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CASE REPORT

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Pfeiffer Syndrome type 2; A case report of cranio-orbitofaciostenosis with bilateral choanal atresia at Muhimbili National Hospital, Tanzania

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Abstract

Pfeiffer syndrome is a rare genetic disorder with heterogenous phenotype and prognosis. Due to its diverse clinical presentation, it can easily be misdiagnosed. Where genetic testing still remains a challenge, antenatal sonogram can aid in early diagnosis. The cranioorbito-faciostenosis demands aggressive management to permit survival instead of uniform early demise.

KEYWORDS

choanal atresia, cloverleaf shaped skull, Pfeiffer syndrome, proptosis

1 | BACKGROUND

Pfeiffer syndrome (PS) is a rare acrocephalosyndactyly syndrome that includes inherited anomalies of the head, feet, and hands originally described by Rudolf Pfeiffer in 1964.[1]

Due to the various clinical phenotypes, Cohen et al[2] described the three subtypes. Type 1 is also known as the "Classic" Pfeiffer syndrome described by Rudolf Pfeiffer who noticed the autosomal dominant inheritance pattern among families, and it is usually associated with a normal life span. Type 2 consists of "cloverleaf skull" due to extreme fusion of the skull bones, severe proptosis, finger and toe abnormalities, elbow ankylosis or synostosis. Type 3 is similar to type 2 except for the clover skull shaped deformity. Additionally, they have proptosis, visceral abnormalities (hydronephrosis, pelvic kidneys, and hypoplastic gallbladder), and severe neurological complication. To date, all cases of Type 2 and 3 have occurred sporadically, their overall prognosis being very poor with an early death. Mild variants tend to be familial and carry a relatively good prognosis.

It is caused by mutations in the fibroblast growth factor receptor (*FGFR*) genes, *FGFR1* (on chromosome 8p11.2-p11), and *FGFR2* (on chromosome 10q26) that promotes early maturation of bone cells in a developing embryo and the premature fusion of bones in the skull, hands, and feet.[2]

Pfeiffer syndrome has been found to be associated with anomalies of the upper airway which can lead to midface hypoplasia, secondary nasal obstruction, choanal atresia, and tracheal anomalies.[4-6] Eye features in severe forms include shallow orbits, severe proptosis, cyclotorsion of the orbits, strabismus, and optic nerve compression from increased intracranial pressure.[7]

There are few cases reported in African patients with other subtypes of Pfeiffer syndrome.[8] Since these babies have a

very short life span, early death occurs within a few days after birth due to underlying visceral malformations especially airway malformations. PS is a rare disorder with heterogenous clinical presentation, and it can easily be misdiagnosed. To the best of our knowledge, this is the first case to be reported from Tanzania.

2 | CASE PRESENTATION

We report a case of a newborn male baby delivered at 38 weeks of gestation age at Muhimbili National Hospital in Tanzania. His mother had a history of prolonged labor, and the baby had face presentation during delivery. She had also undergone multiple vaginal examinations due to poor progress of labor which necessitated delivery through caesarian section. At birth, the baby weighed 3.5 Kg (>90th centile), occipitofrontal circumference was 32 cm (10-25th centile), and length was 44cm (<10th centile). This was her first-born child, and both parents are phenotypically normal and nonconsanguineous.

On admission at our neonatal ward, the baby had difficulty in breathing, he was tachypneic, tachycardic and was receiving oxygen therapy through hood at 5L/min. He had passed urine and meconium within the first 24 hours of life, and bilateral choanal atresia was suspected when Ryle's tube size 8 French failed to pass through both nostrils.

He had a protruding forehead (cloverleaf shaped), craniosynostosis, premature closure of anterior and posterior fontanel, hypertelorism, bilateral proptosis and conjunctival hyperemia, (Figure 1) ptosis, fusion of the elbow joints, brachydactyly, inward deviation (varus deformity) of the big toes from other digits (Figure 2), and a high arched hard palate (Figure 3).

