CASE REPORT

Hereditary sensory and autonomic neuropathy type IV and orthopaedic complications

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Summary Hereditary sensory and autonomic neuropathy type IV (HSAN-IV) is a very rare autosomal recessive disorder characterized by recurrent episodes of unexplained fever, extensive anhidrosis, total insensitivity to pain, hypotonia, and mental retardation. The most frequent complications of this disease are corneal scarring, multiple fractures, joint deformities, osteomyelitis, and disabling self-mutilations. We reported the case of a 12-year-old boy. The goal was to discuss our decision-making and compare this case with cases described in the literature.

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Introduction

Congenital insensitivity to pain with anhidrosis, or hereditary sensory and autonomic neuropathy type IV (HSAN-IV), is a very rare autosomal recessive disorder that is difficult to diagnose and treat. It belongs to the HSAN family, which includes five types [1,2]. HSAN-IV is the rarest form [1] and a few hundred cases have been described [3]. It associates insensitivity to pain with preservation of other tactile sensations, developmental delays, anhidrosis, and thermoregulation disorders [1–4]. The complications of this disease are essentially orthopaedic, but the vital prognosis can often be challenged and the life expectancy rarely reaches adulthood in this clinical form.

Early diagnosis should be suspected in early childhood with excoriated lesions of the extremities (ungual and cutaneous with osteolytic lesions), stomatological involvement beginning in the first year of life when the first teeth appear, with biting of tongue and lips, bone fractures (repeated, often unnoticed, with inadequate bone union), and painless joint dislocations [5–11].

Particular vigilance is necessary so as not to confuse this clinical picture with child abuse.

We report the case of a 12-year-old child with HSAN-IV, who presented multiple orthopaedic complications and whose treatment was often difficult, currently with major, notably articular sequelae.

The objective of this article was to show the problems related to making therapeutic decisions in patients with this clinical form of neuropathy and to analyze a
posteriori our choices and compare them with cases reported in the literature.

Clinical observation

The patient was a 12-year-old boy who was diagnosed with HSAN-IV at the age of 4 years with the association of considerable delay in cutaneous healing (scalp lesions), self-mutilations, periungual lesions, early loss of baby teeth, growth delay, and unexplained episodes of hyperthermia. On the behavioral level, he presented delays in acquisitions associated with hyperactivity. Later, the clinical history was marked by fractures caused by minor traumas.

The first orthopaedic event occurred at the age of 5 years with a fracture of the first three left metatarsals associated with injury to the second toe. Treatment was functional with local care. The wounds evolved toward bone union but with cutaneous necrosis of the second toe requiring amputation. At 6 years of age, the patient presented a left tibial diaphyseal fracture, treated orthopaedically. The course was complicated by a delay in bone union with hypertrophic osseous callous formation (Fig. 1a). Three years later, he presented a new fracture in the left leg, again treated orthopaedically, with valgus malunion (Fig. 1b). At 7 years of age, he presented a fracture of the upper third of the left femoral diaphysis, which was treated with osteosynthesis using elastic stable intramedullary nailing (Fig. 2a). Progression was marked by hypertrophic osseous callous formation complicated by a basiscervical fracture 1 month later (Fig. 2b). This was complicated by acute Staphylococcus aureus osteitis, requiring prolonged antibiotic therapy, repeated surgical draining, and removal of the osteosynthesis material. Six months later, the diaphyseal fracture had healed, but the child presented total necrosis of the proximal extremity of the femur (Fig. 2c). Paradoxically, the functional repercussion was minimal other than the need to compensate the unequal length of the lower limbs. At 8 years of age, he presented a diaphyseal fracture of both bones in the right forearm, treated orthopaedically. This fracture was complicated by septic fistulated pseudarthrosis associated with dislocation of the radial head, radioulnar synostosis, and formation of bony sequestra (Fig. 3). Several surgical drainage procedures were necessary, associated with prolonged antibiotic therapy. Healing could only be achieved with substantial bone resection. At 11 years of age, diaphyseal fractures of the two bones of the left forearm were also treated orthopaedically. As on the contralateral side, a spontaneous infection of the fracture site occurred (Fig. 4), requiring several drainage procedures and surgical débridement as well as long-term antibiotic therapy.

Currently, this child walks and runs with limping and orthopaedic shoe wear to compensate the 4-cm difference in the left lower limb. The upper limbs have been fitted with articulated splints at the elbows.

Discussion

Congenital insensitivity was described for the first time in 1932 [12]. It was a very rare clinical syndrome with a prevalence less than 1/1,000,000, related to genetic anomalies. The most frequently used classification was established by Dyck in 1983 [13]. It includes five types; Table 1 shows the clinical characteristics and the mode of genetic
Congenital insensitivity to pain: Orthopedic complications

Figure 2  a: at 7 years of age: fracture of the upper third of the left femoral diaphysis, treated with osteosynthesis using elastic stable intramedullary nailing; b: progression was marked by hypertrophic osseous callous formation complicated by a basicervical fracture 1 month later; c: six months later, diaphyseal fracture healed, but total necrosis of the proximal extremity of the femur.

Table 1  Clinical and genetic characteristics and transmission modes of the five types of hereditary sensory and autonomic neuropathy described by Dyck [13].

