Saethre-Chotzen Syndrome

A Report of 7 Patients and Review of the Literature

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Introduction: Saethre-Chotzen syndrome is a genetic condition characterized by craniofacial and limb anomalies, with craniosynostosis (mainly coronal) being the most frequent craniofacial finding. Cranial and facial deformities can be extremely variable requiring individualization of treatment strategies. We present our case series to highlight clinical findings, treatment philosophy, and challenges facing Saethre-Chotzen patients.

Methods: A retrospective review was performed on records of patients given a diagnosis of Saethre-Chotzen syndrome at the University of California Los Angeles (UCLA) Craniofacial Clinic (n = 7) between 1980 and 2010. Patients with complete records were included in this study, and review of demographic data, clinical findings, surgical interventions and postoperative follow-up, and stability were performed.

Results: Seven patients (1 male and 6 female) were included in this study. The average age at which the patients were first seen was 6.5 years. Suture involvement was bicoronal (n = 6) and unicoronal (n = 1). There was 1 patient having superimposed metopic synostosis, and there was another patient having Kleeblattschädel deformity. Previous procedures performed for patients before establishing care at UCLA were strip craniectomy (n = 2) and fronto-orbital advancement (n = 2). All patients (n = 7) had fronto-orbital advancements at UCLA. Other skeletal operations included the following: redo forehead advancement and contouring (n = 3), monobloc advancement (n = 1), and LeFort III distraction (n = 1). Five patients reached skeletal maturity, and 2 patients received LeFort I advancement for class III malocclusion, one of which also required a bilateral sagittal split osteotomy of the mandible.

Conclusion: Clinical presentation and severity of deformity in Saethre-Chotzen syndrome are variable. Our current report reviews our treatment strategies and illustrates the predominance of cranial and upper face deformities and frequent need for redo surgeries to address forehead asymmetry in this group of syndromic craniosynostosis patients.

Key Words: craniosynostosis, fronto-orbital advancement, Saethre-Chotzen syndrome, Kleeblattschädel deformity, ptosis

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Saethre-Chotzen syndrome (SCS) is an autosomal dominant condition first described by Saethre[1] and Chotzen[2] in the early 30s of the last century. According to the McKusick[3] classification, SCS can be described as acrocephalosyndactyly type III and clinically presents with distinctive craniofacial and limb abnormalities including cranial vault asymmetry secondary to craniosynostosis (typically bicoronal, less commonly unicoronal),[4] facial anomalies including low frontal hairline, facial asymmetry (often secondary to synostotic anterior plagiocephaly), ptosis, downward slanting palpebral fissure, depressed nasal bridge, prominent ear helical folds, and limb abnormalities including incomplete simple syndactyly of the index and middle fingers and the third and fourth toes.[5]

Cranial and facial elements of the deformity in SCS can be markedly variable and can present a reconstructive challenge, and accordingly, treatment plans may need to be individualized according to each patient's deformity. This article aims to describe different clinical features and associated malformations in 7 patients with SCS, as well as the management plan for each of them to achieve functional and aesthetic restoration. The time frame of the study spans 30 years of experience by the senior author (H.K.K.) and highlights the evolution in surgical treatment.

PATIENTS AND METHODS

A retrospective review of records of all Saethre-Chotzen patients seen and treated by the senior author (H.K.K.) during the period from 1980 to 2019 at the University of California Los Angeles (UCLA) was performed with institutional review board approval (UCLA IRB #11-000925). Twelve patients were seen and treated, but only 7 patients with complete records and who completed the minimum follow-up period (9 years) were included. The assessment included retrospective evaluation of demographic data (age at first consultation and sex distribution) and family history of similar anomalies. Clinical findings including cranial and facial anomalies were recorded, and surgical procedures used to correct each deformity were also noted, because the surgical treatment varied according to each case, time of presentation, severity of the condition, and associated anomalies. Preoperative and postoperative photographs were taken of patients for diagnostic purposes and for evaluation of different surgical treatment outcomes.

RESULTS

Patient Characteristics

Seven patients with complete medical records were identified and included in the study (Table 1), 1 male and 6 female; their age at initial assessment ranged from 2 weeks to 12.8 years (mean, 6.5 years). Four patients had previous cranial operations before care was established at UCLA, one had a strip craniectomy performed during the first 6 months after birth, and 3 patients had a previous fronto-orbital advancement (FOA) with no available operative reports. Two patients had a positive family history of similar craniofacial malformations.

