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A clinical case

Acute Hydrocephalus in a Rare Case of Type 2 Pfeiffer Syndrome: Clinical Presentation and Management

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Abstract

Type 2 Pfeiffer Syndrome is a rare craniosynostosis syndrome characterized by distinct craniofacial and limb abnormalities, with hydrocephalus being a significant complication that demands specialized management.
The objective of this article is to describe the clinical course, therapeutic interventions, and postoperative outcomes of the patient, highlighting the challenges in managing this complex syndromic condition.
This report presents the clinical management of a 3.5-month-old male diagnosed with Type 2 Pfeiffer Syndrome, a rare craniosynostosis syndrome characterized by distinct craniofacial and limb abnormalities. The patient was admitted with signs of increased intracranial pressure caused by hydrocephalus. Clinical evaluation, imaging studies, and multidisciplinary consultation guided the treatment strategy.
The patient underwent successful ventriculoperitoneal shunt placement, however experienced respiratory complications. Postoperative assessments indicated a significant reduction in ventricular size and an improvement in cranial pressure symptoms, contributing to the patient's overall positive outcome. This case underscores the importance of multidisciplinary approaches in treating complex syndromic conditions, offering valuable insights for clinicians facing similar challenges.

Keywords: Pfeiffer syndrome 2, acrocephalosyndactyly, craniosynostosis, hydrocephalus, ventriculoperitoneal shunt.

1. Introduction

Initially described in 1964 by Rudolf Pfeiffer, Pfeiffer syndrome (PS), also known as acrocephalosyndactyly type V, is a rare autosomal dominant craniofacial disorder. It is characterized by multiple-suture synostosis, distinctive facial features, and abnormalities in the hands and feet. The disorder is estimated to affect one in 100.000 individuals [1, 2].

Cohen's classification defines three clinical subtypes of PS, each with its own prognostic implications. Type 1, characterized by autosomal dominant inheritance, represents the mildest form. On the other hand, Type 2, characterized by a cloverleaf skull and extensive involvement of the central nervous system, is the most severe subtype. Type 3, an intermediate subtype, shares similarities with Type 2 but does not have the cloverleaf skull deformity [3].

Diagnosing PS prenatally can be challenging due to its rarity and the various morphological presentations it can manifest. However, it remains feasible through molecular analysis or sonographic examination during the second or third trimester [4]. Abnormal head size and ventricular enlargement could potentially be additional signs of fetal craniosynostosis, which could improve the detection rate before birth [5]. Although the distinct cloverleaf-shaped skull, a common sign of PS Type 2, can sometimes be observed before 20 weeks of pregnancy, only one case of PS Type 2 detected in the first trimester has been reported, as described by Hu et al [6].

In relation to PS, the molecular genetics underlying them is similar to other craniosynostosis, such as Crouzon, Apert, and Jackson Weiss syndromes. These conditions can occur due to mutations in genes like FGFR1/2/3, MSX2, or TWIST. Mutations in the FGFR2 gene on chromosome 10q are commonly associated with types 2 and 3 of PS. Approximately 5% of cases, categorized as either type 1 or 2, are caused by mutations in the FGFR1 gene on chromosome 8p [7, 8].

The postnatal diagnosis of PS mainly depends on clinical assessment, which focuses on determining the presence of craniosynostosis, midface hypoplasia, and abnormalities in the extremities, along with other characteristic features. PS Type 2 is identified by the presence of a cloverleaf skull deformity. Primary anomalies include specific developmental defects, such as white matter disorders. Secondary anomalies arise as consequences of skull deformities and may include intracranial hypertension, hydrocephalus, and Chiari I malformation [1]. Neurological complications in patients with PS are crucial indicators of disease severity and the necessity of treatment.

The prognosis of PS subtypes varies significantly, ranging from relatively mild neurological and developmental manifestations to high mortality rates. Types 2 and 3 are distinguished by severe neurological compromise and are associated with unfavorable clinical outcomes [3].