<table>
<thead>
<tr>
<th>HSAN</th>
<th>Age at onset</th>
<th>Heredity</th>
<th>Neurovegetative disorders</th>
<th>Mental retardation</th>
<th>Locus</th>
<th>Gene</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1 radicular neuropathy</td>
<td>10—15 years</td>
<td>AD</td>
<td>-</td>
<td>-</td>
<td>9q22</td>
<td>SPTLC1</td>
</tr>
<tr>
<td>Type 2</td>
<td>Birth</td>
<td>AR</td>
<td>-</td>
<td>±</td>
<td>12p13.3</td>
<td>HSN2</td>
</tr>
<tr>
<td>Type 3</td>
<td>Birth</td>
<td>AR</td>
<td>+++</td>
<td>±</td>
<td>9q31</td>
<td>IKBKAP</td>
</tr>
<tr>
<td>Type 4</td>
<td>Birth</td>
<td>AR</td>
<td>+</td>
<td>+++</td>
<td>1q21</td>
<td>NTRK1</td>
</tr>
<tr>
<td>Type 5</td>
<td>Birth</td>
<td>AR</td>
<td>±</td>
<td>±</td>
<td>1p13.1</td>
<td>NGFB</td>
</tr>
</tbody>
</table>

HSAN: hereditary sensory and autonomic neuropathies; AD: autosomal dominant; AR: autosomal recessive.
absence of a response to the histamine test confirms sympathecic dysfunction.

The case reported herein shows HSAN type IV, a particularly severe form, notably on the orthopaedic level [5], with an increased occurrence of fractures, dislocations, and infectious and neuroarthropathic complications.

As for our patient and those cited in the literature, the absence of pain sensation makes immobilization more difficult and is the source of hypertrophic osseous cal- lous formation [5,7,8,14], which delays bone union and, because of the micro-traumas and traumas resulting from articular anesthesia, leads to neuroarthropathy [15–18]. This disease, today called neurogenic osteoarthropathy, was described for the first time by Charcot in 1868 [19]. It mainly involves the weightbearing joints [2] and ends in destruction of the joint.

As in our example, most often mental retardation associated with behavioral disorders are found in this form of HSAN-IV [1–4]. These disorders make patient compliance difficult, notably during orthopaedic treatment.

A complete workup of dysautonomy (Holter cardiac and blood pressure monitoring, polysomnography) is necessary, as is prevention and treatment of hyper- or hypothermia to which these patients are exposed.

Another major aspect of the functional as well as vital prognosis of HSAN-IV patients are the infectious complications [5,20]. They are encouraged by a delay in healing and they worsen the joint destruction phenomena. Treatment for our patient consisted in surgical débridements associated with prolonged antibiotic therapy, as recommendy by Bar-On et al. [5].

In the present example, the coxofemoral joint evolved toward destruction of the femoral head associated with dislocation. This infectious or neurogenic osteoarticulopathic state secondary to the traumatic processes is described in a number of cases in the literature [5,7,9,10,21,22]. Paradoxically, because of the absence of pain, the functional repercussion is minimal, with the impression of joint mobility relatively well preserved. The question can therefore be raised as to the value of surgical treatment compared to therapeutic abstention with monitoring. Even though Roberts et al. [23] have described a satisfactory surgical cure by performing a simple capsulorraphy followed by immobilization in a spica cast for 2.5 months, thus stabilizing the hip, the treatment attempts reported by Bar-On et al. [5] and Koster et al. [10] failed. These authors had performed surgical reduction associated in one case with varus osteotomy alone and in the other case completing the surgery with innominate osteotomy of the pelvis. Moreover, a surgical intervention is a trauma that can accelerate the development of upper femoral osteonecrosis. As described by Koster et al. [10] in an HSAN patient with bilateral hip dislocation, with one treated orthopaedically and the other surgically, only the latter was complicated by osteonecrosis of the femoral head. In our observation, the question can be raised a posteriori of the value of having carried out osteosynthesis of the femoral fracture with intramedullary nailing, given the secondary infectious complications. Initial orthopaedic management would perhaps have avoided these complications, but with the risk of other complications, inherent to prolonged immobilization: bedsores, increased osteopenia, and problems.
maintaining adequate body temperature in large cast immobilizations.

Treatment with an external fixator seems just as risky and even a source of a high risk for sepsis: its indication has never been proposed in the literature.

Educating patients so that they protect themselves better from the succession of repeated and unperceived micro-traumas is useful but it is very difficult to implement. These subjects develop behavioral disorders of the psychiatric type and enter into self-aggravating situations that are difficult to interrupt.

Protective appliances, in particular for the lower limbs, can be useful, but they are not always easy to implement, especially because of the cutaneous lesions that they can induce.

Conclusion

This observation illustrates the point to which HSAN-IV exposes the patient to orthopaedic complications that are complex to treat and that present a clinical picture that can be disarming for the orthopaedist. One of the essential factors of treatment remains prevention of fractures through parent education. Treatment of fractures must favor orthopaedic treatment as much as possible, which, as we have seen, does not prevent risks of hypertrophic osseous callous formation and osteonecrosis, even septic. Extensive débridement of bone tissue may be necessary at times to obtain healing, at the cost of major articular sequelae, but, finally, remarkably well tolerated because of the absence of pain sensations in this context.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References