Regarding cranial dysmorphology and involved sutures, 6 patients presented with bilateral coronal synostosis and 1 patient had unilateral coronal involvement. Of the patients with bilateral coronal involvement, there was 1 patient having superimposed metopic synostosis, and there was another patient having Kleeblattschädel deformity. Upper eyelid

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TABLE 1. Patient Characteristics

Total no. patients, n	7
Female, n (%)	6 (85.7)
Mean (SD) age at initial evaluation, y	6.5 (5.2)
Mean (SD) age at final evaluation, y	17.9 (2.6)
Patients with affected family members, n (%)	2 (28.6)
Synostotic sutures, n (%)	
Bicoronal	4 (57.1)
Unicoronal	1 (14.3)
Kleeblattschädel	1 (14.3)
Other craniofacial findings, n (%)	
Midface retrusion	2 (28.6)
Blepharoptosis	7 (100.0)
Epicanthal folds	2 (28.6)
Strabismus	2 (28.6)

ptosis (unilateral in 4 patients and bilateral in 3 patients) was found in all patients (Fig. 1). Other reported facial abnormalities included bilateral epicanthal folds in 2 patients, strabismus in 2 patients (1 with severe head tilt and narrowing of the palpebral fissure), depressed nasal bridge in 4 patients, high forehead in 4 patients, midface retrusion in 2 patients, moderately constricted ears in 2 patients, bilateral low-set ears in 1 patient, and prominent ears in 1 patient (Figs. 2, 3). Exorbitism is apparent in many cases and is emphasized by the concomitant forehead deformity and the midface hypoplasia (Fig. 1). Nonfacial features included broadening of the fingers and toes, with syndactyly that may be unilateral or bilateral (Fig. 4) and, sometimes, clinodactyly.

Surgeries

Bony surgical procedures were customized to each patient's deformity and age at presentation (Table 2). Fronto-orbital advancements and strip craniectomies were performed in 4 patients before initial evaluation at UCLA. Of these patients, 3 received a secondary FOA at UCLA for residual forehead retrusion and asymmetry. Two other patients received primary FOAs at UCLA. Two patients had forehead cranioplasty procedures with split rib and calvarial bone grafts. Posterior vault expansion was performed for 1 patient with Kleeblattschädel deformity at 2 years old.

Although midface retrusion was relatively mild in all of the patients compared with other syndromic craniosynostoses, 3 patients underwent monobloc facial bipartition for the purposes of orbital asymmetry. None of the patients required distraction for advancement.

Orthognathic procedures were performed in 2 patients. In one of them, a severe transverse discrepancy of the maxilla required a maxillary corticotomy and midpalatal split for expansion before the final LeFort I advancement. In the second patient, LeFort I advancement was combined with a bilateral sagittal split osteotomy of the mandible to correct lateral deviation.

Temporal ballooning was markedly evident in 2 patients and required bony contouring in both, and temporal fat reduction was also performed in 1 patient. Other procedures included nasal augmentation with cranial bone graft (n = 1), ptosis correction (n = 2), and bilateral lateral canthopexy (n = 3) (Table 2).

DISCUSSION

The first report on SCS came from the Norwegian psychiatrist, Haakon Saethre, who was consulted for a case of schizophrenia and noticed a condition with characteristic craniofacial and limb anomalies with the patient's mother and half-sister also showing similar findings.[1]

