A case report of the dental management of a patient with Sotos syndrome

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Abstract

Sotos syndrome, a rare disease of cerebral gigantism, is characterised by overgrowth, advanced bone age and a typical facial appearance with mild to severe learning disability. This paper reports a case of an 18-year-old male patient with Sotos syndrome and rare association of optic nerve atrophy who, unaware of his underlying condition, reported to our dental clinics with a complaint of spacing between his lower front teeth. The purpose of this case report is to review the diagnostic characteristics of Sotos syndrome, emphasising the importance of a multi professional dental intervention in combination with active family participation.

Key words: Sotos syndrome, cerebral gigantism, overgrowth condition, learning disability

Introduction

Sotos syndrome was first fully described by Sotos et al., in 1964 (Sotos et al., 1964). It is a genetic disease characterised by a tall stature, gigantism, prominent forehead, frontal bossing, hypertelorism, advanced bone age and learning disability. Dental abnormalities like delayed eruption of teeth, macroglossia, poor oral hygiene and high arched palate have been reported in literature (Leventopoulos et al., 2009). The mode of inheritance is thought to be sporadic but autosomal dominant and recessive forms have been reported (Mangono et al., 1989). The prevalence is estimated between 1 in 10,000 and 1 in 50,000 (Sotos, 1997). Our patient presented with features consistent with Sotos syndrome along with associated inconsistent features which demanded further medical evaluation and a combined treatment strategy. Clinicians should be aware of these particular signs, interpretation of which will lead to a specific diagnosis. Management of this condition is multidisciplinary and the key to effective management is its early detection and proper diagnosis.

Case presentation

An 18-year-old male patient reported to the Department of Oral Medicine and Radiology, D.A. Pandu Memorial RV Dental College Bangalore India, with the chief complaint of protrusion of his upper anterior teeth and spacing in his lower anterior teeth. The patient reported he had an umbilical hernia and undescended right testicle at the time of birth which was operated on immediately. A detailed medical history revealed that the patient had an overgrowth condition with learning disability and behavioural problems. The patient was on phenytoin therapy (400mg/day) for seizures which developed at the age of 12 years. There was no family history of mental retardation or overgrowth and a positive history of consanguinity was revealed. The patient was reported to have delayed milestones with a history of excessive somnambulance and lack of interest in performing any work. On general physical examination the patient was 188cm in height with long and thin extremities. An extraoral examination revealed a macrocephaly, an increase in the vertical dimension of the face, prominent nose and nasal bridge with hypertelorism, down slanting of palpebral fissures, a divergent squint, incompetent lips and mandibular prognathism (Figure 1). A marked mandibular prognathism and a receding hairline could be appreciated at the age of 10 years as observed by the previous photographs produced by the patient (Figure 2). Intraoral examination revealed a high arched palate, macroglossia, lower anterior spacing with class III malocclusion and missing mandibular second premolars. Based on the history and general physical examination, a provisional diagnosis of Gigantism was given. Further investigations revealed normal concentrations in plasma including plasma growth hormone level (0.8ng/ml). Ophthalmological evaluation revealed an optic nerve dysfunction with bilateral optic atrophy, decreased visual acuity and total colour blindness of the left eye. The patient was found to have moderate mental retardation with an IQ of 34, measured using the Binet-Kamath intelligence test (Paul et al., 2010). MRI of the brain was normal except for enlarged sphenoid, frontal and ethmoidal sinus with extensive pneumatisation (Figure 3). A two dimensional (2D) echo cardiogram revealed a floppy mitral valve prolapse and a Doppler study showed trivial mitral regurgitation. The EEG showed evidence of recurrent generalised sharp wave discharges.
Based on the patient’s clinical presentation, general physical examination, his personal and family history together with associated systemic abnormalities, we derived a final diagnosis of Sotos syndrome. A combined treatment strategy was devised for the patient. A dental preventive programme was implemented consisting of oral hygiene instructions, dietary advice and fluoride application. Emphasis was placed on reducing consumption of cariogenic food and a regular dental check up was advised. As our patient had associated valvular defects, aggressive dental procedures were performed under antibiotic coverage, as he was deemed at risk of infective endocarditis. An orthodontic consultation was undertaken for correction of spacing and protrusion. A multidisciplinary approach was followed with the patient being referred to a speech therapist and psychologist to address the issues in coping with behavioural problems. Follow up visits revealed consistent improvement in his overall health, speech and behaviour.

