Current Concepts in Diabetic Neuropathy

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Abstract

Diabetic neuropathies are classified, for the sake of convenience, into four groups. First are the distal symmetrical variety that may be predominantly motor or predominantly sensory. Second are the mononeuropathy syndromes of cranial or somatic nerves. Third are the automatic group and finally, any combination of two or three varieties. Etiopathology of these neuropathic syndromes takes into consideration the biochemical alterations and ischemic changes. The most recent understanding of the role of aldose reductase in the polyol pathway is presented briefly, as is, in the hyperglycemic state, sorbitol accumulation, which results in the decrease of ATPase activity and slowing of nerve conduction. In the treatment of diabetic neuropathies, aldose reductase inhibitors are being used in many centers and their release for general use is anxiously awaited.

Key words: Diabetic neuropathy, aldose reductase, sorbitol, aldose-reductase inhibitors

Diabetic neuropathy is a fairly common condition and has been recognized for more than a century. Our understanding of its causation, however, is still incomplete. Nevertheless, recent biochemical advances seem promising and are very likely to influence our approach to the treatment of this condition.

Since there are many neuropathy syndromes associated with diabetes mellitus, it is more appropriate to speak of "diabetic neuropathies" rather than neuropathy. In considering the association of these two conditions, it should be recognized that the neuropathy may sometimes make its clinical appearance even before diabetes manifests itself. This raises the question of whether neuropathy is a part of diabetes or a complication thereof.

There are many ways to classify diabetic neuropathies. The following grouping of these conditions is given only for convenience of discussion:

I) Distal symmetrical polyneuropathy (sensorimotor)
   a) Painful type: predominantly sensory, generally affecting the lower extremities.
   b) Painless type: predominantly motor, generally affecting the distal parts of the extremities.

II) Mononeuropathy syndromes
   a) Mononeuropathy (any somatic nerve, eg, median, femoral or peroneal)
   b) Cranial mononeuropathy (eg, 3rd, 4th, or 6th nerves)
   c) Mononeuropathy multiplex.
   d) Proximal mononeuropathy (Diabetic amyotrophy)

III) Autonomic neuropathy
   There are many autonomic neuropathy syndromes. The following list is by no means complete.
   a) Gastro-intestinal
      1) Esophageal dysfunction
      2) Gastro-paresis
      3) Diabetic diarrhea
   b) Genito-urinary
      1) Cysto-paresis [with overflow incontinence]
      2) Male impotence
   c) Cardiovascular
      1) Postural hypotension
      2) Arrhythmias

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Clinical Features

It is not our purpose to review the clinical features of all the the conditions mentioned above except to mention some of the less common or less well understood conditions. Numbness, neuritic pain and dysesthesias are easily recognized.

A mononeuropathic syndrome is frequently heralded by pain and paresthesia; the important thing to remember is that the prognosis is uniformly good, although recovery may take two years or more. Thoracic neuropathy or radiculopathy presents with acute chest pain or upper abdominal pain. Its early recognition may prevent an unnecessary surgical procedure. Truncal polyneuropathy and polyradiculopathy have also been described in diabetics.

Diabetic amyotrophy is the term applied to the syndrome of acute onset of pain and weakness in one or both lower extremities, especially the thigh muscles such as the quadriceps and psoas. Rapid wasting develops in the quadriceps and sometimes other muscles such as the glutei, hamstrings, etc. There is gradual recovery over a period of one to two years. The facts that (1) Hugh Garland described this syndrome first as diabetic myelopathy, later corrected to amyotrophy, and that (2) the clinical findings of these patients are not limited to the muscles supplied by the femoral nerves has resulted in multiple names. These include "symmetrical proximal motor neuropathies", "femoral neuropathy" etc. This also illustrates the difficulty in placing this syndrome in the usual classification. The exact pathology of this particular condition is not understood.

Diabetic neuropathic cachexia is the condition applied to the syndrome of acute onset of pain and weakness in one or both lower extremities, especially the thigh muscles such as the quadriceps and psoas. Rapid wasting develops in the quadriceps and sometimes other muscles such as the glutei, hamstrings, etc. There is gradual recovery over a period of one to two years. The facts that (1) Hugh Garland described this syndrome first as diabetic myelopathy, later corrected to amyotrophy, and that (2) the clinical findings of these patients are not limited to the muscles supplied by the femoral nerves has resulted in multiple names. These include "symmetrical proximal motor neuropathies", "femoral neuropathy" etc. This also illustrates the difficulty in placing this syndrome in the usual classification. The exact pathology of this particular condition is not understood.

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This result in an accumulation of sorbitol and fructose, which in turn decreases myoinositol; hence, activity of sodium-potassium-ATPase is decreased. Required energy consumption in the nerve fiber is reduced with a resultant decrease in the nerve conduction velocity.23

Involvement of vasa nervorum due to diabetic microangiopathy23 producing ischemia will decrease the turnover of myelin and slow down the axonal transport system.24 It is conceivable that all these factors, singly or in combination, acting over a long period of time may result in structural damage to the nerves in diabetics.

Treatment

From the above description, it seems plausible that reducing the activity of aldose-reductase may improve or prevent neuropathy in diabetics.27 During the last five years, various diabetic centers have attempted trials of aldose-reductase inhibitors, both experimentally and in patients with diabetic neuropathy. Although the results have not been uniformly impressive, this line of treatment appears to have clear promise for the control of diabetic neuropathy in the future.

Treatment of painful neuropathy with drugs such as diphenyl hydantoin and carbamazepine is well established. Anti-depressive medications, such as amitriptyline alone or in combination with a phenothiazine, have been used more recently for the control of pain.28,29 As far as the use of narcotic analgesics is concerned, caution should be exercised as these conditions generally have good prognosis. We anxiously wait for the release of aldose-reductase inhibitors such as sorbinil or tolrestat for the treatment of diabetic neuropathy.

References


