CHRONIC INFLAMMATORY DEMYELINATING POLYNEUROPATHY IN

DIABETIC PATIENT WITH SYPHILIS

**JUAN MANUEL DUARTE1, FEDERICO RODRÍGUEZ CAIROLI1, IGNACIO SAGUIER PADILLA1,**

**SILVIA G. RAMOS2, RICARDO E. BARCIA1, CECILIA E. ARÉVALO1**

1*Sixth Chair of Internal Medicine, Hospital de Clínicas José de San Martín, University of Buenos Aires,* 2*Immunology Laboratory, Immunology and Histocompatibility Unit, Hospital Carlos G. Durand, Buenos Aires, Argentina*

Pain is a cardinal manifestation of diabetic neuropathy. Neuropathy induced by diabetes mellitus treatment is acute, and appears in patients undergoing rapid glycaemic control1. Pain is rarely considered as a presenting symptom of chronic inflammatory demyelinating polyneuropathy (CIDP)2.

We present the case of a patient with diabetes mellitus (DM) who consulted for painful neuropathy.

**Clinical case**

A 54-year-old woman with a history of type II DM, diagnosed in February 2016, with glycosylated haemoglobin (HbA1c) values of 9.2%. After the initiation of insulin treatment, the glycosylated haemoglobin values were reduced to 6.5% over two months. In this context, she began to experience pain and allodynia of all four limbs which caused her difficulty walking, which is why she consulted at our institution.

|  |  |
| --- | --- |
| Upon admission to the inpatient ward, she was lucid and haemodynamically compensated. Pupils were isochoric and photomotor and consensual reflexes were normal. She reported pain of 10/10 intensity and allodynia in all four limbs, at proximal and distal levels. Muscle strength was reduced (4/5, *Medical Research Council* muscle strengthscale) in the proximal muscles. Bilateral patella and achilles areflexia were confirmed. No alterations of vibratory sensitivity or sensitivity evaluated with the monofilament were found.  An electrophysiological study was indicated, which showed demyelinating sensory and motor polyneuropathy (Table 1). The laboratory data upon admission showed slight hypercholesterolaemia (235 mg/dl, desirable up to 200), an increase in LDL cholesterol (146 mg/dl, desirable up to 100) and serum triglycerides (308 mg/dl, desirable up to 150). Given these symptoms, treatment with intravenous human immunoglobulin was indicated at a dose of 2 grams/kg of weight to occur in 5 days, obtaining complete reversal of symptoms at the end of treatment. Prior to discharge, positive serum VDRL and FTA-ABS (fluorescent treponemal antibody absorption) results were received, and thus a lumbar puncture was performed, the results of which were: glycorrhachia 66 mg/100 ml, CSF protein concentration 60 mg/100 ml, chlorides 129 mEq/l, cells 1/mm3 mononuclear[[1]](#footnote-1), few red blood cells, dark field, spirochaetes were not observed, VDRL in cerebrospinal fluid negative. With these results, neurosyphilis was ruled out. It should be noted that this study was carried out after the resolution of symptoms following immunomodulatory treatment. Treatment with two doses of intramuscular benzathine penicillin was indicated, with a series of serological controls with VDRL negativity. Four months later she had a relapse of the painful symptoms of all four limbs with an intensity of 9/10, without associated weakness, but with difficulty walking. The symptoms reversed completely after another treatment with intravenous immunoglobulins, at a dosage of 2 grams/kg of weight. Thirty days after hospital discharge, the dosage of antiganglioside antibodies was requested from another institution, the results of which were: anti-GM1, anti-asialo GM1, anti- GD1a and | anti-GD1b weak positive in enzyme-linked immunosorbent assay (ELISA) (Table 2). The patient continues to have outpatient controls under treatment with insulin and 600 mg thioctic acid.  **Discussion**  The patient consulted for predominantly painful symptoms, with allodynia, characteristic of small fibre neuropathy3, which coincided with the improvement in glycosylated haemoglobin values due to insulin treatment. The symptoms, at first, could be interpreted as neuropathy secondary to the treatment of diabetes, previously called insulin neuritis, described by Caravani in 19334. It can occur in patients with type I or type II DM treated with insulin, oral hypoglycaemic drugs or, in rare cases, in the context of strict dietary restrictions that cause a rapid improvement in the metabolic control of patients with a long history of hyperglycaemia5. The treatment of this consists of symptomatic management, with a gradual improvement over time6.  However, the patient's electrophysiological examination was compatible with demyelinating sensory and motor neuropathy. Taking into account the course of syndromic evolution and the clinical and electrophysiological criteria proposed by the European Federation of Neurological Societies and the Peripheral Nerve Society, the symptoms were interpreted as an atypical variant of chronic inflammatory demyelinating polyneuropathy (CIDP): absence of F waves in three nerves, significant reduction of conduction velocity in four nerves, developing over more than two months; the atypical manifestation corresponds to the presence of pain as a cardinal symptom7,8. With the immunomodulatory treatment, a rapid reversal of symptoms was obtained, with a relapse four months later and a new response after the administration of intravenous immunoglobulins. Classic distal diabetic polyneuropathy results from axonal loss due to the microangiopathy of the *vasa nervorum*, |

