BMJ Case Reports

## TITLE OF CASE

Apert Syndrome: An informative long term dentofacial outcome

## SUMMARY

The management of patients with Apert Syndrome (AS) is complex and reflects the multisystem disease as a result of premature fusion of cranial vault, cranial base and midface sutures as well as extremity anomalies characterised by syndactyly. Early cranial sutural fusion results in cranio-cerebal disproportion which can lead to crisis surgical intervention due to raised intracranial pressure, ophthalmic and compromised airway concerns. Childhood inventions are often determined by psychosocial concerns and adult surgical interventions are often determined by cosmetic concerns. Treatments are provided by many different specialists within multidisciplinary teams (MDT). The treatment pathway extends from birth well into adulthood and is often associated with a heavy burden of care. Due to the extensive nature of the interaction with these patients MDT members have opportunities to provide enhanced patient-centred care and support.

This case report provides an overview of the current knowledge of the aetiology of AS, illustrates the pathway of surgical and non-surgical management of AS and provides a long-term review of the dentofacial treatment outcomes.

By having a better understanding of the impact of AS and treatment provided, MDT members can not only provide improved clinical treatment but also offer improved patient experiences for those with craniofacial anomalies in particular an increased awareness of the psychosocial challenges they endure.

## BACKGROUND

Craniosynostosis is a condition that describes the premature fusion of one or more skull sutures. The incidence has been estimated to range from 1:2000 to 1:2500 live births and although 80% are “non-syndromic”, craniosynostosis has been associated with more than 150 syndromes. The most common craniosynostosis syndromes affected by mutations in fibroblast growth factor reception (FGFR) include Pfeiffer, Crouzon, Muenke and Apert.[1] Apert syndrome (AS) (OMIM 101200) was first described in 1909 by French physician Eugène Apert who identified individuals with similar facial characteristics alongside syndactyly.[2] Apert syndrome leads to complex functional and structural abnormalities in the face and extremities and requires multi-disciplinary management.

Apert syndrome presents in around 1:60,000 live births. The syndrome usually occurs due to sporadic mutations in FGFR2 however, an autosomal dominant inheritance pattern has also been shown.[3] Wilkie and colleagues found that two variants in FGFR2 mutations are involved in the syndrome: S252W and P253R.[4] FGFR signalling contributes to the proliferation, migration, differentiation, and survival of cells. In Apert syndrome, the FGFR2 mutation leads to enhanced differentiation of osteoblasts and a gain-of-function in FGF signalling leading to inhibition of growth particularly at the coronal suture interface and compensative growth at other sutures.[3]

Apert syndrome is associated with the general features of bicoronal craniosynostosis, exorbitism, midface retrusion and syndactyly of hands and feet. The changes in skull shape can result in raised intracranial pressure creating complications in vision and neurodevelopment. Some individuals also show mild intellectual disability and speech and hearing impairments. Exorbtism can cause corneal abrasions and scarring due to increased eye exposure. Airway compromise causes issues with feeding and sleep apnoea which may require additional surgeries. Cleft palate and conductive hearing loss are often further complications of the syndrome.[5]

In relation to a patient's dentition, individuals with AS are known to frequently present with a delayed eruption pattern. Missing teeth and malformations are also common. Due to the altered jaw sizes, often there is a narrowing of the maxillary arch, class III malocclusion and bilateral crossbite, and crowding of both permanent and deciduous dentitions. Manual dexterity is compromised in these individuals, reducing adequate oral hygiene, causing increased caries and periodontal disease risk.[5,6]

As with other craniofacial anomalies, the rehabilitation of a patient with AS is coordinated and staged within a multidisciplinary team and numerous surgical and non-surgical management with variations and timings of therapeutic interventions set according to individual requirements[5]. These patients and their families often experience a range of emotional and psychological issues associated with the abnormalities and its treatment.[7,8]

