Pfeiffer Syndrome

Pfeiffer syndrome, also known as acrocephalosyndactyly type 1, is a rare genetic disorder that was first described by RA Pfeiffer in 1964. This disease process is characterized primarily by craniosynostosis, broad thumbs, and large first toes. Premature fusion of the lambdoid and coronal sutures, with occasional fusion of the sagittal suture, (Fig. 1) is seen in these patients. This disease process has a spectrum with Aperts and Crouzon syndromes.

Classification

Pfeiffer et al. (4) divided Pfeiffer syndrome into three types based on the severity of their phenotype (Table 1). Type 1 has a relatively poor outcome with death in early infancy or childhood and has a specific inheritance pattern. The major clinical findings associated with type 1 include a Kleebattschädel skull (Fig. 1), severe ocular proptosis, elbow ankylosis, broad thumbs, and broad toes (2, 3, 4). These patients undergo multiple surgeries early in life for craniosynostosis and fusion. Type 1 Pfeiffer syndrome can have a mutation on either of these genes, result in abnormal cell signaling, which is likely the cause of premature osseous fusion (Fig. 3), broad thumbs, broad toes, and variable syndactyly (2,3,4).

Type 2 Pfeiffer syndrome is characterized primarily by craniosynostosis, broad thumbs, and large first toes. Premature fusion of the lambda and coronal sutures, with occasional fusion of the sagittal suture (Fig. 1) is seen in these patients. Type 2 Pfeiffer syndrome has been described in patients who have a mutation in one of the FGFR 2 genes. These patients undergo extensive imaging work up early in life (Fig. 4), broad thumbs, broad toes, and variable syndactyly (2,3,4).

Clinical History

Our patient is a 6-year-old male with type 2 Pfeiffer syndrome who has done remarkably well given the poor prognosis associated with this mutation. This patient was born at 38 weeks gestation after an unremarkable pregnancy. He was born with a Chiari Type I malformation but did develop by the time he was one year old, which is not uncommon in patients with craniosynostosis (1). In October of 2011, our patient began experiencing progressive spinal deformity and neurological deficits (9).

Our patient's sagittal suture was noted to be closed at 2.5 years of age, leading the spine to two hemicords. Each hemicord contains a spinal cord (blue asterisk), and the spinal cord is divided by a fibrous septum (5). Two types of diastematomyelia have been described in the literature, having key distinguishing features. Type 1 diastematomyelia is present when there are two hemicords in each patient's dorsal sac and are commonly separated by a fibrous septum (6). Other associated features commonly seen with type 1 diastematomyelia are hydrocephalus, vertebral anomalies, and skin pigmentation (5,9). Type 2 diastematomyelia is less severe in which both hemicords are contained in a single dorsal sac (6). Typically, a fibrous septum separates the cord in type 2 diastematomyelia with vertebral anomalies and hydrocephalus being less severe (5,9). Our patient has type 2 diastematomyelia with associated vertebral anomalies and syringomyelia.

Conclusion

Type 2 Pfeiffer syndrome is a rare genetic disorder caused by a mutation in the FGFR 2 gene. This disease process has a spectrum with early-onset extensive imaging work up early in life but does not routinely undergo spinal MR imaging. It is unclear if diastematomyelia is a unique finding to this patient or if it is present in other type 2 Pfeiffer syndrome patients and associated with the FGFR 2 gene mutation. This gene mutation may play a role in the development of the fibrous, cartilaginous, or bony septum in diastematomyelia due to its role in the development of osseous and cartilaginous structures.

Summary

1. Pfeiffer syndrome is a rare disease with multiple characteristic anomalies that have been attributed to mutations in the fibroblast growth factor receptor (FGFR 1) and FGFR 2 genes. The type 2 phenotype of Pfeiffer syndrome has been described in patients who have a mutation in the FGFR 2 gene.
2. Our patient has a mutation in FGFR 2 gene and has the type 2 Pfeiffer syndrome phenotype. He has been born with a Chiari Type I malformation but did develop by the time he was one year old, which is not uncommon in patients with craniosynostosis.
3. In October of 2011, our patient began experiencing progressive spinal deformity and neurological deficits.
4. Our patient's sagittal suture was noted to be closed at 2.5 years of age, leading the spine to two hemicords.
5. Each hemicord contains a spinal cord and is divided by a fibrous septum.
6. Two types of diastematomyelia have been described in the literature, having key distinguishing features. Type 1 diastematomyelia is present when there are two hemicords in each patient's dorsal sac and are commonly separated by a fibrous septum. Other associated features commonly seen with type 1 diastematomyelia are hydrocephalus, vertebral anomalies, and skin pigmentation.
7. Type 2 diastematomyelia is less severe in which both hemicords are contained in a single dorsal sac. Typically, a fibrous septum separates the cord in type 2 diastematomyelia with vertebral anomalies and hydrocephalus being less severe.
8. Our patient has type 2 diastematomyelia with associated vertebral anomalies and syringomyelia.

References

- Pfeiffer Syndrome: A Clinical Classification. AJR 135:1225
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- Craniofacial Journal, Jan. 1995, Vol. 32 No. 1
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Discussion (Continued)

Imaging of Type 2 Pfeiffer Syndrome

Pfeiffer syndrome is a rare disease with multiple characteristic anomalies that have been attributed to mutations in the fibroblast growth factor receptor (FGFR 1) and FGFR 2 genes. The type 2 phenotype of Pfeiffer syndrome has been described in patients who have a mutation in the FGFR 2 gene. These patients undergo extensive imaging work up early in life (Fig. 4), broad thumbs, broad toes, and variable syndactyly. These patients undergo multiple surgeries early in life for craniosynostosis and fusion. Type 1 Pfeiffer syndrome can have a mutation on either of these genes, result in abnormal cell signaling, which is likely the cause of premature osseous fusion (Fig. 3), broad thumbs, broad toes, and variable syndactyly (2,3,4).

Type 2 Pfeiffer syndrome is characterized primarily by craniosynostosis, broad thumbs, and large first toes. Premature fusion of the lambda and coronal sutures, with occasional fusion of the sagittal suture (Fig. 1) is seen in these patients. Type 2 Pfeiffer syndrome has been described in patients who have a mutation in one of the FGFR 2 genes. These patients undergo extensive imaging work up early in life (Fig. 4), broad thumbs, broad toes, and variable syndactyly (2,3,4).

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Our patient has type 2 diastematomyelia with associated vertebral anomalies and syringomyelia.

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