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SCN9A channelopathy associated autosomal recessive Congenital Indifference to Pain. A case report

ABSTRACT

Background Congenital Indifference to Pain (CIP) is a rare condition that inhibits the ability of patients to perceive physical pain but otherwise keeps normal sensory modalities. The condition has been mapped to an autosomal recessive trait to chromosome 2q 24.3 with mutations on the SCN9A gene.

Case report A 2 year old Caucasian female presented with CIP. Bite injuries, tongue wounds and unaccounted dental trauma episodes were frequently reported. Preventive instructions and possible treatment modalities were discussed with the parents.

Conclusion The cornerstone of treating CIP patients is an extensive preventive approach alongside regular oral examination at home by parents as well as routine recall appointments with dentists.

Keywords CIP, congenital indifference to pain, congenital insensitivity to pain.

Introduction

Congenital Indifference to Pain (CIP) is a rare condition (about 20 cases have been reported in the literature) that inhibits the ability of patients to perceive physical pain but otherwise keeps normal sensory modalities (OMIM 243000). Synonyms for this condition

mentioned in the literature include “channelopathy-associated insensitivity to pain”, “autosomal recessive asymbolia for pain” and “congenital analgesia”. The condition could often be misdiagnosed as “congenital insensitivity to pain” (OMIM 608654), also known as hereditary sensory and autonomic neuropathy type 5 (HSAN5)[Cox et al., 2006].

The condition has been mapped to an autosomal recessive trait to chromosome 2q 24.3 identifying biallelic null mutations in the transmembrane voltage-gated sodium channel type IX α subunit (SCN9A) [Woods et al., 2014], a 113.5-kb gene comprising 26 coding exons (OMIM 603415). The SCN9A gene mutations that cause CIP create a premature stop signal in the instructions for making the alpha subunit of the NaV1.7 sodium channel [Cox et al., 2010]. As a result, pain signals from the site of injury to the brain are impaired, causing those affected to be insensitive to pain [Shorer et al., 2014].

The present paper reports the characteristics of a girl with CIP. The genetic diagnosis, medical history, oral implications, differential diagnosis and treatment planning will be discussed.

Case Report

A 2 year old Caucasian female patient presented at the Department of Paediatric dentistry and special care, University hospital, Ghent, Belgium as part of a regular oral check-up.

Medical history

Normal anthropometric, cognitive and neurologic development were diagnosed. The patient was able to distinguish between hot and cold sensations and responded well to tickling sensations. Unconscious self-mutilation was reported. Previous bite injuries of thumb and index finger have been reported. The patient has previous history of scratching her own eyes for which protective glasses were advised but the patient's co-operation was reported to be minimal. A radical treatment approach would be splinting of the elbows to prevent self-injury to the eye and fingers. Patient also suffers from osteomyelitis of the left foot and urinary incontinence.

Genetic diagnosis

Two SCN9A mutations were detected (c.3319-2A>G and c.5463dupT as a result of abnormal splicing of the SCN9A mRNA and abnormal SCN9A protein p.Gly1822fs respectively). Further genetic analysis of parents showed that the father is a heterozygous carrier of p.Gly.1822fs and the mother is a heterozygous carrier of c.3319-2AG mutation. Bi-parental inheritance of these mutations are consistent with diagnosis of congenital indifference to pain.

Oral examination

During the first appointment, the parents reported that the patient bit her tongue unconsciously (Fig 1A). The parents encouraged the use of a pacifier at all times as it was found to be very helpful in preventing bite injuries. At the second appointment after six months, the tongue wounds were completely healed. After two months, the patient reported to the clinic after premature loss of lower primary lateral incisor (tooth 72). The reason was not obvious and traumatic avulsion or self-extraction was suspected. Upon clinical examination, tooth 71 and 81 were slightly mobile and agenesis of tooth 62 was observed. Pathologic mobility of the tooth was suspected to be a result of self-mutilation or unaccounted dental trauma.

