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CASE REPORT

Chiari I Malformation in Patients with Pfeiffer Syndrome: Important Aspects of Preoperative Imaging

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ABSTRACT

Chiari I malformation may not be congenital, but may be acquired as a consequence of skull deformities and other associated intracranial factors in patients with craniosynostosis. Pfeiffer syndrome is one of the many conditions associated with Chiari I malformation. Premature fusion of multiple cranial sutures and cloverleaf skull (kleeblattschädel deformity) are often observed in the calvaria of patients with Pfeiffer syndrome. This report is of a male infant, with Pfeiffer syndrome who was noted to have progressive Chiari I malformation, with classical imaging features illustrated. Important aspects of preoperative imaging will be discussed, with a brief review of literature.

Key Words: *Acrocephalosyndactylia; Arnold-Chiari malformation; Cerebral veins; Craniosynostoses*

中文摘要

Pfeiffer綜合症患者的Chiari I型畸形：術前影像的重要性

葉精勤、許其達、林慧文、周明德

Chiari I型畸形不一定是先天性的病患，它可以是頭骨畸形以及因顱縫早閉而引致有關顱內其他相關症狀的結果。Pfeiffer綜合症是與Chiari I型畸形眾多相關病症的其中一種。Pfeiffer綜合症患者的顱蓋骨普遍出現多個顱縫的提早融合與三葉草顱綜合症（kleeblattschädel畸形）。本文報告一名患有Pfeiffer綜合症的男嬰出現進行性Chiari I型畸形的典型影像，並會討論術前的影像及簡要回顧文獻。

INTRODUCTION

Pfeiffer syndrome is associated with premature fusion of multiple cranial sutures, cloverleaf skull (kleeblattschädel deformity), prominent ptosis, thumb and first toe abnormalities, variable syndactyly, and mutated genes for types 1 or 2 fibroblast growth factor receptors (FGFRs). Children with severe forms (types 2 and 3 disease) generally present with considerable neurological and cognitive defects, and may die at a young age.

It is well recognised that there is an association between Chiari I malformation and some congenital craniosynostosis syndromes. Reports also illustrate that Chiari I malformation can develop rapidly in the presence of increased intracranial pressure and