Clinicians, especially neurosurgeons, involved in the care of these patients should possess a thorough understanding of the neurological abnormalities associated with PS. These abnormalities may necessitate neurosurgical interventions or potentially render such interventions more complex. To the best of our knowledge, there is limited literature on patients diagnosed with Type 2 PS, especially when it comes to describing neurosurgical management issues.

The purpose of this case report is to provide insights into the challenges of managing severe hydrocephalus and the complications encountered during the implementation of management strategies for a patient with Type 2 PS.

2. Case report

The male infant, who is 3.5 months old, was hospitalized due to vomiting and lethargy. He was born at 36 weeks of gestation via cesarean section because of placental abruption, which was a significant event in an otherwise uncomplicated pregnancy. Neither parent has a history of genetic disorders, and the mother did not experience any infectious diseases during pregnancy. Diagnostic procedures conducted at the 32-week gestation period using ultrasound imaging revealed cranial deformities in the fetus. At birth, the infant had noticeable craniofacial anomalies, such as a cloverleaf-shaped skull and pronounced bilateral ptosis, but no limb deformities were detected. Since birth, the infant has had compromised gastrointestinal motility, which required the insertion of a gastric tube to aid in the passage of nutrition. Additionally, the infant experienced respiratory distress and was hospitalized at three months of age due to pneumonia.

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During the clinical examination, the male infant patient displayed noticeable physical anomalies. These included a cloverleaf-shaped head (Figure 1A), bilateral proptosis, and conjunctival hyperemia. Additional observations revealed a high-arched hard palate.

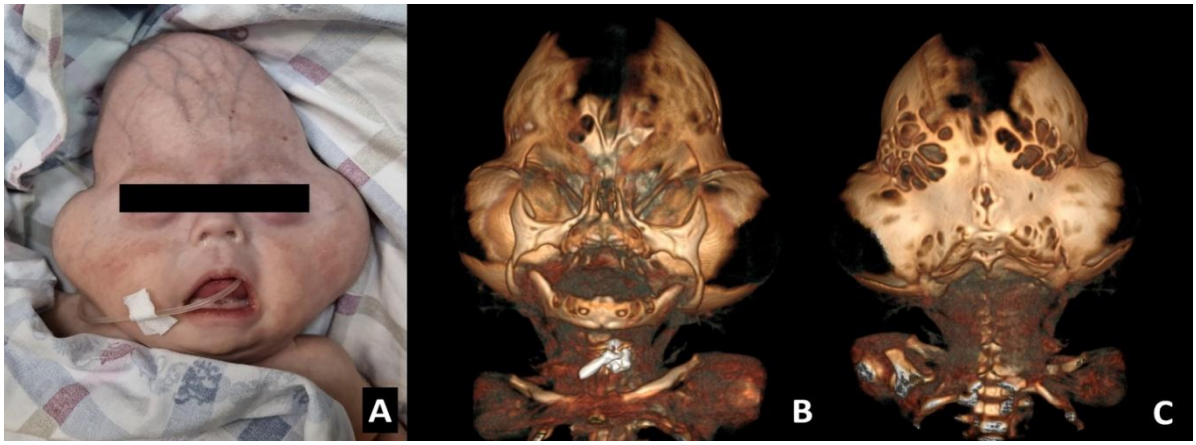

Figure 1 – Cloverleaf-shaped head (A). Three-dimensional CT reconstruction of the skull demonstrating the cloverleaf-shaped skull deformity due to temporal and lambdoid suture fusion, nonfusion of sagittal suture and full-thickness defects throughout the skull. Anterior view (B), Posterior view (C)

Neurologically, the infant showed signs of lethargy and somnolence. Notably, the child exhibited diminished muscle tone in all extremities and was unable to sit, crawl, or control his head. An ophthalmologist's assessment revealed partial optic nerve atrophy in the right eye, highlighting the complexity of the child's condition.

A comprehensive full blood count was performed, and the results were within normal parameters. Although the clinical indicators suggested a genetic cause, genetic testing could not be done due to its unavailability in the current medical setting. Computed Tomography (CT) scans provided detailed insights, revealing a cloverleaf-shaped skull (Figure 1B-C) and anomalies in the cranial base and orofacial regions.

