Original Paper

Posterior vault distraction osteogenesis in Apert syndrome

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Apert syndrome is an uncommon autosomal dominant condition with a varied clinical spectrum which includes premature cranial and facial suture fusion and complex upper and lower limb syndactilies. In this manuscript, we share our posterior vault distraction osteogenesis (PVDO) experience regarding Apert syndrome patients so that a larger patient population may benefit. In addition, we aimed to determine an onset of elevated intracranial pressure in the long term follow up.

A retrospective study was performed on consecutive patients with syndromic craniosynostosis who were diagnosed with Apert syndrome, underwent PVDO between 2012 and 2019, and received at least 2 years of follow-up care. Demographic data, diagnosis, surgery related data, and outcome data (perioperative and mid-term complications and need for additional surgery), were verified by means of medical records, clinical photographs, radiographic images, and interviews with all included patients and/or their parents.

The present study included 14 patients who were diagnosed respectively with Apert syndrome (n = 14). The average posterior advancement distance achieved was 19.37 ± 3.0 mm. Two patients included in this study presented major complications, but neither experienced permanent sequelae or a lethal course. Two Apert patients presented cerebral spinal fluid (CSF) leakage (Clavien–Dindo type II). One patient presented a onset of elevated intracranial pressure at 4 years of follow up.

PVDO is an effective procedure at alleviating intracranial pressure and present a low complication rate.

Keywords: Apert syndrome, craniosynostosis, syndromic craniosynostosis, syndrome, Apert, craniofacial dysostosis, craniofaciostenosis, cranioestenosis

INTRODUCTION

Apert syndrome is an uncommon autosomal dominant condition with a varied clinical spectrum which includes premature cranial and facial suture fusion and complex upper and lower limb syndactilies. Abnormal retruded maxillary morphology, differing levels of exorbitism, and obstructive sleep apnea are frequently presented by Apert patients.(1) Additionally, due to the above mentioned premature fusion, Apert patients usually experience elevated intracranial pressure.(2)

To support and facilitate maximum cognitive development, as well as hand function and dexterity, effective treatment and management of Apert syndrome cases necessitate a dual approach via a multidisciplinary team accompanied by long term follow-up.(3) As there will be successive procedures, careful staging is essential so that each individual craniofacial surgical procedure performed along the reconstructive ladder does not adversely impact the efficacy of any other subsequent procedure.(4, 5)

Beginning in 2009, posterior cranial vault distraction (PVDO) was introduced as a novel technique in treating children with Apert syndrome. (6)There are many benefits to utilizing PVDO, as this procedure results in greater cranial volume than previous procedures, supports hydrocephalus prevention and Chiari type I and papilledema treatment, as well as skull reshaping and reduced turricephaly.(7-13) Additionally, significant cognitive gains have been demonstrated in children following performance of PVDO, and the reduction in elevated intracranial pressure shown in follow up likely eliminates the need for a second procedure.(14) Additional advances in distraction osteogenesis in the treatment of children with syndromic craniosynostosis are now being achieved worldwide in reference centers, thereby reducing relapse risks associated with classical techniques that do not include distraction osteogenesis.(10, 14-18) The major advantages shown by

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posterior distraction over less recent techniques have caused numerous high-volume centers (above 40 syndromic cases/year) to forego classical techniques and modify their treatment algorithms to include PVDO.(3, 8, 9, 19) Despite the above, PVDO is still not utilized as a first-line treatment in Brasil, and we are sharing our PVDO experience regarding Apert syndrome patients so that a larger patient population may benefit. In addition, we aimed to determine an onset of elevated intracranial pressure in the long term follow up.

METHODS

A retrospective study was performed on consecutive patients with syndromic craniosynostosis who were diagnosed with Apert syndrome, underwent PVDO between 2012 and 2019, and received at least 2 years of follow-up care. A prophylactic PVDO was performed on all included patients under 1 year of age, and a therapeutic PVDO was performed on all included patients older than 1 year of age, who already presented signs of elevated intracranial pressure.