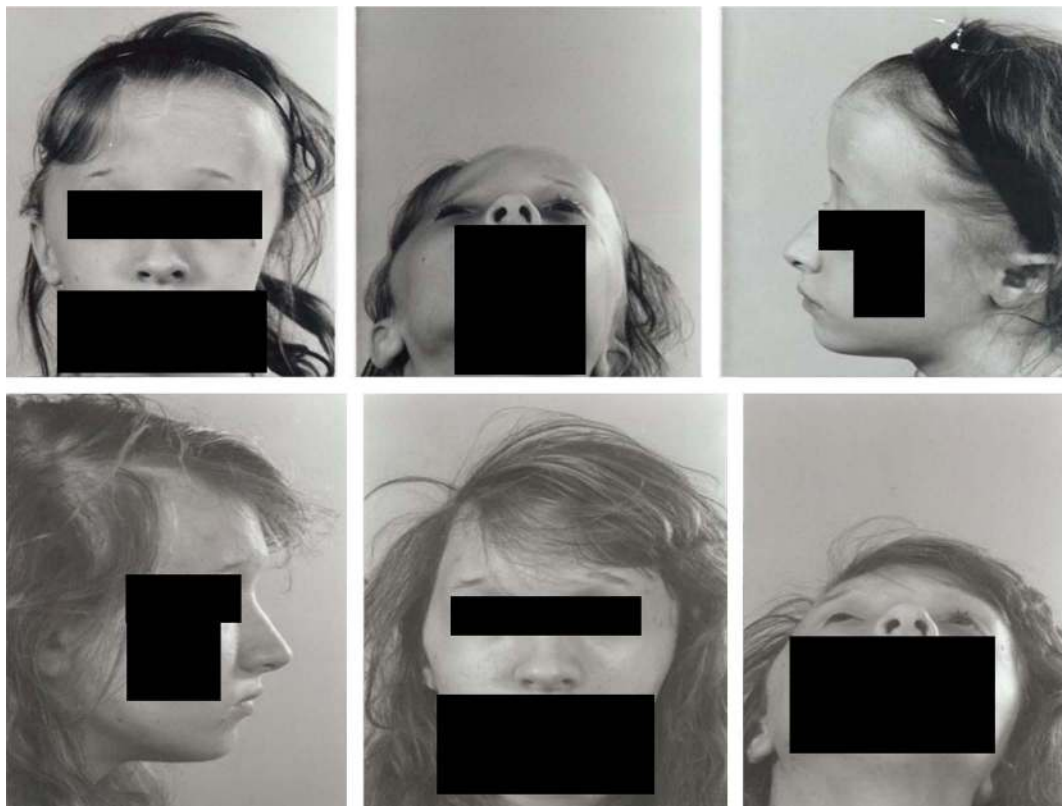

FIGURE 1. A girl with midface hypoplasia, ptosis, exorbitism, depressed nasal bridge, and low-set ear. Note the tracheostomy tube. full color online

