ORIGINAL ARTICLE

Vestibular dysfunction in Apert Syndrome

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Abstract

Objectives: Apert syndrome affects the craniofacial structures resulting in craniosynostosis, craniofacial anomalies and syndactyly. Although many characteristic features are recognized, vestibular dysfunction is a little known feature that can often be present. This can cause a delay in the attainment of gross motor milestones and impair motor function. We aimed to examine this cohort to review the incidence of vestibular hypofunction and to assess the effect on motor function.

Study design: We performed a retrospective analysis of 55 Apert syndrome patients who had undergone audiological review at Great Ormond Street Hospital for Children.

Results: 50.9% of patients experienced balance difficulties; 18.1% of patients (all of whom had delayed motor milestones) underwent clinical examination and vestibular assessment. Results showed only 20% of patients had bilateral vestibular function present; 30% of patients had unilateral and 50% bilateral vestibular hypofunction. Two patients who initially presented with imbalance and vestibular hypofunction experienced significant improvement in symptoms on re-examination following vestibular physiotherapy. Conclusion: Vestibular dysfunction is a feature of Apert syndrome. Although the imbalance may be attributable to mechanical problems arising from syndactyly, it is important to recognize that a vestibular component can coexist. This is not well recognized, poorly understood and scarcely treated. We aim to increase awareness of vestibular dysfunction in Apert syndrome and advocate a high index of suspicion, particularly in the presence of motor milestone delay. Early detection, thorough vestibular assessment and prompt initiation of vestibular physiotherapy can aid vestibular compensation, rehabilitating patients and maximizing their functional attainment.

Key words: Apert, craniofacial, vestibular, balance, compensation

Introduction

Apert syndrome was first described in 1906, and named after Eugene Apert, a French physician. It affects the craniofacial structures and the limbs; it is characterized by craniosynostosis, craniofacial anomalies (including midface hypoplasia) and symmetrical syndactyly of the hands and feet (1).

The estimated prevalence is between 9.9 and 15.5 per million live births and accounts for 4.5% of craniosynostoses. It is an autosomal dominant disorder linked with a mutation in the FGFR2 gene, which maps to 10q25–10q26. The pathogenesis is not clearly understood although it is postulated that the FGFR2 gene alters the protein causing prolonged signalling, thus promoting premature fusion of bones in the skull, hands, and feet (2–5).

The mutation can occur sporadically and autosomal recessive cases have been documented in the literature. For an unaffected parent the risk of having a further child with Apert syndrome is minor; however, for an affected parent the risk of syndromic recurrence in a further child is 50% (5–7).

Additional clinical features include hearing impairment, cleft palate, proptosis, polydactyly and cognitive impairment (see Table I).

Treatment of Apert syndrome patients is complex and requires a multidisciplinary specialist team of paediatricians, neurosurgeons, otolaryngologists, audiological physicians, plastic surgeons, maxillofacial surgeons, ophthalmologists, orthopaedic surgeons, orthodontists, optometrists, physiotherapists, psychologists, speech and language therapists and a myriad of allied health professionals. Their care spans from infancy to adulthood (7).

Treatment is initially focused on the surgical correction of the skull to protect the developing brain and the orbits and management of the airway as they are prone to sleep apnoea. Subsequent surgical treatment focuses on craniofacial reconstructive and corrective orthopaedic surgery. A holistic rehabilitative
approach is adopted with the aim of supporting development while restoring form and function (7).

The impact Apert syndrome has on hearing is well recognized and most agree that there can be a significant level of hearing impairment; however, controversies exist in the literature as to the true incidence and type of impairment (4). Rajenderkumar et al. performed the largest series analysing hearing loss in 70 Apert syndrome patients. They concluded that otitis media with effusion was the main cause of hearing impairment, with a 3–6% incidence of congenital hearing impairment observed (4,9).