Patients with incomplete medical records and/or those patients who did not participate in a full course of follow-up care were excluded from this study.

Demographic data (patient gender and age when the PVDO procedure was performed), diagnosis, surgery related data, and outcome data (perioperative and mid-term complications and need for additional surgery), were verified by means of medical records, clinical photographs, radiographic images, and interviews with all included patients and/or their parents. As each patient included in this series was promptly operated on subsequent to his/her presentation, patient age when the relevant surgical procedures were performed is directly correlated with patient age at presentation.

All subjects enrolled in this study completed consent forms signed by the patients' parents in accordance with the Declaration of Helsinki of 1975, as amended in 1983. Local institutional research ethics board approval was obtained for this study.

SURGICAL TECHNIQUE AND DISTRACTION PROTOCOL

For a great majority of our syndromic craniosynostosis (SC) patients, our standard protocol includes PVDO as a first-line procedure. However, our protocol does not include the performance of PVDO as a first-line procedure for SC patients when a patient presents one or more of the following 3 conditions:

1) Patients presenting malignant exorbitism; 2) Patients presenting severe cranial lacunae, a Swiss-cheese type of bone formation that impairs bone stability during distraction osteogenesis; and 3) Patients presenting important supratentorial collateral emissary veins (CEV) embedded in the scalp that create sagittal sinus venous outflow dependence.

We perform computerized tomography and/or magnetic resonance imaging venograms on all of our SC patients to detect the presence of venous hypertension and critical supra-tentorial CEV, which may generate venous outflow dependence.

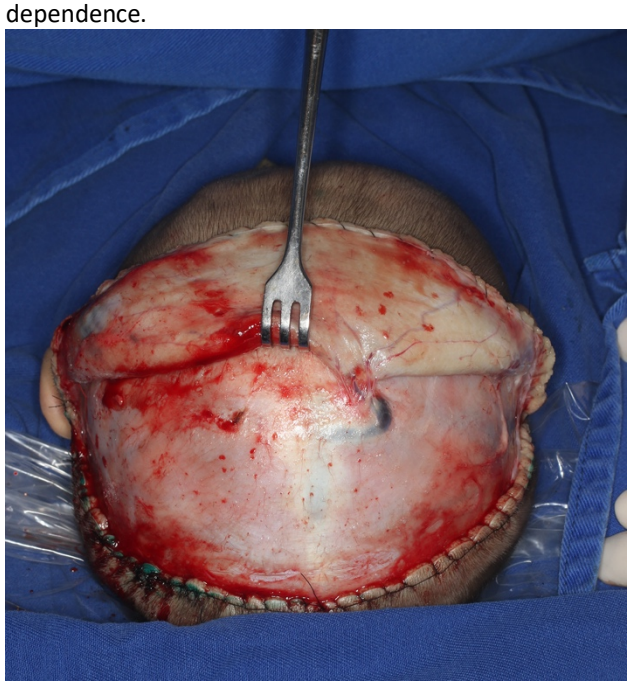

Figure 1 - Computerized tomography imaging venograms showing supra-tentorial collateral emissary veins.

Surgical technique

The patient is placed in a prone position at the beginning of the PVDO procedure, followed by the performance of a coronal incision, and elevation of the coronal flap within the supra-periosteal plane and non-dependent collateral vein is ligated. (Figure 2). Although the periosteum remains attached to the underlying bone, the periosteum is incised, and a posterior craniotomy is marked from the vertex, following the parietal and occipital bones towards the torcula. In order to maintain a hemoglobin level above 10g/dl for each patient, intraoperative transfusion was performed as needed, based on patient blood loss. The craniotomy is performed by the neurosurgeon (EG), and internal mandibular distractor devices measuring between 20mm and 30mm in length are placed.

