CASE REPORT

Diagnosis of Pfeiffer Syndrome with Umbilical Hernia

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ABSTRACT

Pfeiffer syndrome (PS) is a form of acrocephalosyndactyly, a group of rare genetic syndromes, and is characterized by variable degrees of bicoronal craniosynostosis, variable hand and foot malformations and various other associated manifestations. Type I Pfeiffer syndrome is compatible with life. It is characterized by normal intelligence and a classic phenotype of craniosynostosis, broad thumbs, and syndactyly. Types II and III are sporadic in occurrence, with more severe involvement of the central nervous system (CNS) than in type I. Type II is associated with the classic cloverleaf-shaped skull. Neurologic compromise is common in both types II and III.

KEY WORDS: *Autoimmune Pfeiffer Syndrome (PS), Acrocephalosyndactyly, Craniosynostosis.*

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INTRODUCTION

Pfeiffer syndrome (PS) is a rare autosomal dominant congenital disorder, originally described by Pfeiffer in 1964, characterized by bicoronal craniosynostosis, midface deficiency, broad thumbs, big toes and partial variable soft tissue syndactyly of the hands and feet. Based on the severity of phenotype, Cohen proposed the division of Pfeiffer syndrome into 3 clinical subtypes.

Classic Pfeiffer syndrome, designated Type 1, involves individuals with mild manifestations, associated with normal neurological and intellectual development, generally has good outcome and can be found dominantly inherited. Type 2 consists of cloverleaf skull, broad hands and feet, severe exorbitism, central nervous system involvement, elbow ankylosis or synostosis. Type 3 is similar to type 2 but without the cloverleaf skull. Types 2 and 3 have poor prognosis due to severe neurological compromise and various visceral anomalies, and they generally result in early death. Till date, all cases of types 2 and 3 have only had sporadic occurrence.[1]

The diagnosis of Pfeiffer syndrome is challenging and need clinical, radiological exploration and genetic counseling. Radiological exploration can confirm the skeletal abnormalities and associated malformations.

After review of literature we diagnosed and reported the first child in our hospital at National Institute of Child Health Karachi with PS who had bicoronal craniosynostosis, bilateral broad thumbs and big toes, umbilical hernia and radio-humeral synostosis.

CASE

The patient in this case was a girl, born in February 2014, as the second child of a healthy 28-year-old mother and 32 year old father. The First baby child was a 3 year old healthy and normal boy. Second baby child is delivered through C-section at 38 weeks without any complications during pregnancy. The child referred to our hospital for skeletal survey with complains of proptosis, unable to extend elbow properly, unable to flex 2nd and 5th fingers of hands bilaterally.

On skeletal survey multiple craniofacial and skeletal abnormalities were detected as follow.

Bicoronal and sagittal synostosis, copper beaten skull, shallow orbital cavity, hypo plastic maxilla, umbilical hernia, bilateral symmetrical radio humeral synostosis, bowing of lower extremity, broad and medially deviated thumb with hypoplastic proximal phalanx, hypo plastic 1st metacarpal and middle phalanges of 2nd and 5th finger, broad and laterally deviated toe with hypoplastic proximal phalanx of 1st toe.

Figure 1. Photograph of patient's upper torso showing shallow orbits, medially deviated thumb and inability to flex 2nd and 5th finger.

