Congential insensitivity to pain: report of two cases

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Congenital indifference or insensitivity to pain (CIP) is a rare syndrome. It mimics a number of other syndromes categorized under peripheral sensory neuropathies, often making early diagnosis difficult. Two cases from the middle east are presented, highlighting possible diagnostic, and management difficulties.
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INTRODUCTION

Congenital insensitivity to pain is an uncommon syndrome first described by Dearbon in 1932. It is characterized by absence of normal subjective and objective responses to noxious stimuli in patients with intact central and peripheral nervous systems. The condition which is mostly found in young children is also clinically characterized by fractures, which can go un-noticed, bruising, ulceration of fingers and toes, and oral self mutilation.

The purpose of this report is twofold. The first objective is to report two additional cases of congenital insensitivity to pain from the Middle East, particularly from Saudi Arabia, which to our knowledge are the first from this part of the world.

The second purpose is to discuss the possible diagnostic and management difficulties the syndrome can pose for the clinician unfamiliar with the syndrome.

CASE REPORTS

Case 1

On February 11th 1999, an 8 year old female (Patient 1) was referred to the King Fahad Hospital emergency room from a local primary health centre. The presenting complaint was a moderate swelling of the lower right jaw following an extraction three weeks earlier. She was referred to the oral and maxillofacial surgery clinic for consultation and management. The patient, who did not appear to be in distress, had a slightly elevated temperature at 38˚C.

Extra-oral examination revealed, mildly tender right mandibular swelling, corneal opacity, decreased vertical dimension of the jaws on closure, (Figure 1A) scarred and deformed fingers (Figure 1B).

Intra-orally, she had several missing teeth, and the anterior third of her tongue was deformed and scarred. The alveolus in relation to edentulous areas were moderately resorbed. The tongue, palate and buccal mucosa were intact. Extraction socket of tooth number 6 was moderately necrotic.

A clinical diagnosis of sub-acute infection secondary to infected extraction socket was made and patient was treated with debridement, copious irrigation of the socket and anti-biotics. Appointment was given for follow-up.

A further review of the patients case note was remarkable. It revealed previous attendance at age 5 years to the Eye and Pediatric Clinics of the Hospital in 1996.

Her presenting complaint then was, recurrent corneal ulcer and, trophic ulcers of the fingers and toes. Physical examination at the time revealed, clear chest, normal heart sound, and tendon reflex. A clinical impression of familial dysautonomia and Lesch-Nyhan syndrome were respectively made.

On follow-up, radiographs of long bones, and phalanges were ordered, with uric acid test. Reports were negative for bone deformity, except for erosion of the upper middle phalanges. Uric acid test was 223 mol/L. Patient was subsequently referred to the orthopedic and neurology clinics for consultation with a diagnosis of familial dysautonomia or congenital sensory neuropathy, having excluded Lesch-Nyhan syndrome based on the uric acid test result.

Patient failed to return for several years only to represent in 1998 to the Eye Clinic at the KFH with recurrent eye problem and trophic ulcers. She was treated at the clinics, and was later referred to the orthopaedic unit, where new radiographs of long bones were ordered. Radiographic report was negative. The previous diagnosis of congenital sensory neuropathy was affirmed, with congenital insensitivity to pain as differential. The record did not indicate attendance at the neurology clinic.

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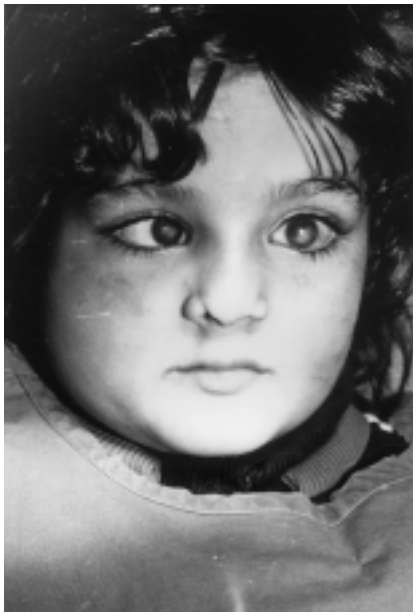

Figure 1(A). Patient (1) Facial profile. Showing slight right mandibular swelling, and corneal opacity.

On questioning, the father claimed, patient was born at full term in her native Yemen. At 11 months, the parents noticed she was fond of bitting on her fingers, toe and lips, often inflicting trauma on self without any emotion. She also often scratched her eyes. At age 2 years, dental consultation was obtained in Yemen for her traumatized lip, and extraction of all anterior teeth was recommended. She has one sister and two brothers. The sister (Patient 2), who is a twin and a year older than Patient 1, has the same problem, but her twin brother is free of this disorder.