A full blood count was obtained which had normal findings; creatinine was 54.6 mmol/L, urea 5.3 mmol/L, sodium 139 mmol/L, potassium 4.5 mmol/L, and calcium 2.03 mmol/L; these values were within normal range.

Skull X-ray showed turricephaly (severe craniosynostoses) (Figure 4).

Cranial ultrasound revealed agenesis of corpus callosum, but otherwise he had a normal brain parenchyma, normal ventricles, no hydrocephalus, or herniation of brain contents. Echocardiography screening showed a moderate patent ductus arteriosus (PDA) of 4 millimeter.

Abdominal ultrasound revealed discrepancies in kidneys size and echogenicity. Right kidney was hyper echoic and measured 35 mm (small) while the left kidney was hypoechoic and measured 49 mm (enlarged). Other abdominal structures were normal.

Genetic testing was not done as it was not available in our setting.

He underwent an emergency bilateral choanal atresia release repair on the 2nd day of life. Bronchoscopy was not done during the surgery to look for underlying tracheal anomalies.

Postoperative management was mainly supportive. The baby was admitted in the general neonatal ward since we did not have a high dependent unit (HDU) or neonatal ICU for critical sick babies in our hospital during that time. His eyes were covered with an eye patch soaked with saline, and topical ciprofloxacin eye drops were instilled two to three times a day to prevent exposure keratitis. Antibiotics were given pre- and postoperatively as the risk of sepsis was high pertaining to the perinatal history and surgery. He was fed with expressed breastmilk through an orogastric tube to maintain optimum nutrition and growth and syrup furosemide 4 mg once daily to prevent pulmonary edema was given for the underlying congenital cardiac defect. He was followed up by pediatric neurosurgery, otorhinolaryngology, and ophthalmologists in the hospital.

Unfortunately, two days after the surgery the baby passed away due to severe respiratory distress and respiratory failure. The exact underlying cause of death was difficult to establish as multiple factors were involved from perinatal history of difficult labor to multiple organ involvement at birth that includes central nervous system, renal and cardiac and postoperative complications. Some possibilities could be