## CASE PRESENTATION

A 14-year-old patient with AS presented with a high steeped forehead, mild hypertelorism and proptosis with anti-mongoloid slant, mildly hypoplastic infraorbital and malar regions and a depressed nasal bridge (Figure 1A). She was experiencing Continuous Positive Airway Pressure (CPAP) dependent obstructive sleep apnoea with reduced nasal airway, particularly on the left side and a narrow nasal aperture. She was in the late mixed dentition with a Class II division 1 incisor relationship on a skeletal 2 base with an increased FMA and increased lower face height. There was fair oral hygiene with moderate lower arch crowding and potentially severe upper arch crowding. The upper had a narrow V-shaped arch form, the incisors were proclined and spaced with the first premolars approximating the distal of the lateral incisors. There was a 12mm overjet, a deep impinging overbite with an accentuated curve of Spee to the lower arch. The molar relationship was full unit Class II and there was a bilateral buccal crossbite and with an upper midline shift to the left. There was deep periodontal pocketing associated with the mesial and distal aspects of the 16 with gingival recession on the buccal (Figure 2A).

The OPG confirmed the presence of unerupted ectopically placed 13,23, 28 and the unerupted and impacted 37,38,47,48. Significant bone loss was evident distal to the 16. Cephalometric analysis confirmed the skeletal 2 relationship with retrognathic mandible and vertical maxillary excess (Table 1). Also evident was the beaten copper appearance to the inner surface of the frontal bone which is indicative of previous raised intracranial pressure (Figure 3B).

Table 1. Lateral cephalogram analysis: (A) Pre Le Fort III distraction (B) Pre orthodontic treatment and surgically assisted maxillary expansion (C) Pre Le Fort I impaction/rotation and BBSO advancement (D) Brace removal.

| **Skeletal AP** | A | B | C | D |
|---|---|---|---|---|
| SNA (º) | 65.8 | 85.8 | 88.3 | 86.7 |
| SNB (º) | 75.3 | 76.2 | 78.7 | 81.8 |
| ANB (º) | -9.5 | 9.6 | 3.6 | 4.9 |
| | | | | |
| **Vertical** | | | | |
| Maxillary-Mand Angle (PP-MP) (º) | 39.8 | 26.1 | 34.2 | 37.4 |
| Y-axis (SGn - SN -7) (º) | 61.2 | 57.2 | 45.6 | 58.0 |
| MP - SN (º) | 37.8 | 25.4 | 32.8 | 32.1 |
| | | | | |
| **Dental** | | | | |
| U1 - Palatal Plane (º) | 109.6 | 116.0 | 102.8 | 101.6 |
| L1 - GoGn (º) | 79.8 | 81.5 | 103.5 | 92.5 |
| Interincisal Angle (U1-L1) (º) | 130.9 | 136.8 | 125.6 | 136.7 |
| Overjet (mm) | 2.0 | 32.3 | 11.9 | 3.1 |
| Overbite (mm) | 0.5 | 9.1 | 3.4 | 1.2 |
| | | | | |
| **Facial Proportions** | | | | |
| AUFH/Total face height (%) | 31.4 | 39.2 | 35.7 | 35.3 |
| ALFH/Total face height (%) | 68.6 | 60.8 | 64.3 | 64.7 |
| | | | | |
| **Facial Convexity** | | | | |
| Downs angle of convexity (NA-APo) (º) | -19.2 | 13.5 | 11.8 | 11.4 |
| Holdaway Angle (NB to H-line) (º) | 9.3 | 18.2 | 15.2 | 13.8 |

Prior to presenting, the patient had undergone earlier surgery which involved a Fronto-orbital advancement and remodelling (FOAR) as an infant and more recently (at age 9) a Le Fort III distraction advancement. Both operations, which are common in AS were undertaken to improve compromised upper airway, although the earlier operation also addressed her cranio-cerebal disproportion and ophthalmic concerns due to early cranial vault suture closure. Additional surgery was also undertaken during infancy to address the syndactyly of hands and feet. Prior to the Le Fort III distraction advancement, there was marked midface retrusion, a reverse overjet and ongoing issues of obstructive sleep apnoea despite CPAP treatment (Figure 3A). The distractor placement resulted in the loss of developing teeth 18,17 and 27 and the probable displacement of the developing 28 tooth bud. It also resulted in bone loss associated with the 16 and limited its long-term prognosis. The distraction was further complicated by a differential advancement resulting in a significant maxillary midline shift to the left. Despite the earlier midfacial advancement she required CPAP and had difficulties with concentration at school.