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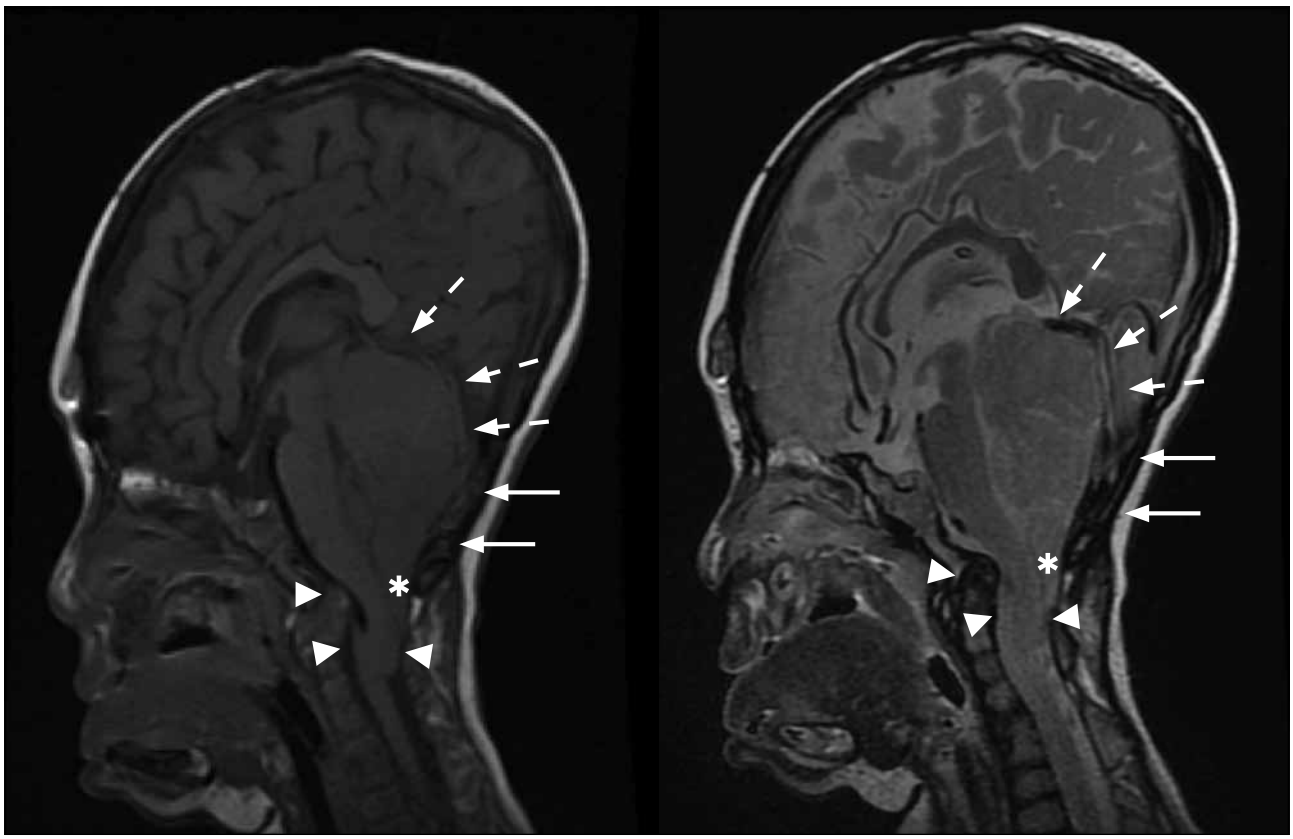

Figure 1. Magnetic resonance images of the brain and craniocervical junction show brachycephaly with small posterior cranial fossa (arrows). Cerebellar tonsillar ectopia is evident, with the cerebellar tonsil (*) herniating down approximately 1.4 cm below the foramen magnum. Associated towering of the cerebellum and beaking of the tectum were noted (broken arrows). Retroflexion of the upper odontoid process, and indentation and kinking of the medulla oblongata (arrowheads) and cervicomedullary junction were seen. No abnormal intramedullary or intra-axial T2-weighted hyperintensity or syrinx was detected. Failure of segmentation of C5–C7 was noted. No spinal stenosis or cord compression was observed at the cervical level.

craniosynostosis.[1] Approximately half of all patients with Pfeiffer syndrome and virtually all with type 2 disease have Chiari I malformation.[2] We report on a full-term male infant with Pfeiffer syndrome and progressive Chiari I malformation.

CASE REPORT

A full-term male infant presented at early infancy with Pfeiffer syndrome in December 2009, with craniosynostosis involving bilateral coronal and lambdoid sutures. He had multiple cranial suture synostoses resulting in cloverleaf and copper-beaten deformities of the skull vault, and the anterior fontanelle opened with moderate tension. He also had severe proptosis due to frontal and maxillary hypoplasia.

Despite repeated posterior cranioplasties and decompressive craniotomies performed for four times in his first two years of life, he suffered from deteriorating oromotor dysfunction and recurrent apnoea. Magnetic resonance imaging (MRI) of the brain and craniocervical junction showed brachycephaly with a small posterior cranial fossa. Cerebellar tonsillar ectopia was evident, with the cerebellar tonsil herniating down approximately 1.4 cm below the foramen magnum. Associated towering of the cerebellum and beaking of the tectum were noted. Retroflexion of the upper odontoid process was also noted. Indentation and kinking of the medulla oblongata and cervicomedullary junction were evident. These findings were in keeping with Chiari I malformation (Figure 1).