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| TABLE 1.-  *Electrophysiological study: Values of motor and sensory nerve conduction* | | | | |
|  | Distal latency | Amplitude | Conduction velocity | F wave  Latency |
|  | (msec) | (mV) | (m/sec) | (msec) |
| Right EPS | 5.7 (< 5) | 2.5 (> 3) | 24 (> 41) | Absent |
| Left EPS | 6.2 (< 5) | 1 (> 3) | 27 (> 41) | Absent |
| Left IPS | 6.6 (< 5) | 1 (> 3) | 28 (> 41) | Absent |
| Right Cub | 3.3 (< 3.1) | 2 (> 7) | 29 (< 31) |  |
| Right Med | 5.6 (< 4.1) | 2 (6) | 46 (< 31) |  |
| Right Cub (sensory) | 4.2 (< 3.5) | 0.5 (> 10) | 33 (> 50) |  |
|  |  |  |  |  |

*Parameters of demyelination are highlighted*

*EPS: External popliteal sciatic; IPS: Internal popliteal sciatic; Cub: Cubital; Med: Median*

*In brackets, reference values for the neurophysiology laboratory*

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| TABLE 2.-  *Result of the dosage of antiganglioside antibodies*   |  |  |  | | --- | --- | --- | | Antibody | Results | Reference value | |  |  |  | | a-GM1 IgM/IgG | 35% | < 20%: negative | |  |  | 20-50%: weak positive | |  |  | > 50%: positive | |  |  | > 150%: strong positive | | a-GM2 IgM/IgG | 14% | < 20%: negative | |  |  | 20-50%: weak positive | |  |  | > 50%: positive | |  |  | > 150%: strong positive | | a-aGM1 IgM/IgG | 40% | < 20%: negative | |  |  | 20-50%: weak positive | |  |  | > 50%: positive | |  |  | > 150%: strong positive | | a-GD1a (IgM/IgG) | 33% | < 20%: negative | |  |  | 20-50%: weak positive | |  |  | > 50%: positive | |  |  | > 150%: strong positive | | a-GD1b (IgM/IgG) | 39% | < 20%: negative | |  |  | 20-50%: weak positive | |  |  | > 50%: positive | |  |  | > 150%: strong positive | | a-GQ1b (IgM/IgG) | 2% | < 20%: negative | |  |  | 20-50%: weak positive | |  |  | > 50%: positive | |  |  | > 150%: strong positive | | a-MAG (IgM) | < 1000 BTU | 0-1000 BTU |   *BTU: Bühlmann titre units*  axonal oedema, deterioration of axonal transportation and deterioration of the myelin sheath9: demonstration of primary axonal damage through electrophysiology or histology is more indicative of diabetic neuropathy. Lotan et al. proposed a score by adding the diagnostic criteria of CIDP in patients with DM: in this case, the course of development of less than six months, proximal motor involvement, involvement of the upper limbs, good metabolic control, as well as more of the electrophysiological signs mentioned previously. The total score was 11 points, with definitive diagnostic criteria of CIDP in a patient with DM10.  Obtaining, after immunomodulatory treatment, a positive VDRL result in serum, confirmed with FTA-ABS, forced us to check for neurosyphilis, which was not demonstrated after analysis of the cerebrospinal fluid. The improvement of the neurological symptoms after administration of intravenous immunoglobulins, prior to the diagnosis of syphilis, should be noted. We found in the literature the report of a case of CIDP secondary to neurosyphilis that was reversed with intravenous penicillin: in that case, | the presence of the infectious agent was demonstrated in the cerebrospinal fluid11.  Pain as a form of CIDP presentation is rare. In a retrospective study of 27 patients, Boukhris et al. described five of them whose clinical presentation was pain: in four it was radicular, and in the rest, allodynia and distal paresthesias1. Topa et al. described the case of a 54-year-old man with type II DM treated with oral hypoglycaemic agents who consulted for burning pain and allodynia in the lower limbs and autonomic symptoms developing over three months, in which CIDP was diagnosed, with improvement after immunomodulatory treatment12.  The link between CIDP and DM is controversial: there are authors who did not demonstrate an epidemiological association between CIDP and DM13; however, other studies suggest that the prevalence of CIDP tends to be higher in patients with DM14.  The presence of autoantibodies has not been considered a useful marker in classic CIDP; however, certain antiganglioside antibodies have been associated with some subtypes of CIDP 14. The weak positive results of the anti-GM1, anti-asialo GM1, anti-GD1a and anti-GD1b antibodies in this case could be correlated with the variant described.  In conclusion, CIDP can be a form of presentation of small fibre sensory neuropathy. We present the case of a patient with type II DM and CIDP, and we consider the different differential diagnoses.    **Conflict of interests**: None to declare |

1. It appears this way in the Spanish, but I presume it should say “mononuclear cells 1/mm3”  [↑](#footnote-ref-1)