Treatment plan

The treatment plan involved: (1) improvement of the patient's oral hygiene and periodontal health, in particular the region of the 16; (2) placement of a rapid palatal expander screw prior to the surgical removal of multiple ectopic/impacted teeth (13,23,27,37,38,47,48) and undertake Le Fort I maxillary osteotomy to enable surgically assisted maxillary expansion and bony recontouring of the pyriform aperture; (3) placement of upper and lower fixed appliances to align and decompensate the dental

arches; (4) undertake a Le Fort I impaction with rotation and mandibular bilateral sagittal split osteotomy (BSSO) advancement; (5) carry out final post-surgical occlusal detailing prior to debond and placement of retainers.

Treatment Progress

Orthodontic treatment was initiated at age 14.3 years with the placement of a maxillary midline Hyrax screw immediately prior to undertaking multiple surgical extractions listed above and a Le Fort I osteotomy to facilitate surgically assisted maxillary expansion and bony recontouring of the pyriform aperture region to significantly widen and enlarge the anterior nares with a view to improve the nasal airway and make the patient less dependent on CPAP. Activation of the midline screw (1cm) over a 2-week period resulted in a large upper midline diastema and this proceeded to the placement of upper and lower fixed edgewise appliances (0.022" MBT prescription). Once co-ordinated 0.019" × 0.025" stainless steel arch wires were in place the Hyrax screw was removed and shortly afterwards presurgical records collected to confirm presurgical arch decompensation and coordination (Figures 1B,2B,3C) (Table 1). A Le Fort I impaction with rotation was undertaken at age 16.1 years to achieve midline correction, allow some autorotation of the mandible and a BSSO advancement to achieve a complete reduction in overjet. Postsurgical intra-oral elastics were required to fine-tune the occlusion, especially for the left buccal segments which required further buccal expansion. Fixed appliances were finally removed at age 16.8 years with upper and lower vacuum formed retainers prescribed (Figures 1C,2C,3D) (Table 1).

## OUTCOME AND FOLLOW-UP

A 5.8 year follow up showed stable correction of the overjet, overbite and dental midlines, although there has been some constriction of the maxillary posterior teeth resulting in a bilateral buccal crossbite. The current posterior occlusion appears stable with no mandibular displacement and retainers were discarded by the patient 2 years previously after the 16 was extracted due to lack of periodontal support. There has been some minor imbrication of the upper left central incisor and lower incisors with slight space distal to the 12, which do not cause the patient any concern. The patient reports an absence of any breathing or masticatory issues and maintains regular dental hygiene visits. She maintains regular employment and is now no longer requiring CPAP and has much improved gingival health.

The case study of this patient illustrates the need for collaboration and interaction between the multidisciplinary team in planning a comprehensive treatment strategy over an extended time frame. Initial surgeries for APS are often "crisis" driven as in this case, where a FOAR surgical procedure was undertaken to address cranio-cerebral disproportion and ophthalmic concerns due to early cranial vault suture closure. A subsequent Le Fort III distraction advancement was undertaken due to ongoing compromised upper airway and issues associated with obstructive sleep apnoea despite CPAP treatment.

Following the eruption of the permanent dentition, combined orthodontic and orthognathic surgeries are often required to restore dental function and aesthetic appearance to the face. For this case a Le Fort I osteotomy use undertaken to facilitate surgically assisted maxillary expansion and bony recontouring of the pyriform aperture, followed by fixed appliances and a further Le Fort I maxillary impaction with rotation and BSSO advancement.