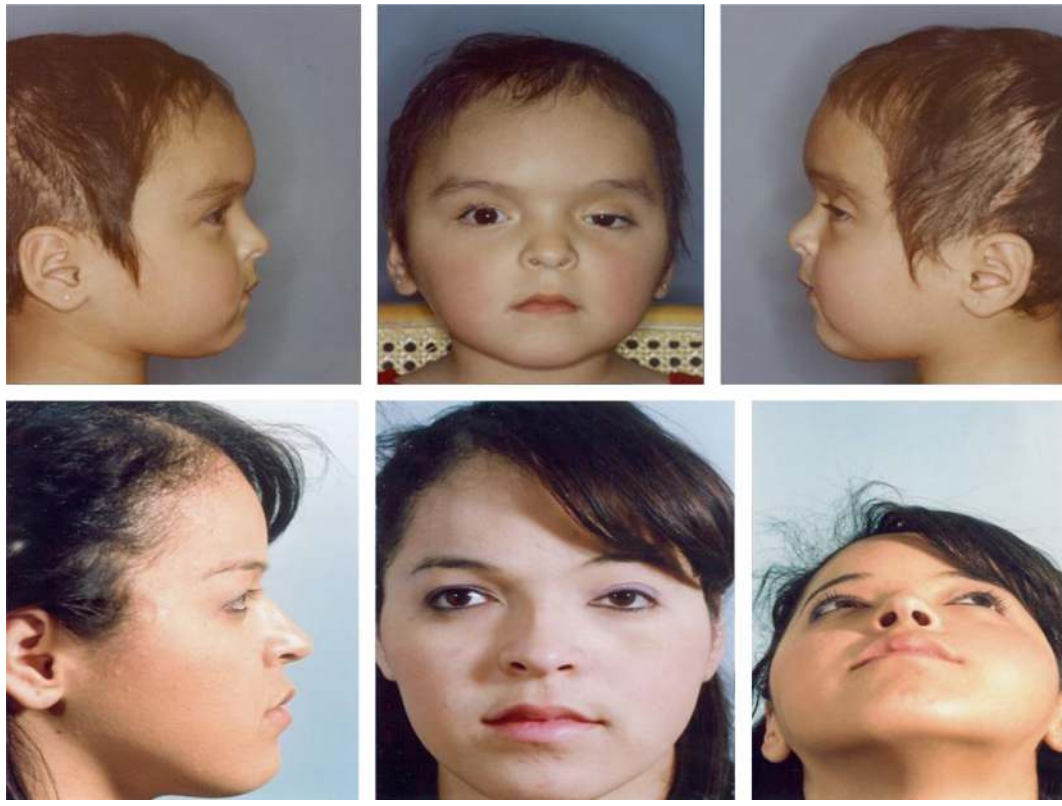

FIGURE 2. A patient with Saethre-Chotzen syndrome showing bilateral ptosis, bilateral epicanthal folds, depressed nasal bridge, high forehead, and low-set ears. full color online

Within a year, Chotzen reported similar—but not typical—findings in a father and 2 sons.[2] Because of the variable phenotypes of the condition, it was not until 1975 when Pantke et al[6] adequately highlighted the details of the syndrome. Incidence of SCS varies from 1 in 25 000 to 1 in 50 000 live births.[5] It is an autosomal dominant inherited condition, although sporadic cases do also occur because of genetic mutations affecting the TWIST1 gene on chromosome 7p21.[7,8] Most cases of SCS are familial rather than sporadic, but the signs in other family members may be subtle.[9]

Although there is no pathognomonic feature associated with this syndrome,[4,5] it typically presents with plagiocephaly or brachycephaly due to coronal craniosynostosis (unilateral or bilateral). Trigonocephaly and "peace sign synostosis" characterized by synostosis of the metopic, bilateral coronal, and sagittal sutures are also known to be associated with SCS, and even pansynostosis can occur.[5,10,11] Regarding the pattern of suture synostosis in our study, bilateral coronal synostosis was the most commonly observed pattern, with only 1 patient having had unilateral coronal synostosis. In 1 patient, there was superimposed

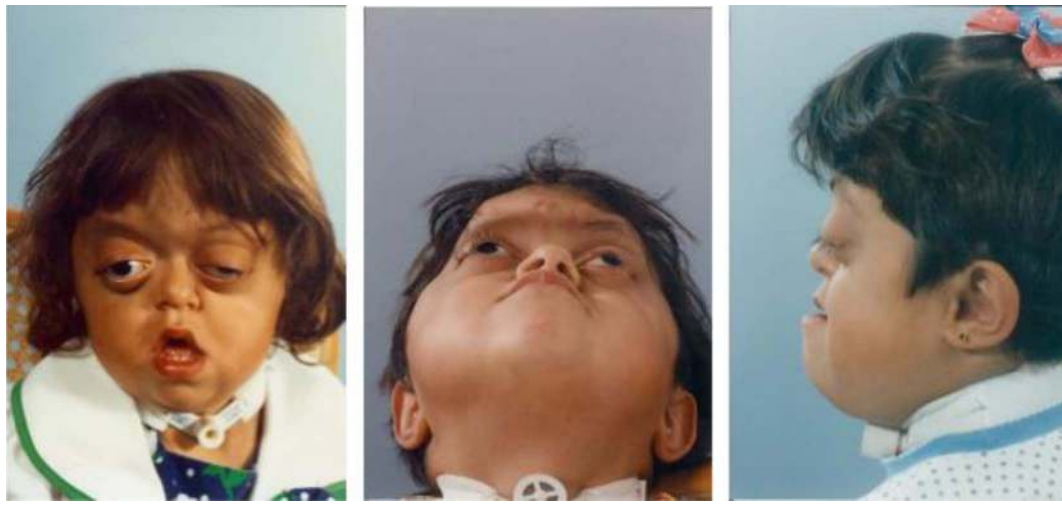

FIGURE 3. A girl with Saethre-Chotzen syndrome with left low-set ear and unilateral ptosis on the same side. full color online

