Brachial Plexopathy as Early Manifestation of Hereditary Neuropathy with Liability to Pressure Palsy (Hnpp) in Infancy

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Abstract

Hereditary neuropathy with liability to pressure palsy (HNPP) is an autosomal dominant disorder characterized by recurrent mono-neuropathies related to minimal trauma or compression. HNPP usually manifests in adolescence or adulthood, being relatively exceptional at an earlier age. A 4-month-old boy with brachial plexopathy as early manifestation of HNPP is presented. Familiar anamnesis, as well as neurophysiological and molecular studies, stands out in early diagnostic suspicion. In this case, the early manifestation and its semiological characteristics accentuate its peculiarity.

Keywords: Brachial plexopathy; Infancy; Hereditary neuropathy with liability to pressure palsy

Introduction

Hereditary neuropathy with liability to pressure palsy (HNPP) is a sensitive motor neuropathy inherited in an autosomal dominant pattern whose anomaly consists of a deletion of the peripheral myelin protein 22 (PMP22) gene, located in the 17p11.2 chromosome region. Its clinical characterization reveals recurrent episodes related to minimal trauma, such as traction and/or external pressure. This diagnosis is rare in the paediatric age [1-4]. We present a case of HNPP with clinical manifestations at an early age (4 months). Familiar anamnesis, as well as neurophysiological and molecular studies, stand out in early diagnostic suspicion.

Case Report

We present a case of a four month infant attending a well-child examination, showing less mobility in left upper limb (the left arm standing in approximation and internal rotation). There were no previous traumatisms of evident traction. Massages and passive exercises of the articulations of the upper limb were recommended showing a progressive improvement with complete recovery after five–six weeks. Neurological examination was normal at six months of age. His father, aged 40, pointed out that he presented weakness in upper right limb, associated to sensitive disorder (numbness) during several weeks when carrying relatively heavy objects (such as the shopping bag). In addition, his sister and her daughter (aged 50 and 28, respectively), as well as his brother (aged 43) referred similar symptoms (his brother worked as a waiter and had to quit his job because of recurrent episodes of weakness and loss of manual skill). His paternal grandfather, who is now dead, seemed to have suffered the same symptoms. Our patient has a six year old sister who refers weakness and recurrent limb paresthesia (her parents did not will to achieve molecular and neurophysiological studies). Pregnancy was normal and showed low fetal movement (an amniocentesis was required because of age over 35: normal karyotype 46, XY). A forceps delivery was required. Birth weight was 3400 g and reanimation was not necessary (Apgar score: 9/10).

A psychomotor retardation and/or motor impairment was gradually appreciated (rolling from back to side at age 11 months, unsupported sitting at 14 months, able to walk unassisted at 20 months of age). Blood analysis (hemogram, calcium and phosphate, ferritin, creatine phosphokinase, liver and renal function tests, thyroid hormones, pyruvate, ammonia and amino acids) and urine analysis (organic acids and amino acids) as well as cranial MRI were normal. He is four years old at present, shows relatively steady unsupported walking, but has difficulties to jump in place with both feet together and stand on one foot. He did not present any additional neuropathic episode.

At age 10 months, electromyography and peripheral nerve conduction studies were normal. At age 15 months, peripheral nerve conduction was normal, except for a slight alteration of median nerve at wrist. At age three years, studies showed a moderate decrease in peripheral motor and sensory nerve conduction velocities with lower limbs predominance, as well as alteration in right median nerve at wrist (distal latency: 5.7 ms) and, to a lesser extent, in right popliteal sciatic nerve at the fibular head (distal latency: 10.7 ms) (Table 1). The neurophysiological studies performed in his father and affected uncles showed generalized slowing of motor and sensory conduction with a higher expressivity in usual focal compression places (ulnar neuropathy at the elbow in all three, and important conduction alteration of the right median and left popliteal sciatic nerves, at carpal tunnel and fibular head, respectively, in his father). A molecular genetic study (Figure 1) was performed in affected relatives by gene amplification using the SALSA P033B kit containing 37 probes, 16 of which are specific for the PMP22 (17p11.2) gene region. The amplified fragments were analyzed with automated DNA sequencing by capillary electrophoresis and showed a hybridization pattern compatible with the presence of reduced PMP22 gene dosage (deletion).