## DISCUSSION *Include a very brief review of similar published cases*

Apert syndrome is a rare disorder of craniofacial development. Differential diagnosis of other craniosynostosis syndromes includes Pfeiffer, Crouzon, Muenke which include overlapping craniofacial features observed in AS but with differing limb/digit defects. AS presents with characteristic syndactyly of hands and feet. A diagnosis of AS is based upon detailed patient history, clinical evaluation and identification of physical characteristics. Of relevance to those providing care for patients with AS include the craniofacial region with immediate concerns relating to cranio-cerebal disproportion with possible airway and ophthalmic consequences associated with early sutural closure. Facial frontal advancement surgery with bipartition if hypertelorism is evident is often undertaken. Early correction of the syndactyly of hands and feet is also required. A lack of midface growth resulting in airway compromise and poor occlusal relationships often requires further surgery during the childhood years to be undertaken balancing the burden of care. It is not until facial growth has ceased that definitive surgical correction and the restoration of a more normal facial appearance is usually undertaken. Due to the variability of functional and clinical needs as well as aesthetic and psychosocial needs patients with AS require tailored staged coordinated treatment plans. Each individual with APS has different psychosocial and functional/aesthetic needs and accordingly, tailored co-ordinated treatment plans are required and commitment for long term follow up is required due to the risk of surgical and orthodontic relapse.

### Patient's perspective

"Looking back on my treatment journey the most difficult stages to cope with related to making friends and socialising and having to take breaks from horse riding during the recovery from surgery. It was hard to have pureed food for a long period of time. There were some challenges as the surgeries were complicated. Recovery was the most challenging. The most enjoyable aspects relate to being able to drive a car following the surgeries because if I hadn't had the surgeries, I might not of been able to drive, surgery has improved by general health and quality life, and I can now eat food that I wasn't able to eat when I was younger. I think things were done very well and I had the best team possible and don't think it could have been done any better."

"My advice to parents/patients with Aperts is don't be discouraged by what you can't do, and don't tell the child that they can't do things because of what they look like. Focus on all the positives that they can do. Don't make anyone make you feel ashamed because you have Aperts and because you can't do something that someone without Aperts can do. It may seem tough now but it's all worth it in the end. Trust the medical professionals, they do a wonderful job, and they will look after you. Having this opportunity will hopefully also help others with Aperts."

Taryn reports that she is currently working at a local airport which has a great work environment and strong support. She enjoys her work and enjoys the financial rewards provided from her job.

## LEARNING POINTS/TAKE HOME MESSAGES *3-5 bullet points*

Patients with Apert syndrome experience a complex and extended treatment pathway with initial concerns relating to cranio-cerebal disproportion with possible airway and ophthalmic consequences associated with early sutural closure.

Surgical and non-surgical treatments are staged and coordinated within the multidisciplinary craniofacial team to address the challenging functional and clinical needs as well as aesthetic and psychosocial needs.

Long term follow up is required due to the risk of long-term relapse.

Patients with AS have challenging psychosocial, aesthetic, functional and clinical needs and strong support and understanding of family, work and social networks are exceptionally important for their wellbeing.

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## FIGURE/VIDEO CAPTIONS

Figure 1. Extra oral photographs A. Pre-orthodontic treatment (Previous Front-orbital advancement and remodelling as an infant and Le Fort III distraction advancement at age 9 years) B. Pre-Le Fort I impaction and rotation and bilateral sagittal split osteotomy (BSSO) advancement C. End of orthodontic treatment D. 5.8 years post treatment.

Figure 2. Intra-oral photographs A. Pre-orthodontic and surgically assisted maxillary expansion treatment B. Pre Le Fort I impaction and rotation and bilateral sagittal split osteotomy (BSSO) advancement C. End of orthodontic treatment D. 5.8 years post treatment.

Figure 3. Lateral Cephalograms A. Pre Le Fort III distraction B. Pre orthodontic treatment and surgically assisted maxillary expansion C. Pre Le Fort I impaction and rotation and bilateral sagittal split osteotomy (BSSO) advancement D. End of orthodontic treatment.

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