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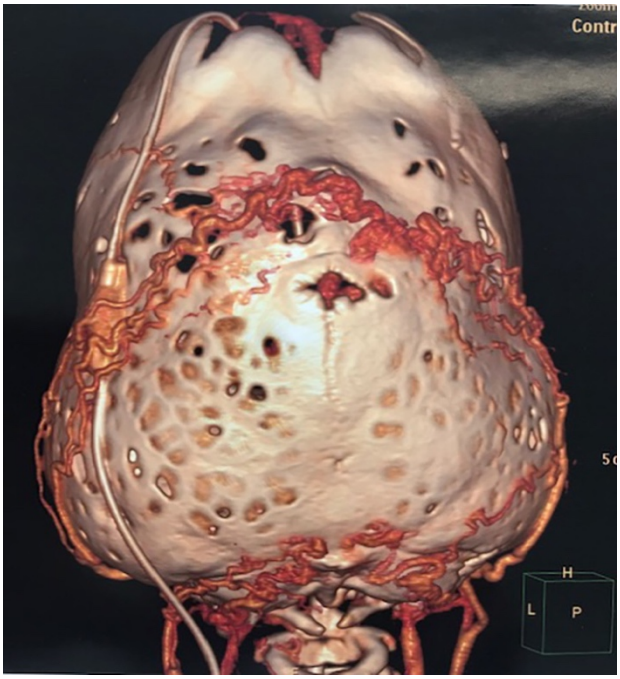

Figure 2 - Photograph showing the supratentorial collateral non-dependent emissary vein that was subsequently ligated for the craniotomy.

Approximately 48 hours after surgery is performed, the distraction activation period commences. The subsequent activation period lasts approximately 20-30 days, and distraction usually occurs at a rate of 1mm per day. Following a 4 week consolidation period, the internal distractor devices are removed utilizing a small incision at the coronal scar.

Approximately 3 weeks before surgery is performed, all patients receive 3 doses of erythropoietin, 1 dose per week, as per our standard preoperative protocol.

We recorded and stratified patient complications utilizing a modified Clavien–Dindo surgical complication scale.(20) Complications recorded as minor only required pharmacologic treatment and/or intervention without hospital admission. Major complications were then sub-stratified into I, II, and III: (I) events requiring initial or subsequent intervention with general anesthesia to treat the resulting condition; (II) events with permanent sequelae; and (III) fatal events.

As part of our standard follow up care protocol, all SC patients undergo annual evaluation to monitor elevated intracranial pressure, and to determine whether subsequent treatment and/or additional surgical procedures are indicated.

Follow up screening for elevation of intracranial pressure and parameters for reoperation were (1) clinical and (2) ophthalmologic; (1) bulging fontanelle, successive headache, vomiting, and restless behavior for more than 15 consecutive days; (2) modification of the status/appearance of the papilledema and/or disc changes. Radiologic (cranial ultrasound or MRI) follow up was performed to detect obliteration of basal cisterns, optic nerve sheath enlargement, empty sella, tonsilar herniation, and progressive hydrocephalus; the last being a criteria for shunt placement.(21)

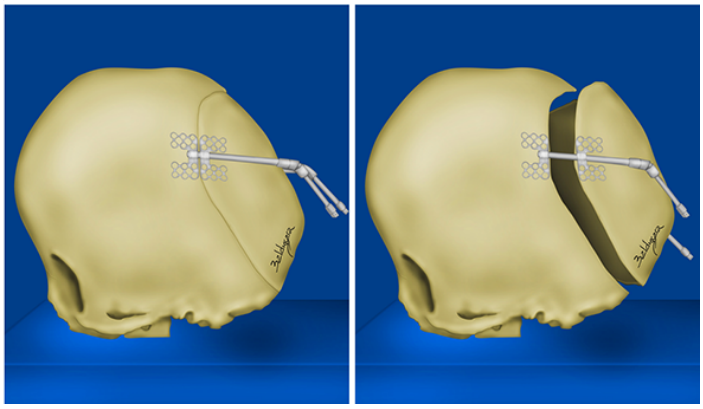

Figure3 - Illustrative drawing depicting the posterior vault distraction osteogenesis.