Figure 1. Profile picture showing, a divergent squint, prominent nose and incompetent lips

Figure 2. Lateral profile view at 10 years of age showing marked mandibular prognathism

Figure 3. T1 weighted sagittal section of MRI image showing enlargement of frontal sinuses but no intra cerebral lesions
Discussion

Sotos syndrome is an overgrowth condition which is diagnosed primarily based on its clinical presentation. Although, there have been previous reports on Sotos syndrome, the present case; a walk-in case into the dental clinic had a rare association of optic nerve atrophy which posed a challenge to both the dental and the medical profession in defining the strategies to meet the treatment needs of the patient.

Aetiology

The aetiology of Sotos syndrome is unknown, it is believed that most of the cases are sporadic and a few autosomal dominant inheritances have been reported. Tatton-Brown et al., (2005) analysed more than 500 individuals with an NSD1 (Nuclear receptor SET domain containing protein) gene abnormality and suggested that these features were due to NSD1 gene abnormality (Tatton-Brown et al., 2005). It is interesting to note that loss of function mutations in the NSD1 gene have been associated with certain dental anomalies like hypodontia and tooth agenesis (Kotilainen et al., 2009). Dental anomalies like hypodontia have been described earlier in a few reports of Sotos syndrome, which were previously absent in the literature. The present case highlights these dental manifestations adding to the reports on dental manifestations in such patients. These dental anomalies have also been linked recently to aberrations in the NSD1 gene. Furthermore, enriched levels of NSD1 have been observed during mouse development in tooth buds, salivary glands and in regions of ossification of the developing bones and periosteum and this could be the reason for oral manifestations in patients with Sotos syndrome.

Clinical presentation

The onset of this syndrome is variable, generally pregnancy is described as normal, however, toxoaemia or pre-eclampsia have been reported in several cases. It is a genetic disorder wherein growth during the first few years of life exceeds normal limits, after which it continues at normal rates. The head is dolichocephalic and hair in the fronto-temporal region seems to be sparse and palpebral fissures are usually down slanting (Sotos et al., 1964). At birth, the mandible appears to be small, pointed in childhood and prominent in adulthood. The other non-specific features like astigmatism, cataract, strabismus, umbilical hernia, vertebral abnormalities and syndactyly were seen in 2-15% of patients (Tatton-Brown et al., 2005).

Growth and skeletal abnormalities

The advance growth is pronounced particularly in the first year of life, after which it stabilises with a height consistently above the 97th centile between the ages of two and six years. Bone age often reflects the accelerated growth velocity and is advanced in 75%-80% of pre pubertal children.

Behavioural abnormalities

A wide range of behavioural problems such as autistic spectrum disorder, phobias, and aggression have been reported in the literature (Finegan et al., 1994).

Cardiac and Neurological manifestations

About 20% of individuals have cardiac anomalies that range from severe to self-limiting form and 25% of the patients develop non febrile seizures at some point of their lives (Buyukgebiz et al., 1990). It has been suggested that children with Sotos syndrome have particular difficulties with speech and articulation. Our patient gave a history of such speech difficulties with poor performance in school, thereby exhibiting delay in social, communicative and cognitive development.

Occular manifestations

Association of Sotos syndrome with optic atrophy is a rarity. Though ocular manifestations have been described in the literature, the presence of primary optic atrophy has been documented only in a few patients (Inoue et al., 2000). Our patient presented with a rare association of primary optic atrophy.

Dental manifestations

Dental abnormalities like malocclusion, high arched palate and macroglossia were reported earlier in literature (Sotos et al., 1964). Although these features are not the mainstay for diagnosis of Sotos or Sotos-like disorders, they can be contributing factors indicating a more serious underlying problem.

Neoplasms

Cohen et al. (1999) critically reviewed neoplasms associated with Sotos syndrome which include Wilms tumour, hepatocellular carcinoma, neuroblastoma, small cell carcinoma, sacroccygeal teratoma, giant cell granuloma of mandible and acute lymphatic leukaemia. A literature review suggests a tumour frequency of about 3.9% (Cohen et al., 1999). However, no such association were found in the present case.