The scans also showed asymmetrical dilatation of the lateral ventricles, signs of progressive hydrocephalus characterized by ventriculomegaly and the effacement of brain fissures, as well as cerebral abnormalities (Figure 2A-D). Based on the comprehensive clinical findings and distinctive radiographic evidence, the patient was diagnosed with type 2 PS.

Figure 2 – Head CT frontal (A-C) and axial (D) view revealing asymmetric enlargement of lateral ventricles and nonfusion of sagittal suture. Frontal (E) and axial (F) view of CT ventriculography sustaining non-occlusive hydrocephalu

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To determine the type of hydrocephalus and eliminate the possibility of aqueductal stenosis, a CT ventriculography was performed. This procedure confirmed the presence of non-occlusive hydrocephalus and allowed for a clear understanding of its nature, leading to a more focused approach in managing and planning treatment for the patient's condition (Figure2 E-F).

Although multiple staged reconstructive surgeries were initially planned after 6 months, the emergence of acute hydrocephalus symptoms prompted us to prioritize ventriculoperitoneal shunt placement. The patient underwent a surgical procedure for the placement of a medium-pressure VPS into the anterior horn of the right ventricle, guided by a neuronavigation system. At a depth of 5 cm, cerebrospinal fluid was aspirated under high pressure. The surgery was completed without any complications. Nevertheless, during the postoperative period, the patient experienced a laryngospasm while being extubated, which led to the need for re-intubation and mechanical ventilation. Due to ongoing respiratory distress, a tracheostomy was performed on the third day after the surgery to ensure a clear airway and improve breathing.

On the third day following the surgery, a CT scan of the head was conducted. The scan revealed a clear decrease in the size of the lateral ventricles, indicating a positive response to the placement of the VPS (Figure 3A-B). Subsequently, on the seventh day after the surgery, a clinical evaluation demonstrated substantial improvements in the patient's condition. This was evidenced by a reduction in exophthalmos and an enhancement in the level of consciousness (Figure 3C).

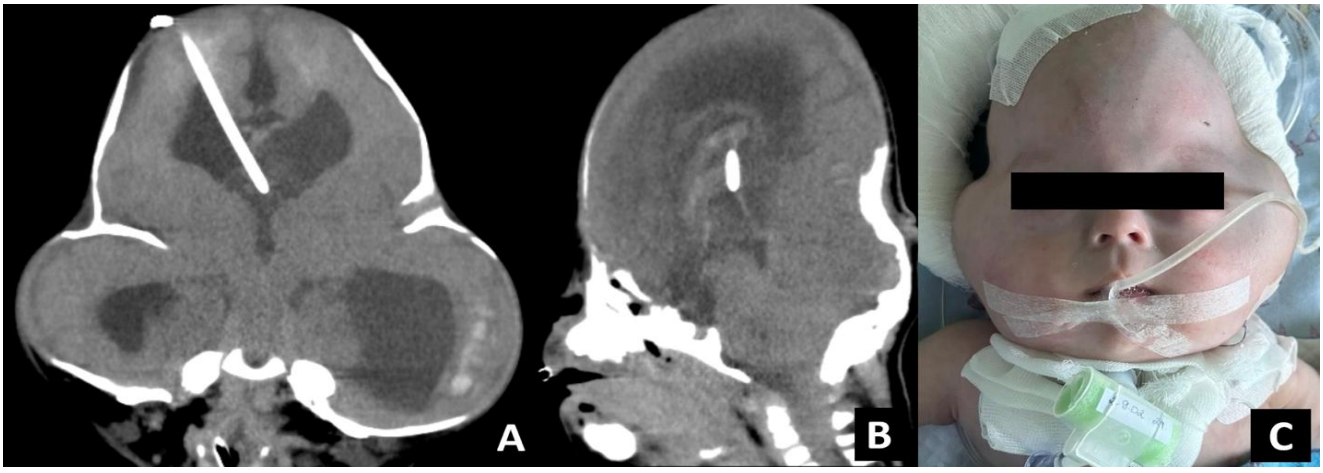

Figure 3 – Postoperative head CT frontal (A) and sagittal (B) view demonstrating the decrease in the volume of the lateral ventricles. Photography (C) on 7th day after surgery showing the regression of exophthalmos

The patient was discharged in satisfactory condition, with recommendations for continued treatment and monitoring by a pulmonologist to address any ongoing respiratory needs.

