Hereditary sensory and autonomic neuropathy type IV orthopaedic complications

Ivo Marik[a], Miroslav Kuklik[a] , Dana Kuklikova[a] and Kazimierz Kozlowsk[b]

Painless fractures with delayed healing or abnormal callus formation require exclusion of a systemic disorder. We report a 9-year-old girl with hereditary sensory and autonomic neuropathy type IV who developed bone changes in the hind foot after a protracted healing of a tibia fracture. Osteomyelitis was considered as a possible cause of destruction of the tarsal bones. Negative sweat test documented anhydrosis. Late diagnosis in our patient occurred because of an unusual clinical course of the disease. *J Pediatr Orthop B* 18:138–140 © 2009 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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[a]Ambulant Centre for Defects of Locomotor Apparatus, Praha, Czech Republic and [b]Department of Medical Imaging, The New Children's Hospital, Sydney, Australia

Correspondence to Dr Kazimierz Kozlowski, New Children's Hospital, Westmead, NSW 2145, Sydney, Australia
Tel/fax: +61 2 94382562; e-mail: Kazimiek@chw.edu.au

Introduction

Fractures with an unusual, painless history, delayed healing process or abnormal callus formation require a thorough medical examination to exclude a systemic disorder. Similarly, the diagnosis of chronic osteomyelitis without systemic manifestations and with normal inflammatory markers (erythrocyte sedimentation rate, C-reactive protein) needs reconsideration.

We report a girl who developed deformity of the left tibia and destructive calcaneal changes after slow healing of a supramalleolar fracture. Osteomyelitis of the calcaneus was considered as a possible diagnosis. Neurological examination of the patient, radiographs and laboratory tests revealed abnormalities characteristic for hereditary sensory and autonomic neuropathy type IV (HSAN IV) [1–8], associated with progressive destructive changes of the tarsal bones, leading to Charcot joint of the hind foot [9]. HSAN constitutes clinically and genetically a very heterogenous group of disorders, affecting small fibrae neurodevelopment with a variable phenotypic expression of the autonomic system [10].

Case report

This patient with a normal family history sustained a fracture of the right radius at the age of 2 years and of the distal left tibia at 3 years. The latter was followed by slow healing, including abscess formation at the distal anterior aspect of the left leg and swelling of the left heel with calcaneal changes suggestive of osteomyelitis.

At the age of 7 years 4 months, she was examined at the Centre for Defects of the Locomotor Apparatus in Prague. HSAN II was diagnosed. However, the parents remarked, she had a dry skin and there was absence of sweating during febrile episodes. She was admitted to the First Paediatric Clinic of Charles University in Prague for some additional tests at the age of 8 years 2 months. The pilocarpine sweating test was performed and the diagnosis changed to HSAN IV. At the age of 9 years 6 months, her height was 126 cm and weight 25 kg. She was limping on her left leg. There was anterior bowing of the left tibia with swelling of the left ankle, hind foot and hallux (Fig. 1). The fingers had dry, eczematoid skin; the distal phalanges were shortened and the nails were small but normal in appearance. All her teeth were present, but they were slightly grey in colour and there were only two large lower incisors. There was chronic gingivitis. Mild mental retardation was present. The summary of examinations and laboratory tests performed during the last 2 years is as follows: the neurologic examination documented normal muscle strength and deep tendon reflexes. There was diffuse tactile hypoesthesia with decrease of pain perception. The temperature, position and vibration sensation were normal.

Electromyography showed normal motor and sensory nerve conduction in both lower extremities. Indirect lymphoscintigraphy showed free lymph flow in both lower extremities. Duplex ultrasonography of the lower extremity vessels was normal. Radiograph examination documented bizarre progressive, destructive and sclerotic changes in the hind foot (Fig. 2a and b).

Pilocarpine filter paper test produced markedly diminished amounts of sweat 0.0239 g (age-matched controls 0.3–0.6 g). Routine blood and urine examinations, C-reactive protein, markers of bone turnover and parathormone were all normal.

