CASE REPORT

AN UNUSUAL NEUROPATHY IN A DIABETIC PATIENT: EVIDENCE FOR INTRAVENOUS IMMUNOGLOBIN-INDUCED EFFECTIVE THERAPY

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SUMMARY - We report the case of a 68-year old type-2 diabetic male patient who was admitted to hospital for progressive weakness in the right lower limb. Although his metabolic control was good, he lost more than 20 kg of weight. Despite intensive physio- and vitaminotherapy, his neurological condition kept on degrading with a severe amyotrophy and pain of the right thigh. He was unable to walk and to stand alone. Besides a yet known sensitive polyneuropathy, the electro-physiological study revealed an obvious motor involvement with signs of demyelination and axonal degeneration. Combined with the albuminocytologic dissociation observed in the cerebrospinal fluid, these specific clinical and electrophysiological features led us to postulate a diagnosis of inflammatory neuropathy. The patient underwent a treatment by methylprednisolone and immunoglobins that rapidly induced a striking improvement of his neurological condition.

This case report illustrates that rare forms of neuropathy such as inflammatory neuropathies close to chronic inflammatory demyelinating polyneuropathy (CIDP) can occur in diabetic patients and superimpose on the more commonly described forms of neuropathies. It recalls the importance of recognizing CIDP-like neuropathies because unlike other forms of neuropathy, inflammatory neuropathies are perfectly curable.

Key-words: diabetic neuropathy, Chronic Inflammatory Demyelinating, polyradiculoneuropathy (CIDP), immunoglobulins, corticosteroids.

RÉSUMÉ - Un cas inhabituel de neuropathie chez un patient diabétique traité efficacement par administration intraveineuse d’immunoglobulines.

Nous rapportons le cas d’un patient diabétique de 68 ans admis en clinique pour altération de l’état général, faiblesse progressive du membre inférieur droit et perte pondérale de plus de 20 kg. Le patient fut dans un premier temps traité par physiothérapie intensive et vitamines B pour ce qui fut considéré initialement comme une mononévrite diabétique. Cependant, son état neurologique continua de s’aggraver avec apparition d’une amyotrophie douloureuse de la cuisse droite. L’analyse par électrophysiologie révélait une atteinte motrice sévère s’accompagnant de signes de démyélinisation et de dégénérescence axonale, en plus d’une atteinte sensitive déjà connue. Un diagnostic de neuropathie inflammatoire fut posé sur la base de la convergence de la symptomatologie clinique, de l’atteinte motrice détectée par électrophysiologie, et d’une dissociation albuminocytologique observée dans le liquide céphalo-rachidien.

Nous avons noté une amélioration franche des paramètres cliniques et électrophysiologiques de ce patient rapidement après qu’une corticothérapie suivie par l’administration intraveineuse d’immunoglobulines fut initiée.

Ce cas clinique rappelle que des formes rares de neuropathie inflammatoire proche de la polyradiculonévrite inflammatoire chronique (syndrome de Guillain-Barré chronique) peuvent survenir chez les patients diabétiques et qu’il convient de les distinguer de l’atteinte sensitive communément décrite. Il insiste sur l’importance de les reconnaître, puisqu’à l’inverse d’autres formes de neuropathie, les neuropathies inflammatoires peuvent bénéficier d’un traitement efficace.

Mots-clés : neuropathie diabétique, polyradiculonévrite chronique inflammatoire, immunoglobulines, corticostéroïdes.
Neuropathy is a common complication of diabetes that already affects 7% to 8% of patients at the time of diagnosis, but up to 50% of them after 25 years of evolution [1]. It can be roughly split into three major categories including symmetrical polyneuropathy, mononeuropathy and autonomic neuropathy [2]. Peripheral polyneuropathy is usually considered as the most common form of diabetic neuropathy. It is predominantly sensory with minor motor involvement and its distribution is usually symmetrical. Neuropathic symptoms (stabbing or burning pain, hyperpathia and hyperaesthesia) can be excruciating and distressing. The Diabetes Control and Complications (DCCT) trial clearly pointed out the benefit of improved blood glucose control on diabetic neuropathy [3]. Nevertheless, beside attempts to achieve tight regulation of blood glucose, there is no specific effective treatment for diabetic neuropathy. This can be highly frustrating for patients and physicians, because once set up, the distal polyneuropathy is irreversible.