3. Discussion

PS is a genetic craniofacial disorder that is characterized by craniosynostosis, midface hypoplasia, broad thumbs and great toes, and varying degrees of soft tissue syndactyly in the hands and feet [1-3]. In such cases, the main goals of surgery are to decompress the brain by providing sufficient intracranial volume and increasing the infraorbital volume. Patients with PS generally undergo multiple staged reconstructive surgeries as part of their treatment plan. However, our patient had acute hydrocephalus and needed immediate surgical intervention for this condition.

A cloverleaf skull is usually caused by the premature closure of the coronal and lambdoid sutures. This closure restricts the growth of the skull base, leading to a decrease in intracranial volume. Consequently, there is an elevation in intracranial pressure and an increased risk of hydrocephalus. At least 40% of patients with PS will experience ventricular dilatation, whereas a smaller percentage will have

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ventriculomegaly [7]. Hydrocephalus can manifest as communicating, as seen in our patient, often due to venous hypertension or CSF flow obstruction. On the other hand, noncommunicating hydrocephalus is typically a result of conditions such as basilar invagination or aqueductal stenosis [1].

The child in this case showed symptoms of acute communicating hydrocephalus, such as vomiting and lethargy. These were confirmed by brain CT and ventriculography, which revealed ventriculomegaly and smoothing of the brain fissures. Prompt intervention is crucial when hydrocephalus appears in PS to prevent further neurological damage. The VPS placement procedure is crucial for managing hydrocephalus in patients with complex syndromic presentations such as PS. It provides significant relief from symptoms and helps prevent potential life-threatening complications [9].

The current literature on the management of hydrocephalus in PS type 2 is limited primarily because the condition is rare. However, case reports and small case series have shown that VPS are effective in relieving symptoms and improving the quality of life in these patients [10-12].

The premature fusion of skull bones can complicate surgical procedure and increase the risk of intraoperative complications [10]. The distorted cranial anatomy poses challenges in the optimal placement of ventricular catheters for VPS. The cloverleaf skull and other cranial deformities present in PS type 2 significantly complicate the typical landmarks in shunt placement. The reduced intracranial volume and altered anatomy can make it difficult to identify optimal sites for ventricular catheter insertion and to navigate the catheter to the desired location within the ventricles. The abnormal skull development can also affect the positioning and vulnerability of major venous sinuses. During shunt placement, there is a heightened risk of injuring these sinuses, leading to significant bleeding [1, 10-12]. Advanced imaging techniques and preoperative planning are critical to avoid these structures during surgery.

Premature fusion of cranial sutures, which is a characteristic of PS, affects the flexibility and expansion capacity of the skull. As a result, this can create difficulties in adapting to normal intracranial pressure changes and make it more complex to determine the most suitable shunt valve settings [1, 11].

In addressing the multifaceted challenges encountered in the surgical treatment of hydrocephalus, especially in patients presenting with craniosynostosis syndromes such as PS type 2, our approach underscores the necessity of meticulous preoperative planning and intraoperative precision. The complexity of these cases necessitates a highly individualized approach to the selection of shunt systems, encompassing both the valves and catheters, tailored to accommodate the patient's specific anatomical challenges and the unique dynamics of their cerebrospinal fluid flow. This level of customization is pivotal in mitigating the risk of postoperative complications and enhancing the overall success rate of the intervention.

Moreover, collaboration among the multidisciplinary team, which includes neurosurgeons, craniofacial surgeons, radiologists, and anesthesiologists, is crucial for navigating the complexities of both the intraoperative and postoperative phases [1]. Our patient had postoperative complications including laryngospasm during extubation, which led to re-intubation and mechanical ventilation. Because of ongoing respiratory distress, a tracheostomy was performed to ensure proper airway management. Despite these challenges, the success of the surgical intervention was evident as imaging showed decreased ventricle size and clinical improvements were observed within the first week after surgery.

