Case Report
Orthodontic treatment and management of limited mouth opening and oral lesions in a patient with congenital insensitivity to pain: case report

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SUMMARY Congenital insensitivity to pain is a rare clinical syndrome characterized by dramatic impairment of pain perception since birth and is generally caused by a hereditary sensory and autonomic neuropathy with loss of the small-calibre, nociceptive nerve fibres. We report a 9-year-old case, with a generalized congenital insensitivity to pain. The patient was referred to our Department by a private orthodontist for severe limited mouth opening and multiple oral ulcers which greatly worsened after starting the orthodontic treatment. The management of his oral lesions of the limited mouth opening and of the orthodontic treatment are described. The management approach aimed to improve mandibular range of motion and associated stretching and a self-modeling mouthguard to avoid cheek self-biting. This protocol allowed continuing the orthodontic treatment to restore the occlusion. Finally, good occlusion, normal function and better quality of patient’s life were achieved.

KEYWORDS: hereditary sensory and autonomic neuropathy, congenital insensitivity to pain, pain, insensitivity, orthodontics, mouth ulcer, literature review

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Introduction
Insensitivity to pain is a pathology described in medical literature from the beginning of the century (1–4). Recently, two groups have been defined: ‘congenital indifference to pain’ (5, 6) and ‘congenital insensitivity to pain’ (CIP) (7). These terms correspond to the two major ascending pathways of pain perception: the ‘medial system’ that project to the anterior cingulated cortex and insula is associated with the affective response to painful stimuli and the ‘lateral pain system’ that project to the somatosensory cortex provides the sensory discriminative component of pain (8).

‘Congenital indifference to pain’ designates individuals with perception of painful stimuli, but with an absence of the affective response. These individuals seem to have a normal neurological pattern, perception of passive movement, normal joint position, unimpaired tactile thresholds and light touch perception. Reflexes and autonomic responses are also normal (5, 9).

Patients with CIP do not distinguish the type, intensity and quality of painful stimuli. They show impairments both in the sensory discrimination of pain and in the affective response (7) involving both the medial and lateral ascending pathways of pain perception. In most cases, CIP is a manifestation of hereditary sensory and autonomic neuropathy (HSAN) involving the small-calibre (A-delta and C) nerve fibres, normally transmitters of nociceptive inputs along sensory nerves.

According to a recent literature review (6), five types of HSANs have been identified as potential causes of CIP, on the basis of different pattern of dysfunction and genetic abnormalities (6, 7, 10, 11) (Table 1). Patients with CIP can be difficult to diagnose because of their...
variable characteristics, the lack of simple diagnostic tests and the paucity of cases reported (12). The heterogeneity of these mutations and the rareness of this pathology may contribute to hide the symptoms to the patient’s parents as well as to the clinicians. The aim of this paper was to report the case of a 9-years-old patient, referred to our Clinic for severe limited mouth opening and multiple oral ulcers, which were severely worsened after the placement of the orthodontic brackets and wires. A working diagnosis of CIP was made, and a management strategy along with a literature review was described.

**Case report**

The patient was referred to the Department of Orthodontics and Orofacial Pain for severe limited mouth opening and multiple oral ulcers. Both problems were severely worsened after starting the orthodontic treatment for the repositioning of upper left central incisor impacted (Fig. 1).

**History**

The patient was a boy aged 8 years and 11 months. He was the first child of a non-consanguineous Italian couple and was born after a trouble-free pregnancy. There is no family history of neurological problems. The clinical history started when the patient was 2 years old. He showed repeated and unexplained episodes of fever up to 40 °C and a walking pattern without charging his right leg. Thirty months later, he was operated on his right tibia with a bioptic diagnosis of osteomyelitis. Since then, several accidents and fractures during childhood have been reported by the patient, always without any perception of pain. Also, temperature perception seemed to be impaired with frequent burns localized to his hands, elbow and knees. In the memory of the patient and his parents, no accident or lesion was associated with crying or any report of pain. He had also several dental cure and primary teeth extractions without anaesthesia and

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**Table 1. HSANs classification and description of the relative features**