Case 2

On 5th of April 1999, a 9 year old girl, sister of patient (1) was referred to the Oral Surgery Clinic at KFH, from the plastic surgery unit for evaluation following a breakdown of a recently revised lip. There was a history of chronic ulcer of the lower lip secondary to self inflicted trauma. The ulcer was found to be directly associated with an existing lower anterior tooth complicating the repair, (Figure 3) hence extraction was recommended. Patient had the same general features like her sister; deformed fingers, toes, lower lip and corneal opacity. (Figures 2 A and B).

The record indicated she had a previous admission at KFH for management of hypopyon corneal ulcer.

Oral examination revealed normal mucosa, including the tongue, which was scarred anteriorly. Orthopantograph showed multiple missing teeth with thin alveolar bone (Figure 3). She was diagnosed at various times as having familial dysautonomia or congenital insensitivity to pain.

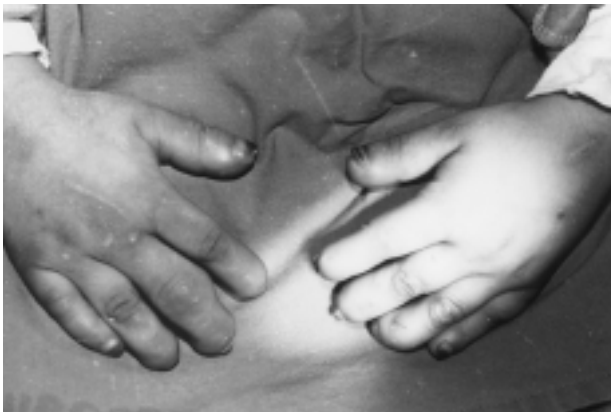

Figure 1 (B). Deformed fingers of Patient (1) is seen.

Histamine test was ordered, and both patients reacted positively.

DISCUSSION

We have reported two cases of congenital insensitivity to pain (CIP). It is a rare condition inherited by a recessive trait.[2,3] Most of the reports and studies in the literature on the condition have been on a non-Arab speaking population[2-5] and few reports have come from the middle east.[7,8] There is no sex predilection for this rare condition.[3] Although both of our cases are in girls; other studies,[2,3] including some from the Middle East, have favored boys and girls respectively. The chances of genetically linked diseases and conditions are known to increase in consanguineous relationships. This type of relationship is common in the middle east, and some reports[7,8] from the region tend to confirm a possible close association between the incidence of CIP and consanguineous relationships. The parents in this report denied a similar relationship.

Congenital insensitivity to pain had been found to mimic many peripheral sensory neuropathies, which can make early diagnosis difficult, particularly to a clinician, who might be encountering it for the first time. Among the conditions in the differential diagnosis that closely mimic (CIP) suggested by various authors,[4-6] are Lesch-Nyhan syndrome, congenital sensory neuropathy with anhidrosis and without anhidrosis, and familiar dysautonomia. According to Brett,[5] sensory loss with insensitivity to pain is a "feature of some rare congenital syndrome of hereditary sensory and autonomic neuropathy (HSAN) seen in childhood, and also of hereditary sensory radicular neuropathy (HSAN type1) seen in adult life with dominant inheritance". According to him the insensitivity to pain relative or general is one clinical finding common to the syndrome presented in childhood.

Absence of pain therefore, characterized by trophic ulcers of the fingers and toes, and self inflicted trauma to the lip and eyes are common to Lesch-Nyhan Syn-

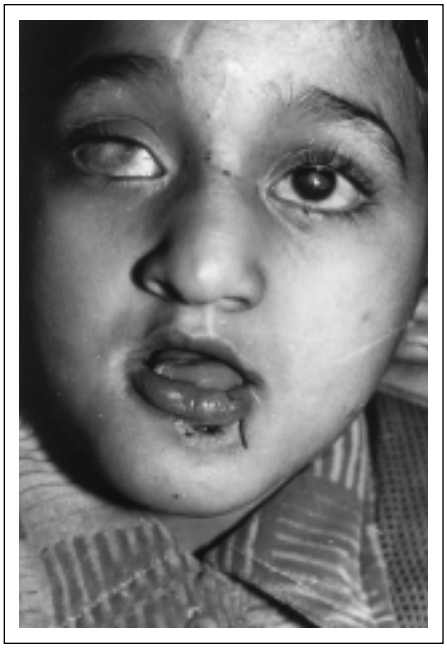

Figure 2 (A). Patient (2) facial profile showing, scarred and ulcerated lower lip, and corneal opacity.