Future research should aim to elucidate the genetic variations contributing to the phenotypic diversity of PS type 2, enabling targeted therapies. Additionally, longitudinal studies are needed to understand the long-term outcomes of patients with PS type 2, particularly those undergoing surgical interventions for associated conditions like hydrocephalus.

4. Conclusions

This case report underscores the complexities of managing hydrocephalus in patients with congenital craniosynostosis syndromes and the efficacy of a multidisciplinary, tailored approach. Successful outcomes hinged on advanced surgical planning, precise intraoperative techniques, and collaborative postoperative care.

Conflicts of interest. The authors declare no conflicts of interest.

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Ethical aspect. Informed consent was obtained from the legal representative of the patient.

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2-типті Пфайффер синдромының сирек жағдайындағы жедел гидроцефалия: Клиникалық көрініс және емдеу

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Түйіндеме

2-типті Пфайффер синдромы — сирек кездесетін краниосиностоз синдромы, айқын краниофасциалдық және аяқ-қол аномалияларымен сипатталады. Гидроцефалия мамандандырылған емдеуді қажет ететін маңызды асқыну. Бұл мақаланың мақсаты — науқастың клиникалық ағымын, емдік араласуларын және операциядан кейінгі нәтижелерін сипаттап, осы күрделі синдромдық жағдайды емдеудегі қиындықтарды атап өту.

Мақалада 3,5 айлық ер балаға қойылған 2-типті Пфайффер синдромын емдеу тәжірибесі сипатталған, ол гидроцефалияға байланысты жоғары бассүйекішілік қысым белгілерімен түсті. Науқастың жағдайын бағалау үшін анамнез деректері және диагностикалық бейнелеу әдістері пайдаланылды.

Науқасқа сәтті вентрикулоперитонеальды шунт қойылды, алайда операциядан кейін тыныс алу асқынулары байқалды. Операциядан кейінгі тексерулер қарыншалардың көлемінің айтарлықтай азайғанын және бассүйекішілік қысым белгілерінің жақсарғанын көрсетті, бұл жалпы оң нәтижеге ықпал етті. Аталмыш жағдай күрделі синдромдық ауруларды емдеуде мультидисциплинарлық тәсілдің маңыздылығын көрсетеді, ұқсас қиындықтарға тап болған клиницистер үшін құнды тәжірибе ұсынады.

Түйін сөздер: 2-типті Пфайффер синдромы, акроцефалосиндактилия, краниосиностоз, гидроцефалия, вентрикулоперитонеальды шунт.

Острая гидроцефалия в редком случае синдрома Пфайффера 2-го типа: Клиническая картина и лечение

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Резюме

Синдром Пфайффера типа 2 — редкий синдром краниосиностоза, характеризующийся выраженными краниофациальными и конечностными аномалиями, при котором гидроцефалия является серьезным осложнением, требующим специализированного лечения. Целью данной статьи является

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описание клинического течения, лечебных вмешательств и послеоперационных результатов у пациента, а также освещение сложностей в управлении этим комплексным синдромным состоянием.

В данном клиническом случае описывается лечение 3,5-месячного мальчика с диагнозом синдром Пфайффера типа 2, госпитализированного с признаками повышения внутричерепного давления, обусловленного гидроцефалией. Пациенту была успешно выполнена вентрикулоперитонеальная шунтирующая операция, однако в послеоперационном периоде возникли респираторные осложнения. Послеоперационные исследования показали значительное уменьшение размеров желудочков мозга и улучшение симптомов повышения внутричерепного давления, что способствовало положительному исходу заболевания. Данный случай подчеркивает важность мультидисциплинарного подхода в лечении сложных синдромных состояний и предоставляет ценный опыт для врачей, сталкивающихся с подобными задачами.

Ключевые слова: синдром Пфайффера 2-го типа, акроцефалосиндактилия, краниосиностоз, гидроцефалия, вентрикулоперитонеальный шунт.

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