Discussion

The HNPP usually manifests during adolescence and/or adulthood, being relatively exceptional at an earlier age [5-10]. Its clinical manifestations usually correspond to anatomical locations

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subject to compression or entrapment, such as the external popliteal sciatic nerve at fibular head, ulnar nerve at the elbow, radial nerve at the humerus and/or the armpit or median nerve in the carpal tunnel [7,9,10]. However, any peripheral or even cranial nerve could be affected. It is characterized by painless motor weakness, which tends to complete recovery in a short period of time, although a certain neurological deficit might persist in adult life.

A favourable prognosis is expected and, in many cases, symptoms are barely perceptible, which justifies the neurophysiological and/or genetic studies in the relatives of a previously diagnosed patient. In this case, the father of the patient, as well as the affected relatives, had an officially recognized degree of disability, and the work duties were conditioned by the symptoms.

In this case, the early manifestation (four months of age), and its semiological characteristics accentuate its peculiarity. Symptoms reflect a brachial plexopathy whose lesion apparently settled on the Erb point, where C5 and C6 roots merge to form the upper trunk of the brachial plexus and therefore affecting the innervation of the deltoid and arm muscles without involving the muscles of hand and forearm. The developmental delay and/or clumsiness in motor skills, as were stated in this patient, are associated manifestations which have been described in the few patients diagnosed in early age [5,6]. They were obviously included in early stimulation programs.

The peculiarities of this case (transient brachial plexopathy without evident etiological factor in an infant) could have caused a delay in diagnostic suspicion. The presence of familiar history facilitated an early diagnosis. The anamnesis data -even without a previous familiar diagnosis- guided to the possibility of a hereditary polyneuropathy. For this reason, molecular and neurophysiological study was mandatory [7]. The neurophysiological studies showed a characteristic

| Nerve | Stimulation-record sites | Amplitude (M=mV, S=μV) | Distal latency (ms) | Conduction velocity (m/s) |
|-------|--------------------------|-------------------------|---------------------|--------------------------|
| Sural | Calf-Ankle               | R                       | N                   | R                        | N                       |
|       |                          | 4                       | >5                  | 2.1                      | <3.5                    | 20                      | >45                     |
| Median sensory | Wrist-Digit 2 | 4                       | >8                  | 4                        | <3.4                    | 20                      | >50                     |
| Ulnar sensory | Wrist-Digit 5 | 5                       | >5                  | 1.8                      | <3.1                    | 40                      | >50                     |
| Median motor | Wrist-APB | 5                       | >5                  | 5.7                      | <4                      | 56                      | >50                     |
| Ulnar motor | Wrist-ADM | 7                       | >6                  | 2.8                      | <3.3                    | 51                      | >50                     |
| Peroneal motor | Ankle-EDB | 0.7                     | >2.5                | 5.1                      | <5                      | 37                      | >45                     |
| Tibial motor | Ankle-AH | 4                       | >3                  | 3.3                      | <5.5                    | 38                      | >45                     |

Table 1: Nerve conduction study results of the patient.
electroneurogram in the patient as well as in the affected relatives: signs of generalized sensitive and motor polyneuropathy showing higher expressivity in usual focal compression places whose specificity allows differential diagnosis with other polyneuropathies [11]. However, we remark the possible need to accomplish evolutionary controls in those cases with early symptoms, since the specific electroneurographic pattern might appear at later stages of the disease, as it occurred in this patient. On the other hand, molecular analysis of the patient and his relatives confirmed the PMP22 gene deletion usually associated to HNPP although there are some cases with point mutation on the same gene [2-4,12]. When neurophysiological and, specially, molecular studies are decisive, as in this case, the sural nerve biopsy (which helps detect focal myelin thickening or tomaculas, characteristic of this pathology) can be avoided [10,13].

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