Further posterior decompressive cranioplasty was planned. Preoperative computed tomography (CT) of the brain was performed to check for enlarged basal emissary veins. The CT image showed signs of Chiari I malformation. The torcular herophili was slightly low lying. Minor emissary veins were noted at the

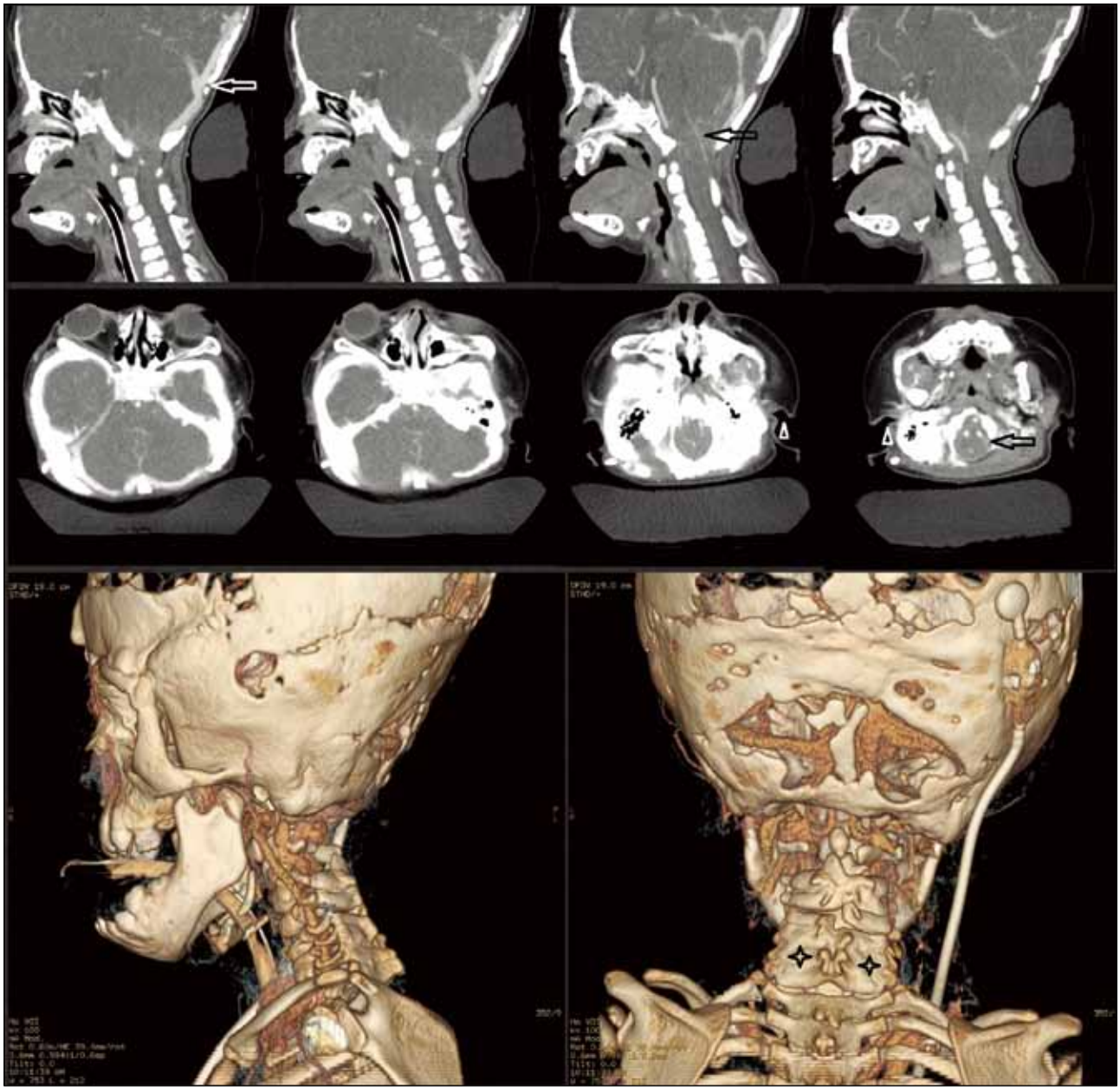

Figure 2. Contrast computed tomography scans of the posterior cranial fossa show the ventricular shunt in situ and the cranioplasties. The torcular herophili was slightly low lying (white arrow). Minor emissary veins were noted at the level of foraman magnum (black arrow). No abnormally engorged venous plexus was seen. Failure of segmentation of C5–C7 was noted (asterisk). No spinal stenosis or cord compression was observed at the cervical level. Narrowing of the bilateral external auditory meatus was incidentally noted (arrowhead).

level of the foramen magnum. No abnormally enlarged venous plexus was seen in the CT scans (Figure 2). The findings were discussed with the neurosurgeons. The small emissary veins were closely observed during the operation and blood loss was minimised.

DISCUSSION

Chiari I malformation is an acquired and progressive finding in multisutural and syndromic craniosynostosis, occurring in 70% of patients with Crouzon syndrome, 75% with oxycephaly, 50% with Pfeiffer syndrome, and 100% with Kleeblattschädel deformity.[3] The pathogenesis of this condition and rationale for treatment are still controversial. Thompson et al[4] have evaluated the occurrence and the extent of herniation of the hindbrain in a population of children

with craniosynostosis by MRI of the craniocervical junction. These authors proposed that herniation of the hindbrain in craniosynostosis is a consequence of brain deformation occurring in response to the physical forces imposed by a combination of the anatomical deformity at the skull base and intracranial hypertension rather than a primary malformation of brain development.[4] Currently, the aetiology is believed to be multifactorial and related to the disproportionately slow growth of the skull relative to the brain, particularly in the posterior fossa, secondary to early fusion of the skull sutures, which occurs secondary to congenital deficiencies in FGFRs; impaired venous sinus drainage; hydrocephalus; and elevations in intracranial pressure.

