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CASE REPORT
Craniofacial/Pediatric

Delayed Postnatal Synostosis without Spheno-occipital Synchondrosis Fusion: A Curious Case of Apert Syndrome

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Summary: Apert syndrome classically presents with craniosynostosis at birth, most commonly of the bilateral coronal sutures, which may lead to cephalocranial disproportion and elevated intracranial pressure, the latter of which is associated with optic atrophy, visual loss, and developmental delays. A small number of patients with syndromic craniosynostosis demonstrate open sutures at birth; however, all previously reported patients of this subtype have been reported to develop premature suture fusion in the early postnatal period and/or require cranial vault expansion for increased intracranial pressure. Here, we report on a patient with Apert syndrome who did not have closed sutures at birth, and only began to demonstrate unilateral coronal suture fusion between ages 4 and 6 years, yet neither developed phenotypic signs of craniosynostosis nor evidence of intracranial hypertension. Moreover, despite demonstrating patency of the spheno-occipital synchondrosis, the patient developed progressive midface hypoplasia, requiring a subcranial Le Fort 3 advancement with external distraction at age 9. Now at skeletal maturity, this patient has a normal cranial shape and will likely never require cranial vault surgery for functional or aesthetic concerns. We are not aware of any prior reports of a patient with Apert syndrome who did not require intracranial surgery over long-term follow-up. *(Plast Reconstr Surg Glob Open 2024; 12:e5558; doi: 10.1097/GOX.0000000000005558; Published online 23 January 2024.)*

Apert syndrome classically presents with craniosynostosis, symmetric syndactyly, midface hypoplasia and developmental delays.[1] Craniosynostosis can cause cephalocranial disproportion and elevated intracranial pressure (ICP), the latter of which may have an incidence as high as 45% among patients with untreated Apert syndrome.[1] Increased ICP is associated with visual loss and developmental delays; thus, traditional treatment consists of early surgical intervention to reduce downstream effects of persistently elevated ICP.[2,3]

Although craniosynostosis is typically present at birth, there are occasional reports of patients with syndromic craniosynostosis who have patent sutures at birth that fuse in the early postnatal period.[1,4,5] However, to our knowledge, there are no prior reports of patients with Apert syndrome for whom intracranial surgery was not indicated for cephalocranial disproportion, cranial shape abnormalities, and/or elevated ICP. Here, we report on a patient with Apert syndrome who did not develop cephalocranial disproportion, cranial vault dysmorphology, or signs of increased ICP over 15 years of comprehensive follow-up, and thus did not require intracranial surgery.

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CASE

A White Hispanic male child was born at 38 weeks of gestation by caesarean section to a mother with a history of polycystic ovarian syndrome and two prior pregnancy losses at 22 weeks of gestation. The pregnancy was complicated by gestational diabetes treated with glyburide. Following birth, the patient was noted to have an acrocephalic skull, a displaced anterior fontanel, a wide posterior fontanel, hypertelorism, and syndactyly of his hands and feet. Genetic testing revealed a heterozygous C-to-G mutation at nucleotide 755 of the fibroblast growth factor

Disclosure statements are at the end of this article, following the correspondence information.

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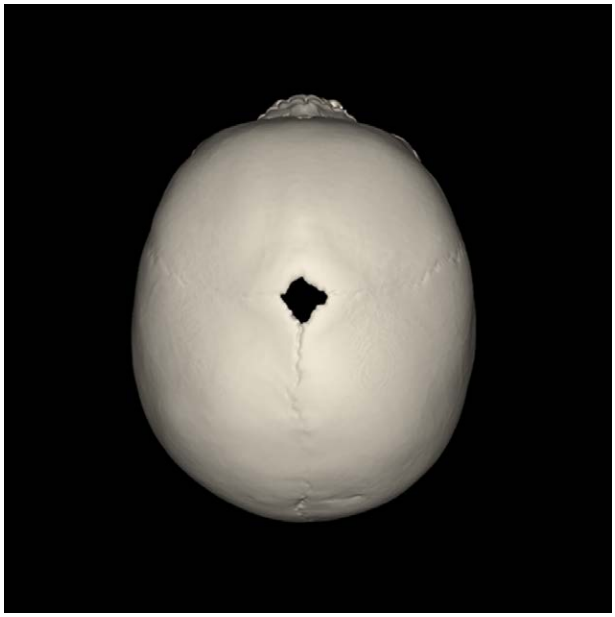

Fig. 1. Birds-eye view of a three-dimensional reconstruction of the skull at age 4.

