Focal and Multifocal Diabetic Neuropathy

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SUMMARY

Diabetic neuropathy is currently the most common neuropathy in the world, and it is associated with a wide range of clinical manifestations. The vast majority of patients with clinical diabetic neuropathy have a distal symmetrical form of the disorder that progresses following a fiber-length-dependent pattern, with sensory and autonomic manifestations predominating. Occasionally, patients with diabetes can develop focal and multifocal neuropathies that include cranial nerve involvement and limb and truncal neuropathies. This neuropathic pattern tends to occur after 50 years of age, and mostly in patients with long-standing diabetes mellitus. Length-dependent diabetic polyneuropathy does not show any trend towards improvement, and either relentlessly progresses or remains relatively stable over a number of years. Conversely, the focal diabetic neuropathies, which are often associated with inflammatory vasculopathy on nerve biopsies, remain self-limited, sometimes after a relapsing course. Other causes of neuropathies must be excluded in diabetic patients with focal neuropathies, and treatable causes must always be sought in diabetic patients with disabling motor deficit.

Key Words: Proximal diabetic neuropathy; diabetic ophthalmoplegia; thoracic neuropathy; inflammatory diabetic neuropathy; nerve biopsy.

INTRODUCTION

Diabetic neuropathy is the most common neuropathy in industrialized countries, with a remarkable range of clinical manifestations. More than 80% of the patients with clinical diabetic neuropathy have a distal symmetrical form, with predominant or isolated sensory and autonomic manifestations (1,2). In the others, and usually in association with symptomatic or latent distal symmetrical sensory polyneuropathy, patients with diabetes might develop a focal neuropathy that includes cranial nerve involvement, limb and truncal neuropathies, and proximal diabetic neuropathy (PDN) of the lower limbs. In this group of neuropathies the disorder tends to occur both in men and women more than 50 years of age, most with longstanding type 1 and type 2 diabetes. The long-term prognosis of focal neuropathy is good in most cases, but sequelae occur. The occurrence of focal neuropathy in patients with diabetes requires first to exclude a nerve lesion owing to a superimposed cause by appropriate investigations. Then, to consider the occurrence of nondiabetic neuropathies more common...
in patients with diabetes, before concluding that the patient is suffering from a focal diabetic neuropathy and discussing which treatment, if any, is needed in addition to control of diabetes.

**CRANIAL DIABETIC NEUROPATHY**

Oculomotor nerve palsies are the most common if not the only cranial neuropathy observed in patients with diabetes.

**Historical Background**

Ogle in 1866, was the first author to mention the occurrence of diabetic ophthalmoplegia (3). In 1905, Dieulafoy published a series of 58 personal cases, in which most of the clinical characteristics of diabetic ophthalmoplegia were described (4). In 1935, Waite and Beetham (5) performed the first epidemiological study on the subject in which they compared the occurrence of oculomotor palsy in 2002 diabetic patients with 457 patients without diabetes. A series of other clinical reports have refined our knowledge on the subject but pathological studies remain scanty with only a few autopsy cases studied (6–8) and the pathophysiology of oculomotor palsies in patients with diabetes remains a matter of discussion.

**Epidemiology**

Such as focal neuropathy observed in other sites of the body, diabetic ophthalmoplegia is uncommon in diabetic patients. In 1933, Gray (9) observed two patients with ophthalmoplegia among 500 diabetic patients examined and Waite and Beetham (5,10) estimated the incidence of oculomotor palsy among patients with diabetes to be 0.8–1.8%. It is interesting to note that in this study, the frequency of oculomotor palsy was 0.8% in patients of less than 45 years of age, against 2.1% after 45 years.

Frequency of involvement of the different oculomotor nerves: the sixth and the third cranial nerves are most commonly affected. In a series of 58 cases of diabetic ophthalmoplegia, Dieulafoy (4) reported 35 cases of sixth nerve palsy, 12 cases of third nerve palsy, five cases of fourth nerve palsy, and six cases of external ophthalmoplegia. The sixth cranial nerve was more often affected than the third one in two series (5,11). Conversely, in other series the third nerve is predominantly affected as the 14 patients reported by Weinstein and Dolger (12), included seven cases of third nerve palsy, six of sixth nerve involvement, and one with simultaneous involvement of both nerves. In an analysis of 811 cases of oculomotor palsies, diabetes accounted for 2.6% of third nerve palsy, 1.9% of sixth nerve palsy, and 0.6% of fourth nerve palsy (13). Finally, in Zorrilla and Kozak’s series of 24 cases, 17 patients had an involvement of the third nerve, including two bilaterally, and seven cases of sixth nerve palsy, but no fourth nerve involvement (14).

**Clinical Manifestations**

In virtually all cases diabetic ophthalmoplegia occurs in patients with diabetes with more than 50 years of age, both in type 1 and type 2 diabetes. Rare cases have been reported in younger patients or even in children (15). The onset is rapid, within a day or two. In many cases, the patient experiences pains a few hours to a few days before noticing diplopia. Pain thus preceded the onset of diplopia in 14 out of the 25 patients