Discussion

A painless, slow-healing fracture or destructive bone changes without pain and fever indicates the possible

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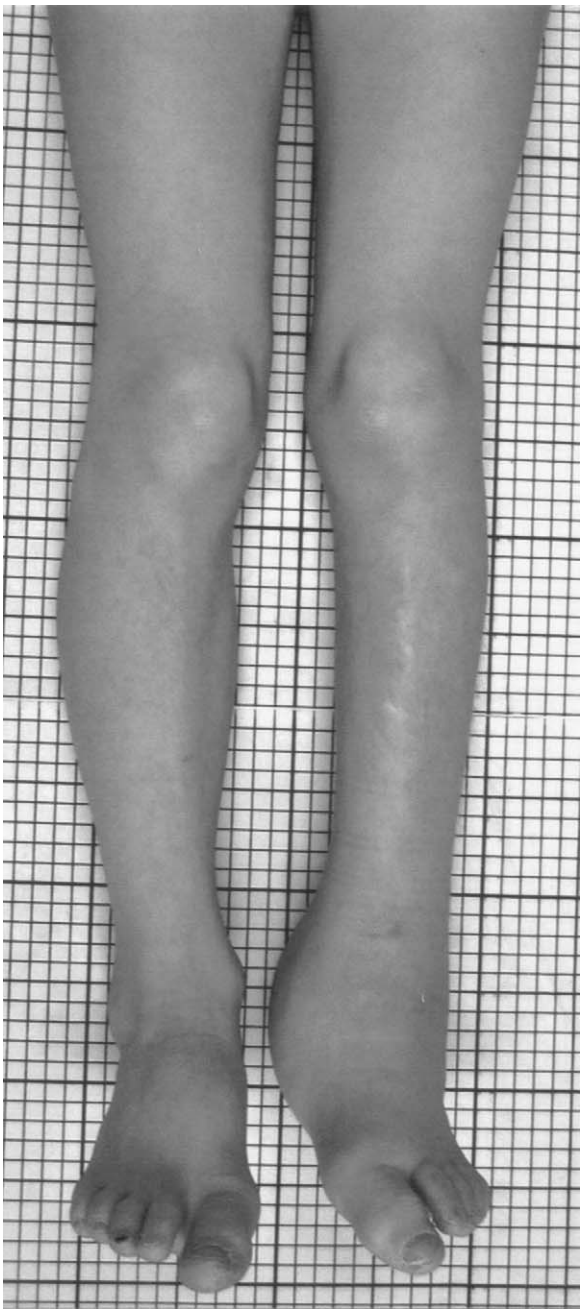
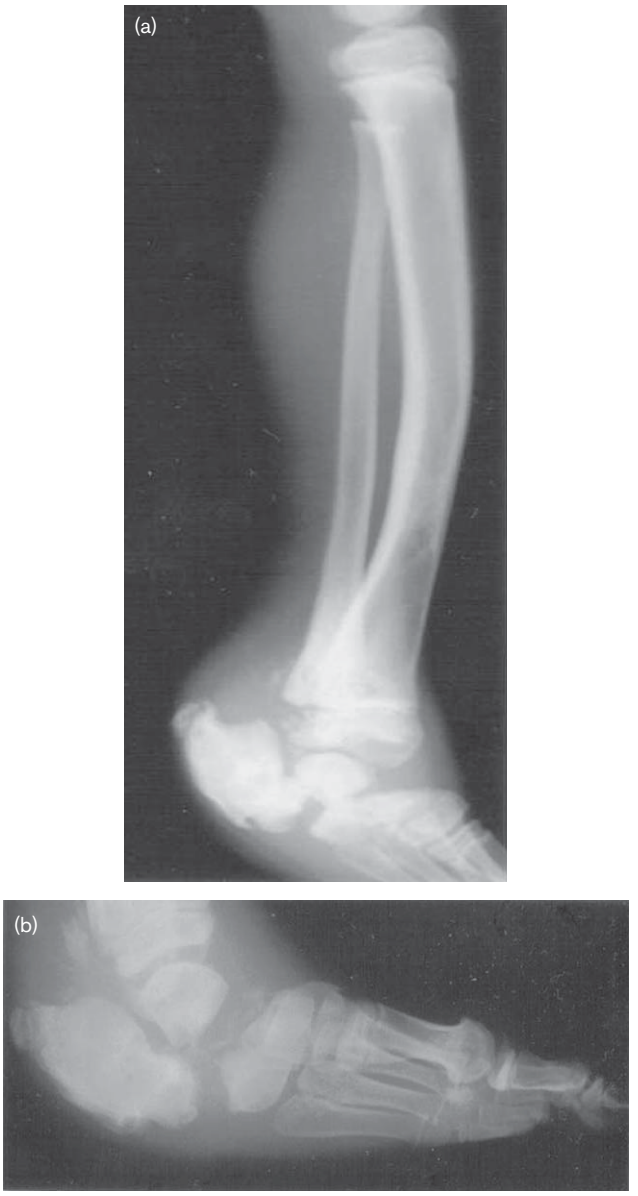
Fig. 1