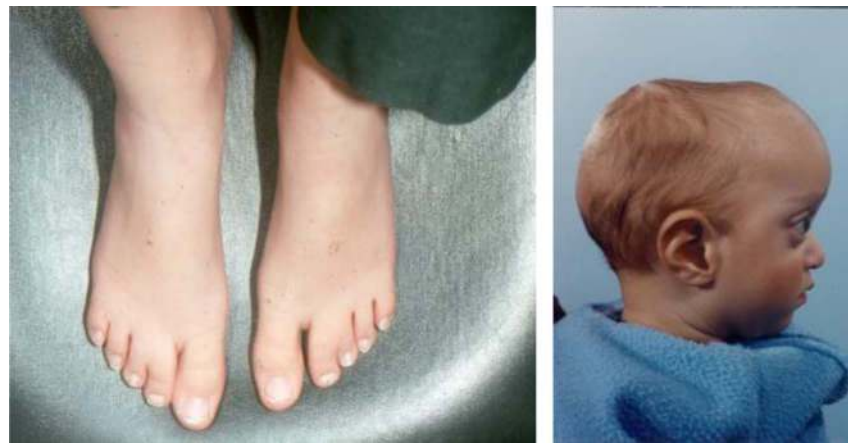

FIGURE 4. (Right) Broadening of the big toes and bilateral incomplete syndactyly of the second web. (Left) Characteristic shape of the skull with frontal bossing and nasal bridge depression. full color online

metopic synostosis, and another patient had the severest synostosis form with Kleeblattschädel deformity.

Other common craniofacial deformities encountered included a low-set frontal hairline, periorbital abnormalities, and external ear anomalies.[4,7] Eye abnormalities consisted of eyelid ptosis, downward-slanting palpebral fissures, hypertelorbitism, epicanthal folds, and, occasionally, blepharophimosis.[5] Eyelid ptosis was the most common facial deformity in our study occurring in 100% of patients, as compared with 53% in the study by de Heer et al.[5] Significant hypertelorbitism was found in 1 patient for which a facial bipartition was performed. Visual anomalies, including strabismus, amblyopia, or even loss of vision, can be found in Saethre-Chotzen patients.[5] In our study, significant strabismus was found in 2 patients; both of them had ptosis, and one also had blepharophimosis and epicanthal folds. Strabismus in this second patient was very difficult to treat, and head tilt could not be surgically corrected. This particular patient also had one of the most difficult-to-correct skeletal deformities encountered, requiring 4 redo forehead contouring procedures with suboptimal aesthetic outcome. In the literature, strabismus has been reported in approximately 56% of patients with craniosynostosis in whom extraocular muscles may be absent, be pathologically thick, be fibrotic, or have anomalous paths and insertions. Surgical planning and treatment of these cases are usually difficult because of the anomalous insertion of extraocular muscles and facial asymmetry.[12]

The ears in patients with Saethre-Chotzen may be low set and rotated, and patients may also have conductive hearing loss.[13] Deformities of the nose include a broad, depressed nasal bridge and nasolacrimal duct stenosis.[5] Three patients (42.8%) had a depressed nasal bridge compared with 65% in de Heer et al.[5] Hypoplastic midface, high-arched palate, and malocclusion are also reported findings.[5] However, it is difficult to find such a "typical patient" who has the whole range of anomalous features mentioned previously. In this study, mild midface retrusion was found in 3 patients, and a high-arched palate was reported in 1 patient (Fig. 5). Similar to other studies, we also found that midface retrusion in SCS is less frequent and less severe than with other craniosynostosis syndromes.[9] Although 3 of our patients underwent monobloc facial bipartition procedures, the rationale for the midface procedure was largely to address orbital asymmetry with only a mild advancement. None of the patients required distraction procedures for advancement.

Although FOA was needed in all patients in this study, 4 of them had previous release performed in outside institutions with strip craniectomies and/or FOA and 3 required reoperation with redo-FOA or forehead cranioplasty. Tessier[14] called SCS "upper face Apert" referring to the lower frontal operation stability and higher reoperation rate in this group of patients. In our most severe cases, we could not achieve satisfying results with redo FOA alone, and multiple bone grafts were necessary to address contour irregularities. Split rib grafts were used in many early cases by the senior author, but in later years, split calvarial bone grafts were preferred, because there is always enough bone in the cranium to reconstruct any defect in the craniofacial complex. In the senior author's experience, and according to some of our previously published reports[15,16] and ongoing research projects about syndromic craniosynostosis, patients with Saethre-Chotzen have the least severe midface retrusion deformity compared with those with Apert, Crouzon, and Pfeiffer syndromes.