Although the audiological aspects of Apert syndrome are well documented, there is limited information and evidence regarding structural inner ear abnormalities. Interestingly, many case reports describe temporal bone abnormalities though scarce comment is made about balance (4,7,9).

Guangwei et al. performed the only study looking at inner ear anomalies; they observed abnormalities on CT temporal bones of all their 40 patients with 90% occurring bilaterally. The most frequently noted abnormalities were dilated vestibule, malformed lateral semicircular canals and cochlear dysplasia (4). This study supports our theory that abnormalities in the vestibular apparatus can occur but there remains no published study focusing specifically on vestibular dysfunction in these patients.

Vestibular dysfunction is a little known and scarcely identified aspect of Apert syndrome. It can cause a delay in the attainment of gross motor milestones and impair motor function. The imbalance is often ignored and, if noted, frequently attributed to the mechanical problems secondary to syndactyly. Our experience suggests that a vestibular component often coexists, which is not well recognized, poorly documented and scarcely treated.

**Method**

This study was a retrospective review of Apert syndrome patients attending for craniofacial assessment at Great Ormond Street Hospital for Children, London. Patients were identified using the computerized clinical documents database. The results were filtered using the terms ‘Apert’ and ‘Audiological Medicine’.

This procedure returned 55 patients whose clinical records were then examined. The aim was to identify how many of this cohort experienced motor delay, reported balance difficulties, underwent CT scan of the temporal bones and attended for formal balance assessment. We then analysed the results including the those of vestibular assessment and changes following vestibular physiotherapy.
Clinical assessment

All 55 patients attended the audiovestibular clinic for audiological assessment as part of the multidisciplinary craniofacial care pathway.

The 10 patients who underwent vestibular assessment all had a detailed clinical history focusing on motor milestones, history of head tilt, imbalance, veering on mobilizing, difficulty walking in the dark or on uneven surfaces, falls and the inability to stand on one foot or catch a large ball. Parental suspicion of dizziness was also examined and where appropriate the child was questioned.

Clinical examination involved the cranial nerves, eye movement (smooth pursuit, saccades, optokinetic and spontaneous nystagmus), gait, tandem gait, Romberg’s test, Unterberger test and foam cushion test.

Objective vestibular assessment was then performed with the child tested independently or secured on the parent’s lap using videonystagmography or electronystagmography, as tolerated by the patient.

Results

Fifty-five patients were included in our cohort, 29 males (53%) and 26 females (47%). All the patients were part of the Great Ormond Street craniofacial assessment pathway and the majority did not have cleft palates. All the patients had undergone serial audiological assessment in our department.

Eleven of these patients had clear documentation of their attainment of motor milestones. Parents reported balance difficulties in 28 patients; complaints ranged from poor coordination, clumsiness, head tilting, delayed milestones to frequent falls. Ten patients attended for vestibular assessment, all of who had delayed motor milestones (see Table II). The mean age when referred for vestibular assessment was 6.3 years, with patients ranging in age from one year to 16 years.

Vestibular assessment results

Of the 10 patients who underwent vestibular assessment, two (20%) had bilateral vestibular function present, three (30%) had unilateral vestibular hypofunction and five (50%) had bilateral vestibular hypofunction. The results are detailed in the Table V.
Vestibular impairment is likely to be present in children whose motor development is not age appropriate: failing to sit, crawl or walk in time with their peers or in those who exhibit head tilt or poor tone. All 10 of the patients who attended for vestibular assessment had delayed motor milestones. Of these 10 children, eight (80%) were subsequently found to have abnormal vestibular function. This finding highlights the importance of questioning parents about the age of attainment of motor developmental milestones. Two patients classified as having a normal response, with bilateral vestibular function present, still suffered from motor delay and symptoms of imbalance. Of these two patients one had global developmental delay and the other was only able to tolerate partial testing, so further assessment has been arranged.