FIGURE 1 Cloverleaf shaped face with Proptosis

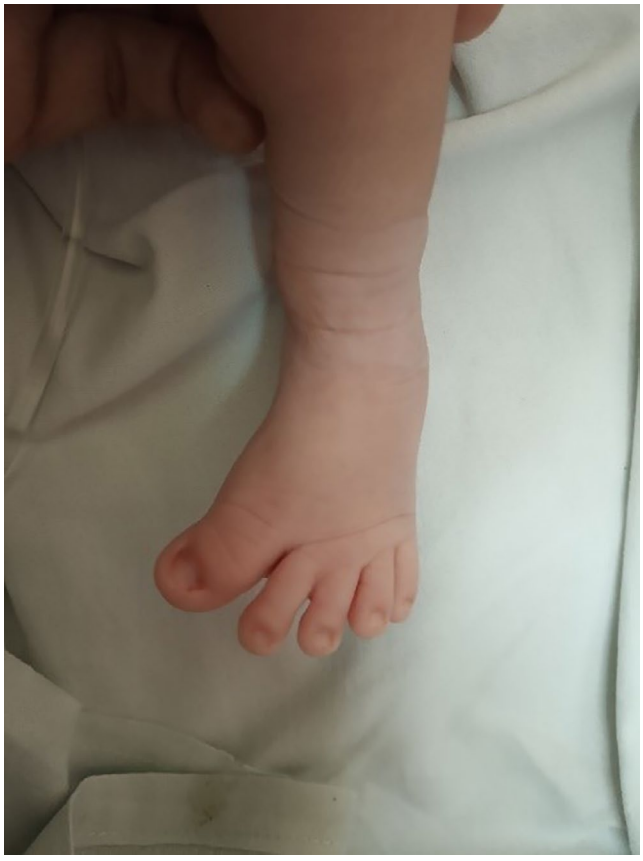

FIGURE 2 Varus deviation and Brachydactyly

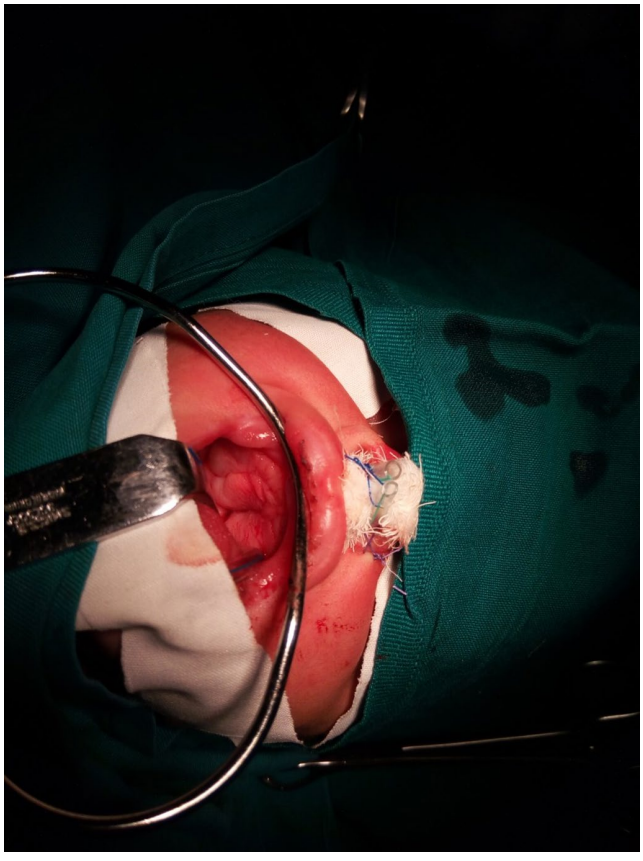

FIGURE 3 High arched palate

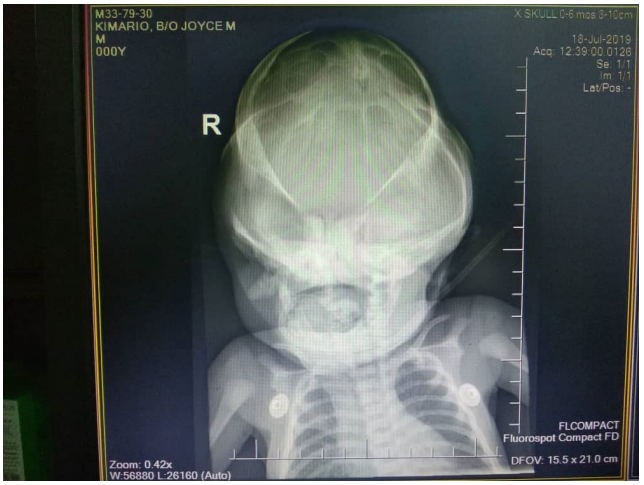

FIGURE 4 Turricephaly due premature fusion of all sutures

tracheal injury following extubation after the surgery (due to an underlying tracheal anomaly which we may have missed) and aspiration pneumonia.

3 | DISCUSSION

Our patient had clinical findings consistent with Pfeiffer syndrome (PS) type 2, which consists of cloverleaf skull deformity due to extensive craniosynostosis, agenesis of corpus callosum, hand and foot anomalies like elbow synostosis, brachydactyly, and varus deformities of the toes, with additional bilateral choanal atresia, cardiac and renal anomalies. PS type 2 has been reported with similar presentation in many literatures from the Western world.[7,9,10] However, Badoe et al[8] reported two cases of Pfeiffer syndrome subtype 3 from west Africa over a 10-year period indicating the rarity of this syndrome in African population. Due to its various clinical presentation, this can easily be missed and perhaps it is under reported.

