

# CRANIOSYNOSTOSIS IN CARPENTER SYNDROME: RADIOLOGICAL CLUES TO A RARE DIAGNOSIS IN PAKISTAN

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## ABSTRACT

Carpenter syndrome is a rare autosomal recessive disorder with incidence of one case per one million live births. We report a case of a 2-month-old boy with Carpenter syndrome having dysmorphic facial features, cutaneous syndactyly, polydactyly and camptodactyly. The Skeletal survey revealed a peculiar tower-shaped skull and small hypoplastic maxilla. This case report serves as an educational resource and reference for the rare occurrence of Carpenter syndrome reported from Pakistan.

**Keywords:** Carpenter Syndrome, Craniosynostosis, Camptodactyly.

## Introduction

Carpenter syndrome, also known as acrocephalopoly syndactyly type II, is a rare genetic disorder caused by a mutation in the RAB23 gene.<sup>1</sup> This gene has a unique function playing a key role during embryonic life in heart and limb formation, neural tube closure, and is also involved with kinesin protein - a protein essential for cilia formation.<sup>2</sup> Carpenter syndrome follows autosomal recessive pattern of inheritance.<sup>1</sup> Its incidence is about one in one million live births.<sup>3</sup>

The term Carpenter syndrome was first coined by George Carpenter who reported craniosynostosis and polysyndactyly in two siblings and later, in 1909, reported a third affected sibling in a published case study.<sup>4</sup> Although this syndrome is rare in medical literature, additional phenotypes have been reported which typically include increased body weight and congenital heart anomalies.<sup>4</sup>

Carpenter syndrome encompasses a wide range of clinical features including congenital cardiac issues, developmental delays, intellectual disabilities, umbilical hernia, cryptorchidism, endocrinal abnormalities such

as hypothyroidism, molar agenesis, bone anomalies and recurrent respiratory infections.<sup>1,5</sup> However, the distinguishing features of carpenter syndrome include craniosynostosis which is particularly defined as premature cranial suture closure, brachydactyly which is abnormal shortening of the fingers or toes due to underdevelopment of the bones, syndactyly defined as fusion of the digits - typically cutaneous type, stunted growth and obesity.<sup>1</sup>

## Case Presentation

A 2-month-old baby from Karachi was referred to our hospital, National Institute of Child Health, largest tertiary care public sector pediatric hospital in Karachi. The child had unusual facial features noted since birth and developed bilateral inguinal hernia approximately at the age of one month.

On examination, the child had dysmorphic facial features with down slanting eyes, flat nasal bridge, small chin, high arched palate and low set ears (Fig.1).

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**Figure 1:** Showing dysmorphic features, down slanting palpebral fissure, high arched palate, low set ears.

Inspection of both hands and feet demonstrated multiple digital anomalies. There was cutaneous syndactyly involving several fingers and toes, with fusion of soft tissues but preservation of individual bony structures. Polydactyly was also noted, characterized by the

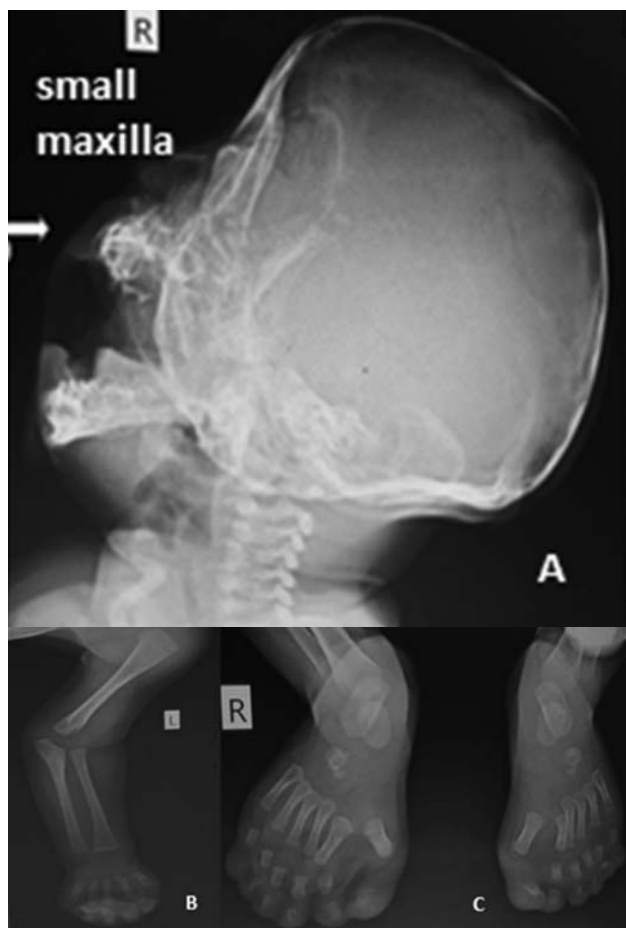
presence of extra digits on both sides. The digits also showed fixed flexion deformities consistent with camptodactyly (Fig.2). No limb length discrepancy or joint contractures were observed. Anthropometric measures revealed height of 50cm and weight of 4 kg.