During the subsequent appointment after one month, parents reported loss of 71 during brushing. In addition, repeated wounds on the tongue were observed (Fig 1B). The sharp edges of teeth 53 and 63 were contoured to prevent mucosal injuries. Parents were advised to check the temperature of food to help faster healing of the tongue and to prevent burn injuries. The patient reported again within 2 months with complaints of bite injuries to the lower lip whereas uneventful healing of the tongue was noted (Fig 2A, 2B). The use of a mouthguard appliance was discussed as a probable solution but considering the non-compliance of the patient, this treatment modality was

postponed. The patient reported again after six months with complete healing of the lip. Physiological mobility of tooth 81 was also observed. The patient was further followed up for two years and reported no adverse oral complications. Regular 6 monthly follow up visits and extensive preventive approach had helped the patient to successfully avoid CIP related oral injuries during the 2 year follow up period.

Discussion

Although the primary consequence of the homozygous SCN9A mutation is the absence of pain sensation, there are associated conditions such as anosmia, self-mutilation resulting in oral lesions, multiple injuries due to repeated trauma, burn-related injuries, orthopaedic complications that include bone deformities from untreated fractures, osteomyelitis, and neuropathic joints later in life [Peddareddygari et al., 2014]. The disease carries substantial morbidity and early-age mortality [Benhalima et al., 2012]. Many people with CIP do not survive childhood due to recurrent injuries [Shorer et al., 2014]. Self-injury, burns, repeat fractures, osteomyelitis and accidental death are the main dangers of this disorder.

CIP is usually recognised by parents at a very early age when the child does not show any discomfort



FIG. 1A Extreme bite wound in the centre of the tongue.



FIG. 1B Repeated wounds on the tongue .



FIG. 2A Bite injury on the lower lip.



FIG. 2B Complete healing of the tongue.

with childhood vaccinations or distress upon injuries [Bennett and Woods, 2014]. If undiagnosed until the first dental appointment, the clinical picture could be confused with child abuse. Unaccounted dental trauma, repeated injuries and parent's inability to explain wounds are a few similarities between child abuse and CIP. Paediatric dentists should be aware of the potential presence of this disease to prevent false accusations of child abuse [van den Bosch et al., 2014]. Other differential diagnoses include self-mutilation associated syndromes and osteogenesis imperfecta. Similar to osteogenesis imperfecta, CIP needs to be considered as a viable diagnosis whenever young patients present with multiple fractures and bruises that are difficult to explain [Sathiaseelan and Rayar, 2003].

Due to the lack of pain perception, a number of oral-related complications could go unnoticed in CIP patients. Brushing injuries to the mucosa, minor and major traumatic dental injuries, TMJ dislocation, alveolar fractures, auto-extraction of teeth, bite and/or burn injuries to the tongue and surrounding oral mucosa, painful episodes of dental caries and/or periodontitis and bleeding of oral soft tissues are certain manifestations that have to be checked by the paediatric dentist during routine recall visits [Manor et al., 2013]. Even though, CIP patients do not need anaesthesia during treatment because of the insensitivity to pain, the tactile sensation is intact and some patients have reported tactile hyperesthesia. Thus, it is possible that the use of anaesthetics can prevent undue tactile discomfort [Labib et al., 2011].

The treatment of CIP is symptomatic. In the late 20th century, all primary teeth were extracted and replaced by full upper and lower dentures in CIP patients [Kouvelas and Terzoglou, 1989] to prevent the child from self-mutilation. However, modern age management consists of patient and parent counselling, learning behaviours to reduce risk of injury and modifying the environment at home to minimise occult trauma [Schalka et al., 2006]. This is particularly

challenging during early childhood.

Conclusion

The cornerstone of treating CIP patients is early diagnosis and extensive preventive approach alongside regular oral examination at home by parents as well as routine recall appointments with dentists.

Conflict of interest

The authors declare that they have no conflict of interest.

Disclosure

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