In some cases though, diabetic patients can develop progressive disabling neuropathy characterized by a prominent motor involvement. Hence, as lately suggested by recent publications, when the course of neuropathy is asymmetrical, subacute rather than chronic and leads to muscular weakness, an inflammatory aetiology, for instance close to chronic inflammatory demyelinating polyneuropathy (CIDP), might be considered [4-9]. It is of cardinal importance to clearly identify this entity because unlike the common sensitive diabetic neuropathy, inflammatory neuropathies are often curable [4, 10-12].

■ CASE REPORT

A 68-year old male patient was hospitalized for progressive weakness in the right lower limb for 3 weeks, with reduced flexion from the leg to the thigh. The patient was not complaining of pain or paresthesia, there was no sign of any kind of trauma, but he could walk only on crutches. He lost more than 20 kg of weight during the last six months. This patient was diagnosed for type-2 diabetes six months earlier (HbA1c: 13%; nl.: 3.9-6.7%). He was at this time hospitalized for a surgical treatment of a right knee anthrax from which he completely recovered. The diabetes was complicated with macroangiopathy (myocardial infarction) and asymptomatic sensitive polyneuropathy. Blood glucose had been quickly controlled by intensive insulin therapy followed by two daily injections of mixed insulin (30/70) along with biguanides. Until his admission, this patient was re-daily injections of mixed insulin (30/70) along with

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nengered the patient to get a tighter control of blood

glucose and we prescribed intensive physio- and vita-

min therapy. The patient then left the hospital for a

month.

He came back thereafter for control in the outpatient clinic. His general condition deeply worsened. He was confused. He kept loosing weight and couldn’t walk anymore. The previously observed crural amyotrophy aggravated with a painful tumescence on the right thigh.

Positive tendon reflexes were present on the left lower limb but absent on the right side. Ankle jerks were absent on both sides. There was a bilateral flexion plantar response. Laboratory tests showed an increased sedimentation rate value: 75 mm/h (< 8 mm/h), as well as CRP: 1.8 mg/dl (< 0.8 mg/dl) that normalized 5 days later, and microalbuminuria: 224.6 mg/g creatinine (< 20 mg/g). Other biological parameters were either normal or non relevant to the case.

Doppler ultrasound study of the neck vessels described severe carotid atheromatosis and cerebral CT-scan showed cortico-subcortical atrophy and leucomacia but no picture suggestive of stroke. The electromyographic study confirmed a yet known sensitive neuropathy but also a significant reduction in motor nerve conduction velocity in peroneal and tibial nerves (< 40 m/s). At this stage of investigation, we concluded for a diabetic mononeuropathy. We challenged the patient to get a tighter control of blood glucose and we prescribed intensive physio- and vitamin therapy. The patient then left the hospital for a month.

The patient underwent a new electromyographic study, as well as a lumbar puncture. The severe motor involvement was confirmed by the markedly slowed motor conduction velocity consistent with a demyelinating process. There was also electromyographical evidence for axonal degeneration as illustrated by the increased number of fibrillations with reduced recruitment and positive sharp waves. Cerebrospinal fluid showed an increased protein level: 1.06 g/l (0.19-0.4 g/l), without white blood cell count. Altogether, these data led us to postulate a diagnosis of inflamma-
tory neuropathy that required a treatment by cortico-
teroid and IV immunoglobins.

The treatment started with intravenous (IV) meth-
ylprednisolone (3 doses of 1 gr. over 3 days) which
already made the patient getting better. He thereafer
received once an IV treatment of immunoglobins
(0.4 g/Kg) over a 5 day period. Improvement was im-
mediate. Less than two weeks after the onset of treat-
ment, the patient was clearly autonomous and able to
walk alone with crutches. He benefited from an intensive
physiotherapy. He completely recovered and has
been reported to be in good condition more than a
year later.