**Figure 2:** Syndactyly, polydactyly and camptodactyly of hand and feet

Undescended testes were palpable in the inguinal region with bilateral reducible inguinal hernia found on genital examination. The Skeletal survey revealed abnormal skull shape with fusion of all sutures resulting in a peculiar tower-shaped skull; craniosynostosis and a small hypoplastic maxilla (Fig.3).

Prenatal history revealed an uneventful pregnancy. Our patient was the first product of a consanguineous marriage. There was no family history of congenital anomalies. Both of his parents were normal. Detailed history as well as clinical and radiological features raised suspicion of a genetic disorder. On the basis of all these findings, a diagnosis of Carpenter syndrome was made. Initially the patient was managed through the outpatient department where symptomatic treatment was provided followed by surgical correction of his skull and facial reconstruction.



**Figure 3:** (A) Lateral skull radiograph showing craniosynostosis and severe midface hypoplasia showing small maxilla. (B) The left upper extremity is severely deformed with fusion of digits. (C) In the lower extremities Pre Axial polydactyly: Additional digit towards first digit of both feet.

## Discussion

Carpenter syndrome is a rare inherited autosomal recessive disorder which occurs due to a defect in RAB23 gene, primarily responsible for regulating developmental pathway that control cell proliferation and specialization and for shaping various body parts.<sup>3</sup> Characterized by a wide array of clinical features, most common manifestations of Carpenter syndrome include craniosynostosis, cryptorchidism (undescended testes), external genital hypoplasia, intellectual disability and obesity.<sup>3</sup> Bradydactyly and syndactyly are the clinical features found in all the cases of Carpenter syndrome.<sup>3</sup> Craniosynostosis refers to the premature fusion of cranial sutures resulting in abnormal skull shape. It may occur as an isolated defect or as part of a syndromic condition such as Carpenter, Apert, Crouzon, Pfeiffer, and Saethre-Chotzen syndromes.<sup>6</sup> Interestingly, craniosynostosis commonly involves coronal sutures in other anomalies while in Carpenter syndrome the typical suture involvement is of metopic and saggital suture.<sup>5</sup> Kadakia et al. reviewed a significant number of Carpenter syndrome cases to identify and evaluate the most efficacious therapeutic interventions having optimal prognostic outcomes.<sup>7</sup> But because of the extreme rarity of this syndrome and lack of a standardized management algorithm, the therapeutic management of Carpenter syndrome remains a clinical dilemma. However, the findings of their study encourages the prompt surgical release of craniosynostosis with concomitant fronto-orbital advancement, particularly cases having elevated intracranial pressure.

Ylikontiola et al. suggested a new technique in patients of craniosynostosis having increased risk of intracranial pressure which tend to cause developmental delays.<sup>8</sup> They suggested Posterior cranial vault expansion by distraction osteogenesis. As they achieved substantial reduction in ICP, cranial shape improvement and normal developmental pattern following the procedure in their patients.

Craniosynostosis disrupts normal skull growth, often resulting in a pointed head shape known as acrocephaly, at times hindering the normal development of brain thus resulting in increased intracranial pressure.<sup>3</sup> Although the reason for intellectual disability in Carpenter syndrome is not clear yet as Anil Batta in his study emphasizes that there is no significant relationship

between intellectual disability and craniosyntosis severity.<sup>3</sup> However, a timely diagnosis and prompt management is still required especially in case of craniosyntosis.<sup>1</sup> As Kadakia et al. in their review article recommend surgical treatment of craniosyntosis especially when associated with increased intracranial pressure.<sup>7</sup> Ylikontiola et al observed in their interventional study that surgical correction of craniosyntosis posterior cranial vault expansion by distraction osteogenesis technique helped individuals avoiding developmental delay and a normal developmental pattern was achieved.<sup>8</sup>

These kind of new surgical interventions should be supported. However, in a third world country like Pakistan with apparently first reported presentation of Carpenter syndrome highly sophisticated and complex surgical interventions remain a distant prospect.

This case is unique in several aspects. Firstly, it reports case of Carpenter syndrome in Pakistani population which is exceptionally rare. Secondly, it highlights the characteristic clinical and radiological features of Carpenter syndrome. Lastly, it suggests surgical correction as a definitive management for craniofacial anomalies aiming to improve quality of life.

The main limitation of this case is the lack of long-term follow-up data. After having surgical correction, the patient lost to follow up; therefore, post-operative outcomes and subsequent well-being of the patient could not be assessed.

Future studies should emphasize early surgical intervention for craniosynostosis and evaluate its impact on intellectual development and quality of life.

## Conclusion

A rare case of Carpenter syndrome was diagnosed in a two-month-old child. Radiological findings demonstrated characteristic features of Carpenter syndrome, including tower-shaped skull, syndactyly, polydactyly and camptodactyly of hand and feet. In such cases surgical intervention for cranial and facial reconstruction has been advised. As Carpenter syndrome is an autosomal recessive disorder, premarital genetic counseling and testing are strongly recommended to reduce recurrence in high-risk populations.

**ETHICAL CONSIDERATIONS:** Informed Consent: Parental consent was obtained.

**CONFLICT OF INTEREST:** None

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