Differential diagnosis

The overgrowth conditions that may be confused with Sotos syndrome are Marfan syndrome, Weaver syndrome, Simpson-Golabi-Behmel syndrome (SGBS), Fragile X syndrome and Bannayan–Riley-Ruvalcaba syndrome. Marfan syndrome shares certain features with Sotos syndrome; however, the outstanding characteristic feature of Marfan syndrome is excessive length of the tubular bone resulting in dolichoostenomelia (disproportionately long and thin extremities) and arachnodactyly which were not
noted in our patient. The classic facial appearance of Weaver syndrome overlaps with that of Sotos syndrome, particularly in infancy. However, the round face in Weaver syndrome with ocular hypertelorism differentiates it from Sotos syndrome. SGBS is an X-linked condition which is also associated with pre and postnatal overgrowth in males. However, other features of supernumerary nipples, diastasis recti and pectum excavatum found in this syndrome help differentiate it from Sotos syndrome. Although Bannayan-Riley-Ruvalcaba syndrome shares similar features of Sotos syndrome; distinctive pigmented spotting of the penis, intestinal polyposis and multiple hemangiomatas and lipomas are more common in Bannayan Riley Ruvalcaba syndrome. The varied clinical manifestations of Fragile X syndrome may sometimes mimic that of Sotos syndrome; however, the prominent characteristics of Fragile X syndrome include large ears and macroorchidism which were absent in our patient (de Vries BBA et al., 1997).

Management strategies
The medical management is multidisciplinary. In the neonatal period, sucking and swallowing difficulties require adjustments of baby food. In infancy and the early years, general and specialised paediatrics follow-up is important because of the possible clinical events, like respiratory infections, seizures and a possibility of increased risk of tumours. Anaesthesia may require special precautions (Adhami et al., 2003). Early in childhood, programmes like infant stimulation, occupational therapy, speech therapy, and adaptive physical education play a significant role in the nurturing of a child with Sotos syndrome. As mentioned previously, some Sotos patients develop behavioural problems during school age. As a result, parents and school staff may have to spend a significant amount of time with these children because they can interfere with social interaction and family functioning. Genetic counselling should be provided to the individuals and family members regarding the nature, inheritance, and implications of genetic disorders, to help them make important medical and personal decisions. As the mode of inheritance of this syndrome is an autosomal dominant type, it is important to know the relative risks from the affected individual.

Dental considerations
A preventive dental programme must be implemented early for these patients in order to avoid premature loss of teeth, unnecessary pain and sepsis which may compromise both their general and dental health. Approximately 8% of patients with Sotos syndrome have been reported with cardiac anomalies, which is of relevance in dental management. Particular emphasis should be placed on the dental management of such patients pertaining to possible underlying cardiac abnormalities, uncooperative behaviour, reduced IQ and seizure disorders. Extensive dental procedures should be performed under antibiotic prophylaxis to reduce the risk of infective endocarditis, however, this may need to be modified according to policy in individual countries. Patients with prosthetic valves generally have higher INR levels (3-4) which may require monitoring for dental procedures. A complete evaluation of seizure disorders is necessary prior to initiation of dental treatment in such patients. Seizures may begin abruptly owing to triggers of seizure activity, hence, any known triggers should be avoided. To minimise the risk of injury and aspiration in these patients, all the dental instruments used should be secured by dental floss and, preferably, a rubber dam should be used. Gingival overgrowth is a significant oral complication among seizure disorder patients on phenytoin therapy and frequent professional scaling and follow-up is required. In this case study, our patient did not complain of gingival enlargement. Xerostomia may be observed in patients on phenytoin therapy used for longer periods, and topical fluorides should be prescribed to decrease risk of developing caries. Mental disability in patients with Sotos syndrome may complicate the dental treatment. Behavioural modification therapies should be employed for patients with mild learning disabilities and those with severe disabilities would require treatment under general anaesthesia.

Conclusion
To conclude, Sotos syndrome, previously described as a rare disorder, is constantly being reported with diverse clinical presentations. This could be attributed to genetic mutations or arising de-novo. Establishing a definitive diagnosis and meeting the treatment needs of the patient poses a challenge for the practitioner. The importance of establishing a diagnosis and defining treatment strategies for patients affected with Sotos syndrome is necessary. This case report describes the features of this disease and highlights the importance of a multidisciplinary approach in management of the patient with emphasis on the dental considerations in Sotos syndrome. Patients with Sotos syndrome require an interdisciplinary management approach from different specialties of medicine, and further research is required in this

Conflicts of interest
The authors declare no conflict of interest for this study.
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