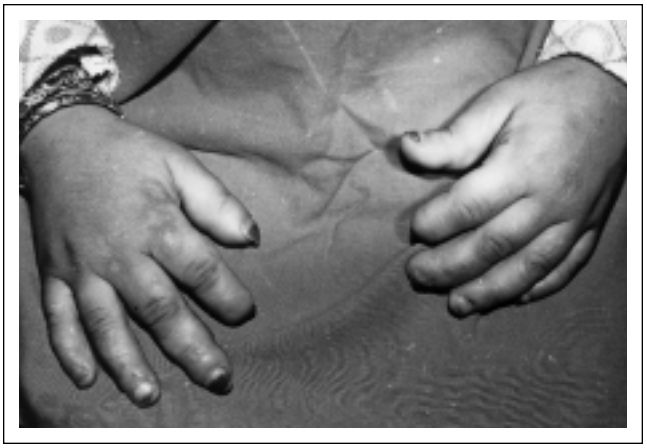

Figure 2 (B). Deformed finger of Patient (2) is noted.

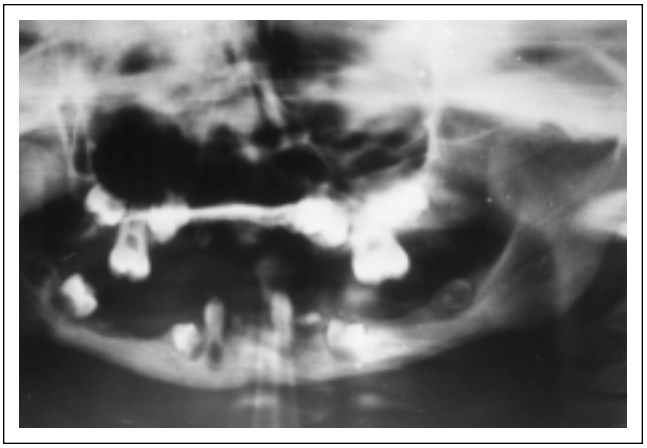

Figure 3. OPG of Patient (2) showing multiple missing teeth, and thin alveolus.

drome, CIP, and familial dysautonomia. These conditions also have age of onset at birth or early childhood. Diagnosis can thus become difficult if the clinician is unfamiliar with the various types of peripheral sensory neuropathies.

However, careful clinical examination, history and specific tests, will often differentiate one condition from the other. Maaya *et al*.[4] in studies on diagnosis and misdiagnosis in familial dysautonomia, reviewed the methods of diagnosis in 122 patients. In all cases, diagnosis was based on the clinical history, physical examination, and results of histamine test. The result showed that 69 (56 %) of patients were diagnosed in the first year of life, and 3 (2 %) from 10.1 to 20 years of life.

In the 19 cases of Lesch-Nyhan syndrome reported by Christie *et al*.,[10] only 4 was correctly diagnosed at ages between 18 months and 10 years. The above examples highlight the general difficulty in diagnosis, that can be posed by peripheral sensory neuropathies. In our cases, even though physical examination, and clinical examination were done, histamine test was not conducted until we saw the patient. This would have earlier eliminated familial dysautonomia, and congenital sensory neuropathy. According to Brett,[5] histamine test for differential diagnosis in familial dysautonomia is reliable with no false negative results.

Other parameters, such as temperature perception and physiological pain reaction if measured could also be early pointers to CIP. It is generally reported[5,6,9] that while these parameters are normal or present in CIP, they are absent or lost in congenital sensory neuropathy, Lesch-Nyhan syndrome, and familial dysautonomia.

Three orthopedic manisfetations of CIP are: recurrent fractures, neuropathic (Charcot) joints and osteomyelitis.[3,6] These features were not prominent in our cases, and could be a rare exception. Some peculiar oral/dental features have been noted in familial dysautonomia. Besides oral self mutilation, which is common to all, the absence or marked reduction of fungiform papillae, and taste buds should easily exclude familial dysautonomia.

In the present reports, no record of intra-oral examination was noted, until patients presented to the oral surgery clinic. This should be routine in all suspected cases of congenital neuropathy presenting in childhood. The racial background of patients with peripheral neuropathy can also be an important clue. While familial dysautonomia is found exclusively among Ashkenazi Jews, other syndromes have been reported among different races.

The clinical course and prognosis in patients with peripheral neuropathy is different. Early diagnosis and proper management are therefore essential in helping patients to cope relatively well with their conditions.

Patients with CIP have a fairly good prognosis. Even though they keep injuring and traumatizing themselves, this behavior improves with age as they seem to learn other clues to help avoid injury.[5]

Lesch-Nyhan and familial dysautonomia patients however do eventually succumb to various systemic complications somewhere along the way, thus making long term prognosis poor. Regarding oro-dental self mutilation. Mass and Gadoth[11] in their recent review of oro-dental self-mutilation in familial dysautonomia advocated elimination of sharp edges of teeth to reduce injury.

This in our opinion is by far preferable to the routine serial extractions earlier prescribed for our patients in the course of their condition. Since CIP patients do have a fair to good prognosis, future oral rehabilitation can become an arduous task.

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