Chiari I malformation can develop rapidly, starting in the first month of life, because of a disproportion between hindbrain growth and an abnormally small posterior fossa as a consequence of the premature fusion of the lambdoid and cranial base sutures.[3] In a review of 21 patient with Chiari I malformation, Hopkins and Haines[1] found that the time from first MRI to development of tonsillar herniation ranged from 11 days to 18.5 years. The status of the sutures at the posterior cranial fossa and skull base are determining factors in development of Chiari I malformation in patients with craniosynostosis syndrome. Decreased volumes of posterior cranial fossa and foraminal stenosis in skull bases are detrimental to hindbrain development. Careful MRI evaluation is therefore recommended for the types of craniosynostosis likely to develop hindbrain herniation.

Stenosis of the jugular foramen can also give rise to venous hypertension, resulting in intracranial hypertension and / or hydrocephalus.[3,5] Proposed mechanisms include constriction theory, a primary role for FGFR mutations, and persistence of the foetal pattern of intracranial venous drainage.[5] Taylor et al[6] analysed the anatomy of intracranial venous drainage in angiography studies of 23 children with complex craniosynostosis without other factors such as hydrocephalus. These authors found that abnormalities of venous drainage particularly affecting the sigmoid-jugular sinus complex produced a state of venous hypertension that was responsible for most cases of intracranial hypertension in this group of patients.[6] There is a close inter-relationship between Chiari I malformation and venous hypertension that is associated with the development of collateral emissary veins. An enlarged basal emissary vein is common in syndromic craniosynostosis, and is usually associated with jugular foraminal stenosis or atresia.[7] Disruption of the emissary veins during surgery can produce massive haemorrhage. CT or contrast-enhanced MR venogram can document the presence of these emissary veins and will play an important role in operative planning.[8]

An anomalous posterior fossa venous drainage pattern, preventing safe posterior fossa decompression, has also been reported in patients with Chiari I malformation type 1 multisutural craniosynostosis and crowded posterior fossa structures.[9] Therefore, careful evaluation of the posterior fossa venous drainage pattern with CT or MR venogram should be performed prior to considering posterior fossa decompression with or without occipitocervical fusion or calvarial vault remodelling procedures in patients with multisutural craniosynostosis. Radiologists should alert neuro-surgeons to any anomalous posterior fossa venous drainage noted on imaging studies that would increase the expected risks associated with surgery.