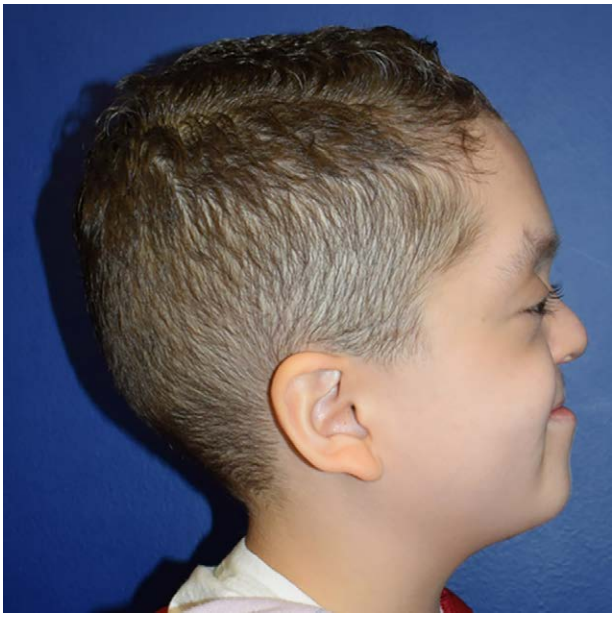

Fig. 3. Profile view of the patient at age 9 before subcranial Le Fort 3 advancement with external distraction.

receptor 2 gene, substituting a tryptophan (TGG) with a serine (TCG) codon at position 252 (p.Ser252Trp), characteristic for Apert syndrome.

The patient received head computed tomography (CT) scans at ages 1 week; 8 months; and 1, 4, 6, and 7 years. Cephalic indices were 0.74, 0.82, 0.83, 0.85, 0.86, and 0.86, respectively. Suture patency was evaluated using fine-cut CT scans and their three-dimensional reconstructions. Open calvarial sutures were evident in the first four scans (Fig. 1), but in the latter two scans, the left coronal suture demonstrated fusion (Fig. 2). The sphenooccipital synchondrosis (SOS) was patent in all scans. (**See figure, Supplemental Digital Content 1**, which displays the axial view of the SOS at age 7, **http://links.lww.com/PRSGO/D39**.) However, the patient developed progressive midface hypoplasia (Fig. 3). In the absence of skull dysmorphology or signs of elevated ICP via biannual ophthalmology and annual craniofacial surgery evaluations, the patient did not undergo intracranial surgery. To treat his midface retrusion, he underwent subcranial Le Fort 3

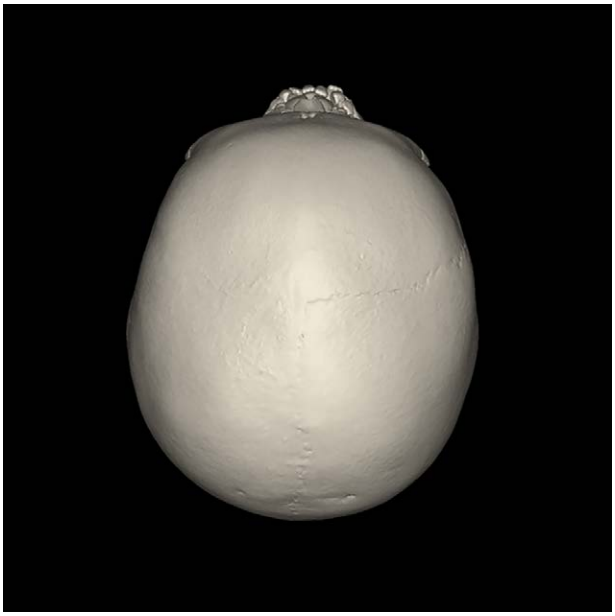

Fig. 2. Birds-eye view of a three-dimensional reconstruction of the skull at age 7.

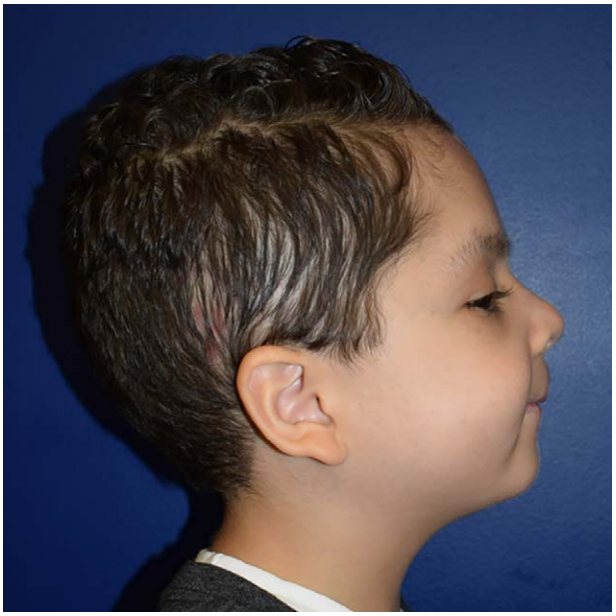

Fig. 4. Profile view of the patient at age 9 after subcranial Le Fort 3 advancement with external distraction.