In all syndromic craniosynostosis patients including Saethre-Chotzen, we follow a surgical algorithm that includes multiple operative sessions and nonsurgical procedures, which are related to the degree of functional and cosmetic deformities, and patient age and growth. The main objectives are to correct cranial and facial deformities and to avoid any increase in the intracranial pressure with its sequelae on cognitive brain function and also on vision. Generally, the algorithm of management is quite similar to the management protocol of Apert syndrome,

TABLE 2. Surgery Characteristics

Description	n (%)	Age, Mean (SD), y
Fronto-orbital advancement	5 (71.4)	7.1 (6.8)
Primary	2 (28.6)	0.5 (0.3)
Secondary	3 (42.8)	11.5 (4.2)
Posterior cranial vault expansion	1 (14.3)	2.4
Monobloc bipartition	3 (42.8)	13.8 (4.1)
Forehead cranioplasty*	2 (28.6)	11.3 (4.1)
Orthognathic procedures†	2 (28.6)	18.1 (0.8)
Eyelid procedures	3 (42.8)	7.1 (6.8)
Ptosis correction‡	2 (28.6)	6.6 (7.5)
Canthopexy/canthoplasty§	3 (42.8)	13.8 (7.5)

*One patient had 4 bone grafts for correction of contour deformities of the skull.

†One patient had a surgically assisted rapid palatal expansion before LeFort I.

‡One patient had 2 ptosis procedures, and 1 patient had 3 ptosis procedures.

§One patient had 2 lateral canthopexies.

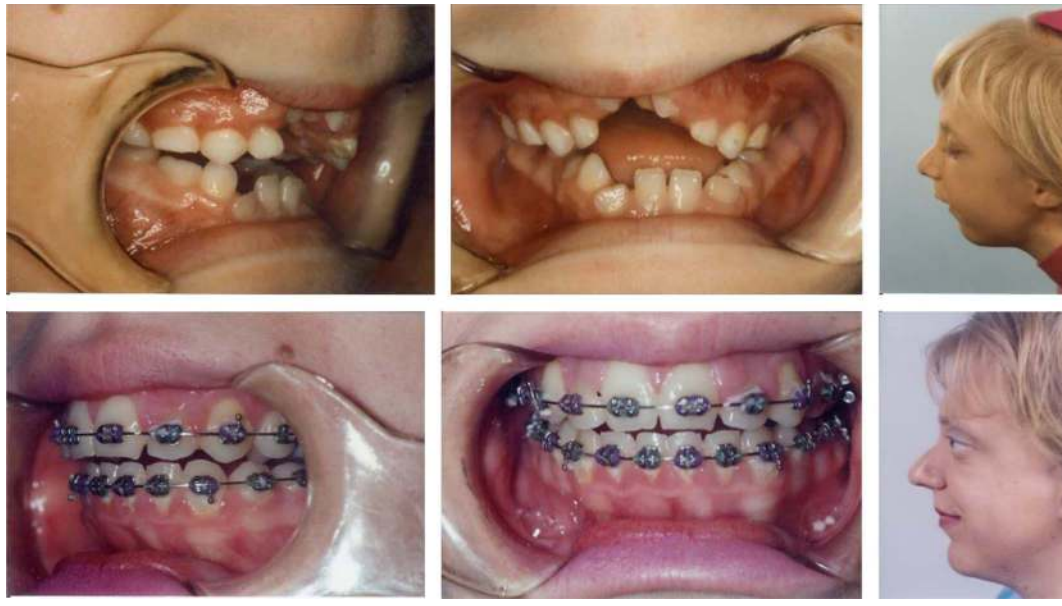

FIGURE 5. Patient with high-arched palate with maxillary collapse and occlusion problem (top), and the same patient after having LeFort 1 and chin advancement (bottom). full color online

which was described by Allam et al[15] in 2011; however, every case should be considered independently according to type and degree of deformity.

CONCLUSIONS

This study describes the senior author's experience with the management of patients with the rare SCS. It also elaborates on the variety of clinical presentations and severity, different treatment options available, and evolution of treatment philosophy over 3 decades. Because the severity of deformity and age at presentation can be variable, treatment plan must be customized to each patient and his or her needs. Forehead deformity is the most challenging problem in Saethre-Chotzen patients, as reflected in increased reoperation rates for FOA and the need for forehead cranioplasties to address contour irregularities in many patients. Conclusions, however, cannot be generalized because of our small sample size given the rarity of this condition, and more studies about the clinical aspects and management of Saethre-Chotzen should be encouraged to draw more solid conclusions.

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