The results show that imbalance is a feature of Apert syndrome that needs careful screening and assessment. Case note review showed that 50.9% of our cohort reported balance difficulties and 20% had delayed motor milestones; however, only 18.1% received formal vestibular assessment. These findings prompted us to develop a balance assessment protocol at our institution to improve our screening and assessment rates.

Initial findings in both patients D and E revealed bilateral vestibular hypofunction. Following diagnosis, parental education and initiation of vestibular physiotherapy, improved motor function was observed. Testing in patient D, two years and six months after diagnosis and initiation of vestibular physiotherapy, shows a significant improvement in motor function and reported daily activity. This signals that vestibular compensation is possible; hence, dysfunction should be identified early.

Kaga et al. performed a review of a longitudinal study examining vestibular compensation in children with congenital and acquired vestibular loss. Kaga’s findings support our results; he concluded that vestibular dysfunction in infants and children with congenital or acquired vestibular loss can be compensated for by the visual and somatosensory systems with children obtaining near normal function by the age of 10 years (10).

We advocate vestibular physiotherapy in all children with vestibular dysfunction to aid vestibular compensation. In addition, physical activity, racket sports and exercise challenging hand-eye coordination are encouraged to help develop compensatory inputs from visual, somatosensory and proprioceptive senses.

Of the 10 patients tested, three had a CT scan of the temporal bones (see Table III); these patients reported significant difficulties and had abnormal vestibular function on testing. Patient E, Figure 1, had grossly dysplastic vestibules and semicircular canals with bilateral vestibular hypofunction on assessment. Patient D, Figure 2, had vestibular dysplasia with bilateral vestibular hypofunction and patient H had a dilated vestibule with mild bilateral vestibular hypofunction.

Although the numbers are small, the inner ear CT anomalies (see Table IV) are in keeping with others reported in the literature and also with the results of vestibular assessment (4,10). This supports our theory that structural inner ear abnormalities may impact on balance as well as hearing.

It remains unclear how the observed anomalies affect vestibular function and on the incidence of these abnormalities in the normal population. There has been no published literature linking the observed anatomical abnormalities, e.g. vestibular dysplasia with imbalance and quantifying the resultant effect. Further work is needed to examine this, especially since some children with absent semicircular canals display vestibular nystagmus in response to rotational testing. Tzuku et al. observed this finding and postu-

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Table IV. CT scan abnormalities.

<table>
<thead>
<tr>
<th>CT temporal bones abnormalities</th>
<th>Patient E</th>
<th>Patient H</th>
<th>Patient D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Small middle ear clefts bilaterally with intact ossicular chains</td>
<td>Grossly dysplastic vestibules and semicircular canals</td>
<td>Dilated vestibule</td>
<td>Vestibular dysplasia</td>
</tr>
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</table>

Figure 2. CT petrous temporal bones showing vestibular dysplasia in Patient D.
lated that vestibular-like cysts may be serving as rudimentary balance organs (11).

Consideration of CT scan of the temporal bones alongside CT scan of the head for surgical treatment planning is advised to screen for structural abnormalities with minimal excess exposure to ionizing radiation.

Although we did not examine hearing profiles in our cohort it is important to consider that structural anomalies of the inner ear may impact on both hearing and balance, and resultant symptoms may be worse if both are affected. Furthermore, imbalance in Apert syndrome is multifactorial and in addition to vestibular abnormalities, balance will also be affected by syndactyly of the feet.

The small sample size was a limitation of this study as was the fact that not all those reporting symptoms received vestibular assessment. The sample size was also affected by patients not attending clinic review due to the burden of multiple medical appointments. However, in view of the rarity of this genetic disorder and paucity of information, the authors believe this work increases awareness and provides a structure on which to build a body of evidence in regard to vestibular function in Apert syndrome.

Conclusions

Apert syndrome can cause a variety of inner ear anomalies resulting in both audiological and vestibular dysfunction. The vestibular causes of imbalance in Apert syndrome are little understood, under-diagnosed and rarely treated. We advocate a high index of suspicion, particularly in the presence of motor milestone delay. Assessment should include a detailed vestibular history and clinical examination with subsequent vestibular testing if indicated.