RESULTS

The present study included 14 patients who were diagnosed respectively with Apert syndrome (n = 14). Patient age when surgery was performed ranged from a minimum of 4 months up to a maximum of 46 months, with the average patient age being 12.9 months (The median is 10.5 months). Among 14 Apert syndrome patients, 10 were prophylactic and 4 therapeutic showing clinical or radiological signs of elevated intracranial pressure.

The average posterior advancement distance achieved was 19.37 ± 3.0 mm. Two turns of the distractor arms corresponded 1mm, one turn 0.5mm.

Two of the Apert syndrome patients included in this study underwent previous strip craniectomies at a different medical facility without improvement in cranial morphology, but subsequently underwent PVDO at our Hospital, resulting in improved Chiari type I. Three Apert syndrome patients included in this study, all of whom had been scheduled to undergo PVDO procedures, underwent fronto-orbital advancement (FOA) instead, due to the presence of important CEV with associated venous outflow dependence. Four additional patients underwent FOA for other reasons.

Only two patients included in this study presented major complications, but neither experienced permanent sequelae or a lethal course. Two Apert patients presented cerebral spinal fluid (CSF) leakage (Clavien–Dindo type II). The distraction process for one of these Apert patients was ended before completion due to meningitis, which was treated with antibiotics. The same Apert patient presented a hydrocephalus following distractor removal, requiring placement of a shunt. The other Apert syndrome patient who presented CSF leakage, experienced a complication related to the distractor arm, and the distraction process was

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temporarily discontinued for 72 hours. Once the leakage stopped, the distraction process was continued to completion. Average blood transfusion volume per kilogram per patient was 22.75 ± 9.30 ml. All patients were transfused. Blood transfusion commenced at the scalp incision. Four patients had Chiari I improved with PVDO. One patient who underwent a prophylactic PVDO presented a recent onset of elevated intracranial pressure showing modification of the status/appearance of the papilledema and/or disc changes in addition to a clinical features at 4 years of follow up and is scheduled for a secondary PVDO. All patients in these series presented 5-digit hand and were included in our hand reconstruction regimen.

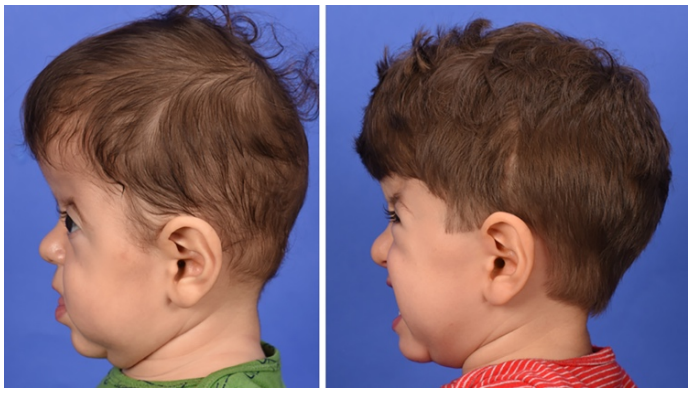

Figure 4- Preoperative and 4 year postoperative photograph of posterior vault distraction osteogenesis.

DISCUSSION

Data from the literature reveals that Apert syndrome patients share high levels of intraoperative blood loss as a unique characteristic.(14, 22, 23) In a study from Birmingham Children's Hospital, the highest incidence of serious complication was with an Apert syndrome cohort of 9 patients, with one Apert patient presenting severe bleeding, two other Apert patients presenting CSF leaks, and one Apert patient requiring a shunt.(24) Death is also reported in Apert syndrome patients. (25) Complications descriptions for intracranial procedures in SC vary according to craniofacial groups.(26-29) Serious complications for transcranial procedures can reach 59%, with a mortality rate of 4.5%.(30) Blood loss in patients with SC is likely related to venous hypertension, and significant bleeding may occur, especially in the presence of CEV from the sagittal sinus to the scalp, or if there is any injury to the posterior sagittal sinus, coronal flap, or dural undermining, prior to craniotomy. Eminent surgeons from the Craniofacial Center, Seattle Children's Hospital also acknowledged that Apert Syndrome is one of the most significant predictor of increased blood loss. (23)