**DISCUSSION**

As recently suggested by several authors, this diag-
osis of inflammatory neuropathy might be evoked in
a diabetic patient when motor symptoms are predomi-
nant and more severe than expected. It is essential to
identify this entity which can superimpose on the com-
mon diabetic neuropathy, because unlike other causes
of neuropathy, inflammatory neuropathy is quite often curable (Table I). Krendel et al. described two categories of progressive inflammatory neuropathy that respond to anti-inflammatory and/or anti-immune treatments [4]. As for our patient, the
first one mostly occurs in type-2 diabetic patients
along with pain, atrophy of one thigh and weight loss.
In contrast to the non inflammatory vascular disease
that accounts for acute mononeuropathy, it corre-
sponds to a multifocal axonal neuropathy caused by
inflammatory microvasculopathy with collections of
lymphocytes around small vessels. The second cat-
egory is related to chronic inflammatory demyelinat-
ing polyneuropathy (CIDP), an acquired autoimmune
disorder of the peripheral nervous system character-
ized by a more symmetric and distal distribution of the
lesions. It mostly occurs in type-1 diabetic patients
without weight loss. Segmental demyelination and re-
myelination, onion bulb formations, and infiltration by
mononuclear cells of the endoneurium are hallmarks
of this CIDP-like neuropathy [4, 5, 7, 9].

Both forms of inflammatory neuropathies exhibit
electrophysiological criteria for demyelination pro-
cesses such as slow conduction velocity, prolonged
distal latencies, conduction block, as well as for den-
ervation activity (fibrillations and positive sharp
waves) [7]. The CSF analysis reveals a typical profile
with increased protein content without rise of cell
counts [4, 5, 7]. Although nerve biopsy can be helpful
to rule out other etiologies such as amyloidosis, vas-
culitis and toxic neuropathies, it is not fully required
in cases of typical inflammatory neuropathy. Indeed,
axonal loss, presence of onions bulbs, regenerative

| TABLE I. Differential diagnostic of neuropathies in diabetic patients (see text for details). |
| Mode of Presentation | Distal Polyneuropathy | Focal/Multifocal Neuropathies | Inflammatory Neuropathies |
| Distribution | Insidious/Chronic | Acute | Progressive onset/Subacute |
| Metabolic Control | Symmetric/Distal | Cranial/Thoraco-abdominal/Limb nerves | Mostly asymmetrical and proximal |
| Accompanying Symptoms | Poor | Poor | can be good |
| Electrophysiological Features | Autonomic neuropathy | Diabetic amyotrophy | Category 1: Weight loss (+)* Category 2: Weight loss (−) IDDM |
| Etiopathogenesis | Sensory involvement | Motor involvement | Motor involvement |
| Treatment/Efficacy | Ischemic/Metabolic Distal axonopathy of dying-back type | Ischemic disease of vasa nervorum Vascular occlusion | Immunmediated inflammatory disorder Category 1: Inflammatory vasculopathy Category 2: Demyelinating neuropathy |
| Outcome | Vitamin and physiotherapy(−) | Tighter metabolic control and physiotherapy(+) | Immunotherapy(++++) |

* Krendel et al. 1996
clusters and wallerian degeneration can also be observed in other forms of diabetic neuropathies [5, 7]. In contrast, clinical improvement after antinflammatory treatment or immunotherapy is considered as an important criterion to confirm the diagnosis of inflammatory neuropathy versus other forms of neuropathy. Uncini et al. even suggested that in doubtful cases, a therapeutic trial with one of the established treatments for CIDP (plasma exchange, IV immunoglobins, steroids) should be used to help defining the diagnosis [7].

Idiopathic CIDP most often occurs alone but may accompany plasma cell dyscrasias, virus infection, connective tissue diseases, neoplasia and others diseases, such as diabetes [12, 13]. Of interest is the recent study by Gorson et al. who showed that diabetic patients with CIDP have clinical features similar to those with idiopathic CIDP [9]. However, their nerve conduction studies and nerve biopsies show more severe axonal loss and the degree of improvement following treatment is less favorable. In our case though, the clinical improvement after steroid and immunotherapy was immediate. Noteworthy was the observation of a reactivation of EBV infection. Although the link between EBV infection and CIDP has not yet been clearly established, EBV is a known precipitant for the acute form of demyelinating polyneuropathy (AIDP or Guillain-Barré syndrome) [14]. Although clear evidences are lacking, it is tempting in the present case to establish a link between the reactivation of the EBV infection and the onset of the inflammatory neuropathy.

In conclusion, through the presentation of the present case report, we aimed to draw the attention of the community of diabetologists on the importance of identifying inflammatory neuropathies. This diagnosis might be evoked in diabetic patients when the motor involvement is prominent and rapidly evolutive. Therapeutic trials with corticosteroid and/or immunoglobins can be useful to ascertain the diagnosis.

REFERENCES