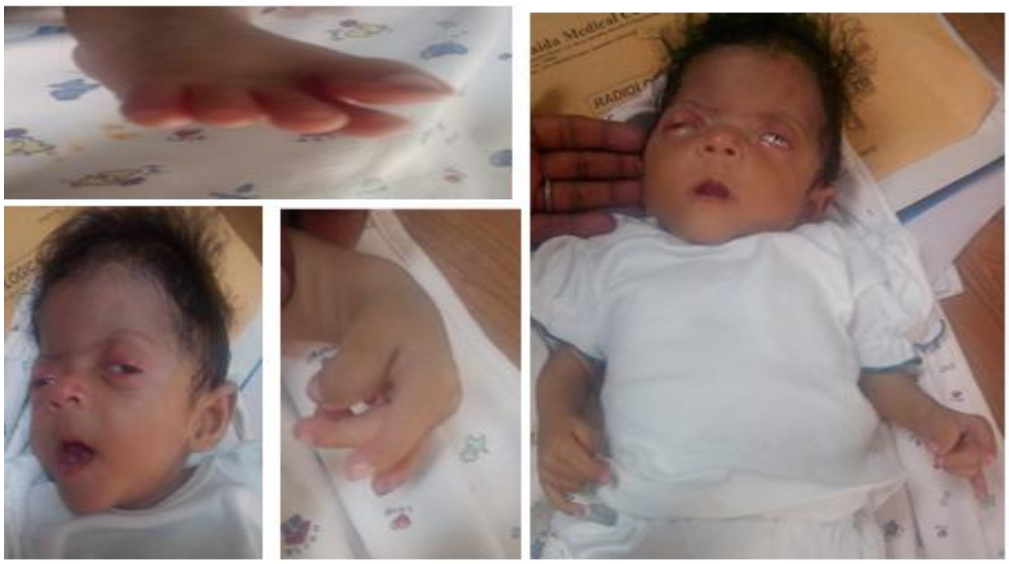
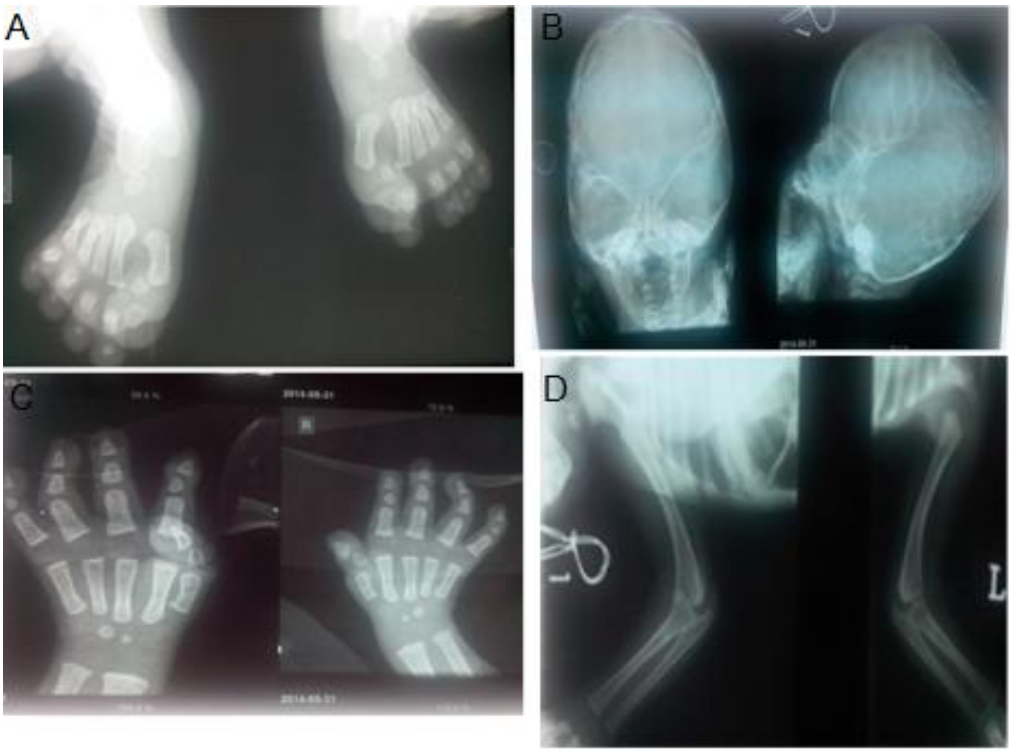
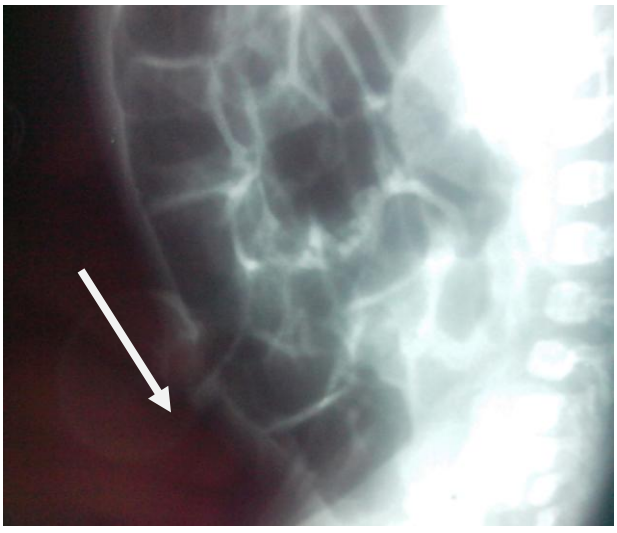


Figure 2. Radiograph of body parts.