Apert syndrome patients likely to develop neurological complication and hydrocephalus are not good candidates for PVDO, and it is therefore critical to recognize this cohort of patients during examination and screening.(3) Among this cohort are those severe syndromic craniosynostosis patients who present cranial lacunae at the posterior region, and/or other clinical and radiological characteristics of elevated intracranial pressure. Coll and collaborators showed that a smaller area of the foramen magnum and a greater degree of cerebellar tonsillar ectopia is present in Crouzon/ Pfeiffer patients compared with children with Apert syndrome, being those more likely to present hydrocephalus. As we did not measure the foramen magnum in our series of Apert syndrome patients, we could not corroborate this finding. Further assessment on our data may show similar correlation. (31)

The wide spectrum of SC patients is evidenced by the presence of cranial lacunae, which is accompanied by severe exorbitism in Pfeiffer syndrome patients, but not always associated with severe exorbitism in Apert syndrome patients.

For SC patients from this particular cohort (patients presenting cranial lacunae type of bone formation, also referred to as severe cranial lacunae), we perform craniectomy and total calvarial remodeling when the patient is between 3 and 4 months of age, not only to alleviate intracranial pressure, but also to improve cloverleaf calvarial shape morphology. (3, 32) Although available data reveals merely a weak correlation between elevated intracranial pressure and cranial lacunae morphology,(21) our experience has demonstrated that performing this type of surgery on a patient at 3 to 4 months of age facilitates bone cuts which are imbricated into the dura mater and sagittal sinus, and enables removal and remodeling with reduced bleeding.

Distraction activation is suspended as per our standard PVDO protocol, if a CSF leak occurs or severe wound breakdown is evident. The activation phase is suspended if a local infection is present, but thereafter resumed following a course of antibiotics. The skin is re-sutured or a local flap is made in cases where patients experience severe wound breakdown, so that distraction activation is not interrupted. In this study, approximately 16% of our patients required corrective procedures and a return to the operating theater, which is higher than the rate reflected in prior relevant national PVDO data.(8)

There is an ongoing debate regarding appropriate duration of the PVDO consolidation phase. Some craniofacial groups advocate keeping the distractors in place for at least 3 months,(24) while other groups recommend distractor removal as early as 4 weeks after surgery or immediately after the activation phase is complete.(3, 13)

Early distractor removal can be appropriate where: (1) the hypertensive brain progressively expands after distraction, which prevents recurrence of the bone flap; (2)

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periosteal cells present enhanced osteogenic potential in patients with an FGFR2 mutation;(33) and (3) as the posterior bone flap is neither devascularized nor detached from the dura mater, it is likely that osteogenesis will occur more rapidly than would be the case with back table bone remodeling.

Our group protocol limits the consolidation phase to 4 weeks only as there is an increased likelihood of a patient experiencing local trauma, device exposure, and local infection, if the distractors are left in place for an extended period.

This study is not without limitation. Up until 2019, our cohort of included patients represented a small sample size. In light of this, our group subsequently recruited a major cohort in the following two years, and the number of complications experienced by participating patients has significantly decreased. Notwithstanding the foregoing, the present study utilizes data from the largest cohort of Apert syndrome patients who have undergone PVDO in Brasil, a procedure pioneered by our group in Brasil, associating neurosurgical and craniofacial plastic surgery skills and expertise.

DISCLOSURES

Ethical approval

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the local Ethics Committee

Consent to participate

The patient gave consent to use his information and images for research proposes.

Consent for publication

The patient gave consent to use his information and images for publication.

Conflict of interest

The authors declare no conflicts of interest with respect to the content, authorship, and/or publication of this article.

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