advancement with external distraction at age 9 (Fig. 4). His comorbidities include aortic stenosis, asthma, gastroesophageal reflux disease, eosinophilic esophagitis, and chronic otitis media. He has been diagnosed with autism spectrum disorder, attention-deficit/hyperactivity disorder, anxiety, mild hearing loss, language learning disorder, and learning impairments in mathematics and reading. His most recent follow-up was at age 15, with no plans for further surgical intervention. (**See figure, Supplemental Digital Content 2,** which displays the profile view of the patient at age 14, **http://links.lww.com/PRSGO/D40**.)

DISCUSSION

Surgical interventions in syndromic craniosynostosis aim to optimize outcomes related to ICP, airway compromise, exorbitism, and psychosocial development.[3] Existing treatment algorithms endorse early cranial vault expansion to prevent morbidity associated with elevated ICP.[2] Despite fusion of the left coronal suture between ages 4 and 6, the patient did not demonstrate radiological or clinical evidence of cephalocranial disproportion or increased ICP over 15 years of comprehensive follow-up. We are not aware of prior reports on a patient with Apert syndrome who did not require intracranial surgery.

There are existing reports of patients with syndromic craniosynostosis who were born with open calvarial sutures but developed premature fusion in the early postnatal period and ultimately required a cranial vault expansion. Connolly et al[4] described a series of 15 patients with postnatal progressive craniosynostosis, among whom one had Apert syndrome and demonstrated open cranial sutures on CT scans at age 8 months, but subsequently underwent fronto-orbital advancement and skull expansion due to suture fusion and increased ICP at age 3. Hoefkens et al[6] reported on 9 patients with Crouzon syndrome who developed postnatal craniosynostosis and elevated ICP from ages 6 to 17 months. In both series, despite demonstrating open sutures at birth, all patients subsequently developed symptoms of increased ICP and required cranial vault expansion.[4,6] Similarly, Coomaralingam and Roth[5] reported on a patient with Apert syndrome who did not demonstrate craniosynostosis at birth via skull radiographs but underwent skull remodeling surgery at age 10 months, presumably for cephalocranial disproportion and/or progressive synostosis. The patient described herein is phenotypically distinct from the aforementioned cases in that he has not required cranial vault surgery for functional or aesthetic concerns.

This report has implications for our understanding of the underlying genetic and pathophysiologic forces in Apert syndrome. Although the patient tested positive for the p.Ser252Trp mutation of fibroblast growth factor receptor 2 found in 64% of patients with Apert syndrome, he demonstrated a milder phenotype with no cephalocranial disproportion.[7] Moreover, despite the patency of major calvarial sutures and the SOS in early childhood, the patient nonetheless exhibited progressive midface hypoplasia. The SOS is believed to be an important site of midfacial growth in the cranial base, with studies demonstrating an association between premature SOS fusion and midface hypoplasia in syndromic craniosynostosis.[8] In contrast to previous work from our group that demonstrated at least partial SOS closure in all patients with Apert syndrome at age 6 or older, this patient did not demonstrate any SOS fusion at his most recent CT scan at age 7.[8] We hypothesize that his midface retrusion may have developed as a result of several influences, including coronal and/or facial sutural fusion and intrinsic mesenchymal growth patterns of the maxilla.[9,10] Although a single occurrence precludes generalization to all cases of Apert syndrome or syndromic craniosynostosis, we provide well-evidenced support via sequential CT scans and clinical photographs that progressive midface retrusion can develop even in the absence of premature SOS fusion.

CONCLUSIONS

We report on a patient with Apert syndrome who did not require intracranial surgery for cephalocranial disproportion, cranial shape abnormalities, or intracranial hypertension. Our findings support previous assertions that craniofacial changes in syndromic craniosynostosis arise from complex interactions among cranial, cranial base, and subcranial abnormalities rather than a singular driving force.

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DISCLOSURE

The authors have no financial interest to declare in relation to the content of this article.

PATIENT CONSENT

The patient provided written consent for the use of his image.

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