A:Bilateral deviated toe with hypo plastic proximal phalanges
B: Synotosis with copper beaten skull, hypo plastic maxilla and shallow orbital cavities
C:Broad medially deviated thumb with hypo plastic 1st metacarpal and middle phalanges of the 2nd and 5th finger bilaterally
D:Bilateral symmetrical radio humeral synotosis

Figure 3. Lateral abdominal radiograph conned view shows umbilical hernia with herniated bowel loops (white arrow)



DISCUSSION

Pfeiffer syndrome characterized by premature fusion of cranial sutures that prevents the skull from growing normally and affects the shape of the head and face, resulting in brachycephaly, hypo plastic maxilla, shallow orbits, proptosis, exophthalmos accompanied with broad and deviated thumbs and big toes and sometimes elbow ankylosis.[2,3] Upper airway obstruction may be present in patients with midface hypoplasia and secondary nasal obstruction due to choanal atresia.[4] Pfeiffer syndrome also known as Acrocephalosyndactyly type V, Noack syndrome and Craniofacial-skeletal-dermatologic dysplasia. Cohen in 1993 classified this syndrome into 3 clinical subtypes.

Type 1 Pfeiffer or "classic" Pfeiffer syndrome involves individuals with mild manifestations including brachycephaly, midface hypoplasia, and finger and toes abnormalities. It is

associated with normal neurological and intellectual development, and generally has a good outcome. Type 2 consists of trilobated skull deformity (cloverleaf skull), extreme proptosis, finger and toes abnormalities, elbow ankylosis or synostosis, developmental delay and neurological complications. The cloverleaf skull can cause limited brain growth, and the extreme proptosis can cause severe visual impairments. Type 3 is similar to type 2 but without the cloverleaf skull.[5] In Pfeiffer types 2 and 3, there may be choanal anomalies, laryngotracheal abnormalities, hydrocephalus, seizures, sacrococcygeal anomalies, and increased risk of death.[6] Type I Pfeiffer syndrome is thought to be autosomal dominant, although often it may be the result of fresh mutations. Types II and III are sporadic. Type 1 Pfeiffer syndrome is caused by mutations in *FGFR1* (5%) or *FGFR2* (95%), whereas types 2 and 3 Pfeiffer syndrome are caused by mutations in *FGFR2* (100%) only.[7, 8]

Skull X Ray shows the major malformation of the cranium including coronal craniosynostosis, cloverleaf appearance of the skull with bulging in the temporal regions, a widely open sagittal suture. Indeed, cranio-facial CT scan with three-dimensional reconstruction shows these abnormalities better, because it provides direct visualization of the sutures of the cranial vault and shows the cranio-facial bony anatomy. X-rays of the feet and hand shows broad and short big toes and thumbs with incorrectly formed phalanges. X-rays of the upper limbs may show ankylosis of the elbows involving the radius, ulna and humerus. Transfontanellar Ultrasonography is the primary imaging technique in the newborn for detecting congenital hydrocephalus, which is the most common abnormality in Pfeiffer syndrome type II.[9] The prognosis depends on the severity of associated anomalies, mainly the severity of the central nervous system compromise. Patients with type 1 syndrome have, in general, a good prognosis. Patients with types 2 and 3 usually expire early in infant or childhood even though some may survive with aggressive medical and surgical management. Treatment of Pfeiffer syndrome require multidisciplinary management by neonatologists, pediatricians, specialists in orthopedics and plastic surgery, ophthalmologists and neurosurgeons.[10]

Pfeiffer syndrome (PS) is a form of acrocephalosyndactyly, a group of rare genetic syndromes. The diagnosis of Pfeiffer syndrome is challenging and need clinical, radiological exploration and genetic counseling. By diagnosing this entity with the help of non-invasive radiological modalities we can timely decides further management of this congenital anomaly as well as its outcomes.

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