Bilateral choanal atresia a rare developmental condition is associated with craniosynostosis syndromes like Apert, Pfeiffer, and Crouzon. In our patient, despite early repair and release of bilateral choanal atresia we still had an early death possibly due to other various underlying causes. Successful outcomes have been reported in some but it also depends on the type of the atresia.[5]

Pfeiffer syndrome has also been associated with other systemic anomalies like tracheobronchial tree anomalies, congenital heart defects, renal, aqueduct stenosis, hydrocephalus, cerebellar and brain stem herniation, low-set ears, external auditory canal stenosis or atresia and, unusually, hydronephrosis, pelvic kidney and hypoplastic gallbladder, micro phallus, cryptorchidism, growth and mental retardation[4,5,7] We also found cranial, cardiac, and renal involvement in our patient associated with this syndrome.

Pfeiffer et al[8] has reported three cases of congenital heart defects with this syndrome; these are ventricular septal defects, atrial septal defects, patent ductus arteriosus, infundibular, and valvular stenosis. The heterogenicity of congenital heart disease in these patients suggests that this disorder is variable and this correlates with our patient.

The ocular manifestations may be due to the pathological process or due to secondary complications of premature fusion of the skull bones. Common ophthalmic findings in severe forms of PS include shallow orbits, severe proptosis, cyclotorsion of the orbits, strabismus, and optic nerve compression from increased intracranial pressure. Severe proptosis and conjunctival hemorrhage were also found in our case which increases the risk of exposure keratitis and globe rupture.

Outcomes with surgical intervention are limited. Aim of the surgery is decompression of the brain and remodeling of the skull, expansion of the bony orbits to accommodate the globes with eyelid closure, and opening of the nasopharyngeal airways. Despite the timely intervention, death occurs due to postoperative complication like respiratory difficulty, arrhythmias, feeding difficulties, and temperature instability.[9] Our patient had an overall poor outcome as many factors were involved from perinatal insults as a result of difficult labor and delivery to multiple organ involvement and postoperative complications making it difficult to establish the underlying cause of death.

Many reports have described tracheal anomalies in Pfeiffer syndrome.[4,6] However, we did not do bronchoscopy in this child to look for tracheal anomalies, perhaps airway malformation and postextubation injury could have been a causes of respiratory failure in our patient. We recommend that whenever possible, bronchoscopy should be done to patients when there is a risk airway malformation.

Due to lack of resources, unavailability of a proper HDU, or neonatal ICU where close monitoring could have been done better, compounded with the various risk factors from our patient's clinical presentation, we faced many challenges in managing this baby.

Research on molecular genetics has shown familial linkage of Pfeiffer syndrome with mutation fibroblast growth factor receptor-1 (FGFR 1). Identical mutations in the fibroblast growth factor receptor gene have been reported in other craniosynostosis deformities like Crouzon and Jackson-Weiss syndrome resulting in variable expression with distinct phenotypes; nevertheless, they do not have hand and foot abnormalities like Pfeiffer syndrome.[3]

In Tanzania, genetic testing still remains a challenge, and most syndromes are diagnosed clinically. Antenatal sonogram especially 3D ultrasound is highly promising to detect these conditions early during pregnancy.[11] This will help with safe deliveries of these babies who sometimes may experience complications like malpresentation as in our case.

4 | CONCLUSION

The overall outcome depends on the clinical subtype of Pfeiffer syndrome. The prognosis in our patient was very poor due to various factors from labor complications to multiorgan involvement. Genetic counseling should be done to parents as familial cases have a risk of recurrence.

ACKNOWLEDGMENTS

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CONFLICT OF INTEREST

None declared.

AUTHORS CONTRIBUTIONS

ZK, JT, and IA: admitted the patient and followed up throughout the hospital stay. IA: prepared the manuscript. AZ, AM, HN, and KM: provided their expert opinion on the management and helped to do bedside imaging studies for the patient like echocardiography and ultrasounds. AA and RL: are surgeons who did the bilateral choanal atresia release repair.

CONSENT FOR PUBLICATION

Written informed consent was obtained from the patient's legal guardian (mother) for publication of this case report and the accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

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