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<tr>
<th>Types of HSAN</th>
<th>Features</th>
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<td>HSAN I</td>
<td>Autosomal dominant neuropathy is characterized by a late onset during the second decade of life; reflexes are absent and autonomic involvement is usually limited to reduced sweating and urinary dysfunction. This disease, caused by a mutation in SPTLC1 gene encoding a subunit of serine palmitoyltransferase, determines the loss of all diameters of axons, mainly C and A delta fibres.</td>
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<td>HSAN II</td>
<td>Autosomal recessive neuropathy is characterized by diffuse impairment of discriminative touch and pressure sensation. Also known as ‘Morvan’s syndrome of uncertain cause,’ it has been recently associated with mutations of a novel gene termed HSN2. Biopitic exams show a severe loss of myelinated fibres with relative preservation of unmyelinated one.</td>
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<tr>
<td>HSAN III</td>
<td>Autosomal recessive neuropathy determines widespread autonomic dysfunction associated with loss of pain and temperature perception. Clinical diagnosis is facilitated by fungiform papillae on the tongue along with an Ashkenazi Jewish ancestry. HSAN III is caused by a mutation in lκB kinase complex associated protein, IKBKAP. Half of patients with this deficiency die before age 30.</td>
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<tr>
<td>HSAN IV</td>
<td>Extremely rare autosomal recessive disorder associated to diffuse thermal and pain insensitivity, self-mutilation, anhidrosis and recurrent episodes of elevated body temperature with preservation of other sensory modalities. The absence of unmyelinated fibres and losses of small myelinated ones is represented and an association with mutations and polymorphism in the TRKA gene (encoding the receptor tyrosine kynase for nerve growth factor) have been found.</td>
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<td>HSAN V</td>
<td>Onset in childhood with pain and temperature insensitivity is similar to the precedent type except for variable autonomic involvement.</td>
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HSAN, hereditary sensory and autonomic neuropathy.
without any pain. The patient had always been anosmic. He was ticklish, and little itch was reported after incidental contacts with nettle. Sweating was reported to be normal even if several episodes of hyperthermia were reported since his childhood. Little, but continuous problems of incontinence was reported too, confirming a minor but present autonomic involvement.

Dental and clinical examination

Both parents were fully informed about the clinical procedures and gave their written consent, prior to start clinical examination and treatment.

The patient was under orthodontic treatment for repositioning of upper left central incisor impacted in late mixed dentition (Fig. 2).

At the clinical examination, no signs and symptoms of temporomandibular joint disorders were found according to Research Diagnostic Criteria for temporomandibular disorders (Axis I: IIA, IIB and IIIa, IIIb, IIIc) (13). Muscle palpation was not painful, but masseter muscles were tense and rigid. The mandibular range of motion was reduced as both the unassisted and assisted mouth openings limited to 25 mm (Fig. 3) to the right and left laterotrusion were 6 and 5 mm, respectively, and protrusion was 3 mm. When asked, the parents reported patient’s habit to chew his cheeks until provoking oral ulcers. During oral examination, the patient showed numerous fibrous scars and bleeding ulcerations all over cheek mucosa, more pronounced on the right side (Fig. 4).

Pupils and eye movements were normal. The following reflexes were tested and resulted normal: corneal,
Treatment and management

Our patient presented a severe limitation of mouth opening as a possible consequence of thick fibrous scars after cheek biting. The habit to chew his cheeks worsened after starting the orthodontic treatment. Also lateral movements and protrusion were very limited. Our first goal was to improve the range of motion. The therapeutic protocol included patient and family members counseling, together with stretching exercises of the masticatory muscles.

Counseling aimed at changing maladaptive habits and behaviours using strategies such as habit reversal. Great importance was given to motivate and carefully instruct the patient and to achieve a good compliance. It was stressed that habits do not change spontaneously and that the patient himself with aid of the parents is responsible for the change. For this reason, the patient was invited to practice the new behaviour throughout the day with the help of post-it notes as reminders.

To stretch muscles, the patient was asked to increase the mouth opening by positioning the thumbs on the upper arch approximately on the incisive area and index fingers on the lower arch and always on the incisive area. The patient was also instructed to use a number of tongue depressors piled together as a reference for the amount of jaw opening by positioning the tongue depressors between arches without touching them with teeth; the patient was asked to add one tongue depressor a day to verify the increased mouth opening. To further stretch the muscles, the patient was asked to use the piled tongue depressors with a pen in

Diagnosis

Although there is a lack of bioptic and genetic data, the clinical features, the history of numerous painless injuries during childhood, the impairment in pain and temperature sensitivity and the autonomic abnormalities suggested an impairment of the sensitive system, with a defect of small-calibre fibres (7, 19). Moreover, the absence of anhidrosis (always associated to HSAN IV) and the minor autonomic involvement with the preservation of the sympathetic skin response led to a working diagnosis of HSAN V (10, 20, 21).
between to have a lever action. These exercises had to be performed each day, every 2 h, holding the mandible stretched for 1 min for six times (22).

The second step of our treatment was to manage his oral ulcers and to avoid self-bite damages at the same time to continue the orthodontic treatment to restore his occlusion. With this aim, we prescribed to wear a fulltime self-modeling mouth-guard, normally used for martial arts (Fig. 5). This toll was employed with the aim of remove by resin shields patient’s cheeks from his teeth.