Ventricular dilatation is another salient MRI finding in Chiari I malformation and craniosynostosis. Three types of cerebrospinal fluid (CSF) hydrodynamic disturbance are observed: progressive hydrocephalus with ventricular dilation; non-progressive ventriculomegaly; and dilation of the subarachnoid spaces.[9] Clinical and radiological findings strongly suggest that three different mechanisms are involved in the pathogenesis of hydrocephalus: primary cerebral maldevelopment, brain atrophy, and CSF outflow obstruction.[10] Hydrocephalus is rarely observed in non-syndromic craniosynostosis and, in these patients, it is usually attributable to coincidental disorders.[9,10] Conversely, it is a common feature of syndromic craniosynostosis, affecting at least 40% of patients with Crouzon, Pfeiffer, or Apert syndrome.[10] Shunt-dependent hydrocephalus is predominantly associated with Crouzon or Pfeiffer syndrome while, in Apert syndrome, the usual finding is non-progressive ventriculomegaly, which may also occur in some cases of Crouzon syndrome.[9,10] The pathogenesis of progressive hydrocephalus remains obscure, and a hypoplastic posterior fossa and a venous outlet occlusion at the skull base as the main causative factors have been discussed in the literature.[9,10] Clinical evaluation is mainly aimed at identifying progressive hydrocephalus. However, diagnosis is difficult, because the head circumference is no indicator of progressive hydrocephalus, and intracranial hypertension may coexist due to CSF accumulation or craniostenosis.

Ventricular dilatation will often become evident only after decompressive surgery. Therefore, careful monitoring of intracranial pressure and ventricular size in the pre- and post-operative period is important. Secondary shunting of hydrocephalus may be considered if the intracranial pressure remains high despite adequate cranial decompression.[10]

Remodelling the cranial vault in an attempt to increase the intracranial volume and thus control intracranial hypertension has been the mainstay of surgery for syndromic craniosynostosis. However, there are reports, as for this patient, of craniosynostosis in the cranial vault expansion, followed by development of hindbrain herniation and hydrocephalus.[9,10] Thompson et al[11] reviewed 34 patients with craniosynostosis, who had been evaluated by MRI following surgery to assess the frequency of hindbrain herniation and hydrocephalus. These authors concluded that cranial vault expansion in complex craniosynostosis may fail to address the underlying aetiology of intracranial hypertension.[11] Furthermore, both hydrocephalus and hindbrain herniation may develop after such surgery. Neither the increase in intracranial volume afforded by cranial vault expansion nor shunting of the hydrocephalus precludes the persistence of abnormal intracranial pressure. Therefore, MRI surveillance should be continued even after decompressive surgery.

CONCLUSION

Chiari I malformation appears to be an acquired and progressive condition that develops in syndromic craniosynostosis due to a disproportion between hindbrain growth and an abnormally small posterior fossa, which is a consequence of the premature fusion of cranial base sutures. Venous hypertension caused by stenosis of the jugular foramen resulting in intracranial hypertension and / or hydrocephalus can also be present in these patients. Development of emissary veins and anomalous venous drainage in the posterior cranial fossa further complicate remodelling decompressive surgery. Careful MRI evaluation is recommended for the forms of craniosynostosis that are likely to develop hindbrain herniation, and dedicated venographic assessment of the posterior cranial fossa should be performed as part of preoperative planning.

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