Patient's legs showing shortening of the left lower extremity, lateral bowing of the left leg with scars and marked swelling of the ankle.

Fig. 2



(a and b) Radiographs of the left leg and left foot show anterior bowing of the tibia and oedema of the ankle. Marked disorganization of the joint architecture, bony sclerosis of dysplastic tarsal bones and small bony fragments in the area of hind foot, consistent with chronic impacted fracture characteristics of Charcot's joint.

presence of a sensory neuropathy. Normal inflammatory serum markers make the diagnosis of osteomyelitis unlikely. Diagnosis of the type of neuropathy is made on the clinical history, a neurological examination and some laboratory tests.

HSAN IV is a rare disorder with less than 50 cases reported up to 2006 [1–8]. Early diagnosis is rare because of the initially confusing symptoms and signs. HSAN IV is characterized by high fevers secondary to anhydrosis during hot weather since infancy, lack of pain sensation and inability to distinguish hot and cold followed by painless injuries of the extremities and oral structures, often with self-mutilation. Corneal scarring is common. Thick skin, dystrophic nails and patchy hypotrichosis of the scalp are further clinical manifestations. Skin and bone lesions heal poorly. Mental retardation with severe learning problems is usually present.

The reason for late diagnosis in our patient was an unusual clinical course for HSAN IV. Insensitivity to pain was of a minor degree, the temperature sensation was normal and self-mutilation was absent. In addition, her hairs and nails were within normal limits and no eye complications were present. Her mental development was only slightly affected. She was not a bright student but attended a normal school. However, owing to the poor healing of the tibial fracture and a history of high fevers during the hot weather during infancy, the diagnosis of HSAN IV could have been considered earlier. Progressive destruction of tarsal bones – a complication of HSAN IV – was initially misdiagnosed as osteomyelitis. This diagnosis, however, was excluded as the patient did not have clinical signs and symptoms of osteomyelitis and the erythrocyte sedimentation rate and C-reactive protein were normal. In addition, the absence of osteoporosis in bones adjacent to an inflammatory process would indeed be unusual.

Important in the differential diagnosis of HSAN IV with other forms of congenital sensory neuropathy – HSAN I, HSAN II, HSAN III and HSAN V – are the clinical history and neurologic examination. The hallmark of HSAN IV is the negative sweat test. HSAN I is a disorder of adults. Occasionally, it may occur in teenagers [7]. HSAN II appears early in infancy and affects both the upper and lower extremities [11–13]. HSAN III is a severe autonomic disorder present since birth [14]. HSAN V has many of the features of HSAN IV. However, the HSAN V patients are mentally normal, have a normal pattern of sweating and different sural nerve biopsy microscopy findings [7]. HSAN I is inherited as an autosomal dominant trait. HSAN II–V are autosomal recessive disorders. Other sensory neuropathies such as syringomyelia, tabes and mononeuropathies are unlikely to cause confusion for a researcher familiar with HSANs.

We did not perform nerve biopsy studies as it would not be of practical benefit to the patient and it would not change the diagnosis or her management. Congenital insensitivity to pain with anhydrosis is caused by mutations in the neurotropic tyrosine kinase receptor type 1 gene located on chromosome 1 (1q21–q22) [1,14–16].

Conclusion

Delayed fracture healing should alert orthopaedic surgeons about the possibility of an HSAN. Although the HSAN IV gene and its chromosomal location are known, no gene therapy is available at present. Early diagnosis is important. Control of the orthopaedic complications is essential for a better prognosis.

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