A tongue grid was used to avoid tongue interposition and increase the overbite. Nevertheless, the use of this appliance was difficult because of severe tongue lesions (Fig. 6). The lesions could be ascribed to patient’s insensitivity to pain and in the inability of controlling the tongue pushing on the grid after the painful stimuli.

Results

After 6 weeks, the unassisted mouth opening was incremented by 25 mm to 32 mm and mandibular movements improved, allowing a better function.

After 1 year and 8 months, the orthodontic treatment was finished and a fixed retainer was applied to the lower arch from canine to canine. The orthodontic treatment allowed to obtain the eruption of the impacted maxillary incisive, normal values of overjet and overbite, the alignment of all teeth, and bilateral Class I canine and molar occlusion (Fig. 7). The post-treatment panoramic radiograph shows mesial inclination of the third molars: their extraction has to be re-evaluated (Fig. 8).

After our treatment, we referred the patient to a neurophysiologist for an histological and genetic support to the clinical diagnosis, and to other physicians (dermatologist and plastic surgeon) to further improve his functioning.

Today, the patient is followed up periodically to check the retainer, the occlusion and the mandibular dynamics. The improvement of mouth opening is stable, assessing around 32 mm. The use of the mouthgard has been still recommended during the sleep to avoid not voluntary check self biting.

Discussion

We reported a patient seeking treatment for a reduced mouth opening and oral mutilations as a consequence of self-biting of tongue, lips and oral mucosa. His characteristic medical history with burns, accidents and fractures without any perception of pain, together with the outcome of clinical tests led us to a working diagnosis of CIP. The patient underwent a clinical examination which showed a limitation of the range of mandibular movement. Instrumental tests revealed impairment of the first facial nerve (olfactive sense) and absence of pain perception (FPT).

Our therapeutic protocol included patient and family members counseling together with stretching exercises of the masticatory muscles (22). To manage the oral ulcers avoiding self-biting and to continue the ortho-
dental treatment, we prescribed a self-modeling mouth-guard to be worn full-time.

After our treatment, we referred the patient to other physicians (dermatologist and plastic surgeon) to further improve the mandibular range of motion. Nevertheless, our simple and conservative therapeutic protocol succeeds in increasing the range of motion and improving patient's quality of life.

Several updates and reviews have been published in the recent years (6, 23), reporting the management of patients with CIP undergoing anaesthetic (24, 25), surgical (26) and dental procedures (27–29). Nevertheless, as far as we know, this is the first case remarking the peculiarities and the problems that patients affected by CIP may present during an orthodontic treatment and the possible dysfunctional implications.

Congenital insensitivity to pain is a sensory syndrome in which a patient does not respond to painful stimuli. This disease may have autosomal, recessive or dominant transmission associated with absence or severe loss of small myelinated fibres and possible decrease in the number of unmyelinated fibres (30). Recent researches point towards gene mutations as the cause of CIP. The mutations are in the neurotrophic tyrosine receptor kinase 1 gene, which is the receptor for nerve growth factor (12, 31–33). A first diagnosis is generally established during early childhood when the family refers to a physician, reporting loss of pain perception or frequent trauma.

Although the lack of neuropathological and genetic data does not allow a definitive classification of the case described in the manuscript, both clinical features and neurophysiological data suggest a selective defect of small-calibre nerve fibres with preserved sweating and with intact large diameter nerve fibres, which best fit with the diagnosis of HSAN V. Patients with these...
autonomic pathologies can be often very difficult to diagnose because of their variable presentation, the lack of simple diagnostic tests and of the apparent rareness of this condition (12, 34).

Probably, when the little boy had repeated and unexplained episodes of fever and the incident to his right tibia, it could have been posed a diagnosis hypothesis of impairment of pain perception (35, 36). Surely, molecular analysis and genetic investigation have to be performed to confirm the clinical diagnosis.

In Dentistry, the most important characteristic of CIP is the self-mutilating behaviour that leads the child to oral ulcerations on lips, tongue and cheeks, self-extraction of teeth and also finger and hand biting (12, 37). This condition represents a challenge to the dentist, especially to the paediatric dentist, who is concerned with an early intervention and because patients can be below normal with respect to intelligence, development and psychological adjustments.

The observation of a premature loss of teeth may be of value for an early diagnosis (27–29). As oral ulcerations and premature loss of teeth may represent early manifestations of this rare disorder, dentists should always keep in mind that these clinical signs can be because of CIP. An early diagnosis and appropriate dental approach is indispensable to avoid severe injuries to the oral mucosa.

A multidisciplinary diagnosis and treatment, further than an open-minded approach is indispensable with this kind of patients. The reported approach tailored on the individual patient takes into account the functional aspect as well as the psychosocial condition with a favourable cost-benefit ratio.

References


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