration of parent/carer training was started very early. She succumbed to a Respiratory-Syncytial-Virus and Pseudomonas pneumonia complicated with sepsis at the age of two years and 11 months.

### KEY WORDS:

*Bohrning-opitz syndrome, genetic, dysmorphism, gene mutation*

### INTRODUCTION

Bohring-Opitz Syndrome (OMIM BOHRING-OPITZ SYNDROME; BOPS #605039), is a sporadic, rare genetic disorder with an unknown aetiology.<sup>1</sup> Cardinal symptoms include feeding difficulties, Intra Uterine Growth Retardation, microcephaly, trigonocephaly, micro/retrognathia, flammeus nevus, prominent eyes, abnormal palate, and BOS posture (posture with shoulders externally rotated and adducted, elbows and wrists flexed in ulnar deviation, and ulnar deviation of the metacarpophalangeal joints).<sup>2</sup> Approximately 50% of Bohrning-Opitz syndrome cases have been attributed to de-novo truncating mutations in the ASXL1 gene.<sup>1,3</sup> The disease is often fatal in early childhood, due to obstructive apnoea and unexplained bradycardia.<sup>4</sup> Approximately 31 cases have been reported worldwide.<sup>1</sup> Any addition to the limited studies done on Bohrning-Opitz Syndrome will greatly benefit the medical fraternity.

### CASE PRESENTATION

Our three-year-old patient was born at 38 weeks of gestation on 20th September 2011 via elective (two previous scars) lower segment caesarean section with an Apgar score 8/9. She was the third child of a non-consanguineous Malay couple with the other children being normal. The pregnancy was complicated with Gestational Diabetes on diet control and her birth weight was 1.95 kilograms which was small for gestation age.

Clinically she had mild upper airway obstruction causing stertor with mild laryngomalacia, moderately severe feeding

intolerance with poor suckling reflex and underlying gastroesophageal reflux disease. She also had recurrent generalized seizures.

On examination, we noted dysmorphism. Her craniofacial features include microcephaly with small anterior fontanelle, hemangioma over the forehead, low set ears, cleft palate and micrognathia. Ophthalmic findings were retinopathy with left eye corneal ulcer. Cardiovascular findings were atrial septal defect with patent ductus arteriosus. Musculoskeletal deformities were left hand pre-axial polydactyl, a typical BOS posture, bilateral developmental dysplasia of the hip, and sacral pit with tuft of hair. In addition to that, she had generalized hyperlaxity of joints with no obvious subluxation or dislocations.

### INVESTIGATIONS

She was investigated for TORCHES infection which was negative. Her seizures warranted an EEG, this showed intermittent focal background slowing and epileptiform pattern over both occipital regions suggestive of occipital epilepsy. MRI brain which was done in December 2011 showed hypoplasia of the Corpus Callosum. Flexible Naso-Pharyngo-Laryngoscope (FNPLS) indicated features in keeping with tubular epiglottis with evidence of inflammation and reflux. Echocardiogram showed an ejection fraction of 60% with an atrial septal defect and patent ductus arteriosus. The National Institute of Medical Research Malaysia concluded that the chromosomal analysis showed features in keeping with 46 xx-Bohrning Opitz Syndrome overlapped with C syndrome.

### TREATMENT

Upon diagnosis, goal directed therapy was initiated immediately. Her seizures were controlled with sodium valproate. The recurrent lung infections were managed with inpatient intravenous antibiotic therapy and assisted ventilation. Feeding was initially started via a nasogastric tube which was later converted to a percutaneous endoscopic gastrostomy tube. Nutrition was optimized via advanced formula feeds with vitamin supplementation. Occupational and physiotherapy was started to optimize activities of daily living and limb range of motion. Holistic care with integration of parent/carer training was started as early as possible to empower the family to adequately care for the patient.

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### OUTCOME AND FOLLOW-UP

Our patient had recurrent aspiration pneumonia requiring inpatient therapy, which resolved on most occasions. However, she succumbed to a Respiratory Syncytial Virus and Pseudomonas pneumonia complicated with sepsis on 26 August 2014 at the age of three years and 11 months.

### DISCUSSION

After consultation with a geneticist, it was concluded that the chromosomal analysis in addition to the clinical features showed that our patient had 46 xx-Bohring Opitz Syndrome overlapped with C syndrome. C syndrome or Opitz Trigonoccephaly Syndrome usually has overlapping features with BOS and is caused by mutations in the TACTILE gene.<sup>2</sup>

Our patient had key diagnostic features of Bohrning Opitz Syndrome which were microcephaly, palatal abnormalities, facial flammeous nevus, low-set ears and a typical BOS posture.<sup>2</sup> Our patient also had hypoplasia of the corpus callosum, retinopathy, failure to thrive and GERD which is fairly consistent with many other cases of Bohrning-Opitz Syndrome reported so far.<sup>5</sup> Our patient had an atrial septal defect with patent ductus arteriosus, consistent with the fact that cardiac abnormalities are seen in almost half of patients with this condition.<sup>2</sup>

Emphasis on parent/carer education and training allowed them to be involved in every stage of care. Mortality rates remain very high in this condition and are most commonly

attributed to infections<sup>2</sup> as was the case in our patient. The take home learning experience will undoubtedly be the management plan which focused on full family empowerment and involvement. This allowed excellent doctor patient/family relationship and significantly helped in the bereavement period.

### CONCLUSION

Next generation chromosomal analysis technology and sharing of evidence based knowledge on the condition, will enable clinicians from developing countries such as Malaysia to overcome the diagnostic challenge of Bohrning-Opitz Syndrome and offer expert therapy to patients.

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