Identification of inner ear and vestibular structural anomalies with CT scan may be an important aid to diagnosis and should be considered. The mainstay of management is vestibular physiotherapy.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Motor milestones</th>
<th>Balance complaints</th>
<th>Age at assessment</th>
<th>Vestibular assessment findings</th>
<th>Conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>Delayed</td>
<td>Poor head control and not yet walking</td>
<td>18 months</td>
<td>Right vestibular hypofunction</td>
<td>Abnormal</td>
</tr>
<tr>
<td>B</td>
<td>Delayed</td>
<td>Initially very floppy with head tilt to both sides. Has never walked independently</td>
<td>16 years</td>
<td>Right vestibular hypofunction</td>
<td>Abnormal</td>
</tr>
<tr>
<td>C</td>
<td>Delayed</td>
<td>Frequent falls</td>
<td>Eight years</td>
<td>Vestibular function present bilaterally but limited testing tolerated</td>
<td>Normal</td>
</tr>
<tr>
<td>D</td>
<td>Delayed</td>
<td>Unable to crawl or walk</td>
<td>18 months</td>
<td>Bilateral vestibular hypofunction</td>
<td>Abnormal</td>
</tr>
<tr>
<td>E</td>
<td>Delayed</td>
<td>Mild head tilt towards the right. Unsteady on feet. Sways to the right on walking. Support required when walking on uneven surfaces</td>
<td>Four years</td>
<td>Bilateral vestibular hypofunction</td>
<td>Abnormal</td>
</tr>
<tr>
<td>F</td>
<td>Delayed</td>
<td>Walks with wide based gait. Walking only aged three years</td>
<td>13 years</td>
<td>Bilateral mild vestibular hypofunction</td>
<td>Abnormal</td>
</tr>
<tr>
<td>G</td>
<td>Delayed</td>
<td>Clumsy, falls frequently</td>
<td>Five years</td>
<td>Mild right vestibular hypofunction</td>
<td>Abnormal</td>
</tr>
<tr>
<td>H</td>
<td>Delayed</td>
<td>Walks with a wide based gait. Falls over easily. Difficulty walking on uneven surfaces</td>
<td>Four years</td>
<td>Bilateral mild vestibular hypofunction</td>
<td>Abnormal</td>
</tr>
<tr>
<td>I</td>
<td>Delayed</td>
<td>Not crawling or walking. Has global developmental delay</td>
<td>One year</td>
<td>Normal</td>
<td>Normal</td>
</tr>
<tr>
<td>J</td>
<td>Delayed</td>
<td>Walks holding onto furniture. Feels frightened and insecure while walking</td>
<td>Nine years</td>
<td>Bilateral vestibular hypofunction</td>
<td>Abnormal</td>
</tr>
</tbody>
</table>

Table VI. Summary of change of symptoms following vestibular physiotherapy.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Clinical history</th>
<th>Initial results on assessment</th>
<th>Clinical history following vestibular physiotherapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient E</td>
<td>Commenced walking independently at 2 years, 4 months. Initially swayed to both sides on walking and required support. Had head tilt to the right</td>
<td>Aged 18 months: Bilateral vestibular hypofunction</td>
<td>Aged months 30 months: No longer wobbly on walking</td>
</tr>
<tr>
<td>Patient D</td>
<td>Unable to crawl or walk at 18 months</td>
<td>Aged 18 months: Bilateral vestibular hypofunction</td>
<td>Aged three years: Improved gait. Able to now walk upstairs Aged four years: Walks on uneven surfaces. Able to run and climb a climbing frame</td>
</tr>
</tbody>
</table>
alongside general physical physiotherapy and parental education. Early detection is important as vestibular compensation is possible with improved locomotor function and ultimately an improvement in quality of life.

**Declaration of interest:** The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

**References**