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Describe the Various Types of Neuropathy Observed in Patients with Diabetes

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Introduction- The most widely recognized neuropathic syndrome found in individuals with diabetes is diabetic peripheral neuropathy. Diabetes is the commonest reason for neuropathy around the world, creating an extensive range of disorders including diverse forms of nerves and pathological mechanisms such as ischemic, metabolic, compressive and immunologic.[12] There are different forms of diabetic neuropathies (diffuse or focal) which present with various clinical sign and influencing distinctive parts of the nervous system. The common forms of neuropathies are autonomic neuropathies and chronic sensorimotor distal symmetric polyneuropathy (DPN). Diagnosis of DPN is reached by excluding other disorder that exhibits the same signs.[3] Approximately, 8% of general population suffer from long standing pain are caused by the neuropathic pain.[4] Around 50% of chronic diabetics' individuals (more than 25 years) will develop neuropathy which affect their daily living.[5] Hyperglycaemia is the chief reason of advancement of all neuropathies, counting PDN. The Diabetes Control and Complications Trial (DCCT) demonstrated that good glycaemic control will lessen the occurrence of neuropathy up to 60%.[6]

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Describe the Various Types of Neuropathy Observed in Patients with Diabetes

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I. Introduction

The most widely recognized neuropathic syndrome found in individuals with diabetes is diabetic peripheral neuropathy. Diabetes is the commonest reason for neuropathy around the world, creating an extensive range of disorders including diverse forms of nerves and pathological mechanisms such as ischemic, metabolic, compressive and immunologic.[12] There are different forms of diabetic neuropathies (diffuse or focal) which present with various clinical sign and influencing distinctive parts of the nervous system. The common forms of neuropathies are autonomic neuropathies and chronic sensorimotor distal symmetric polyneuropathy (DPN). Diagnosis of DPN is reached by excluding other disorder that exhibits the same signs.[3] Approximately, 8% of general population suffer from long standing pain are caused by the neuropathic pain.[4] Around 50% of chronic diabetics' individuals (more than 25 years) will develop neuropathy which affect their daily living.[5] Hyperglycaemia is the chief reason of advancement of all neuropathies, counting PDN. The Diabetes Control and Complications Trial (DCCT) demonstrated that good glycaemic control will lessen the occurrence of neuropathy up to 60%.[6]

II. Signs and Symptoms of Neuropathy

The pain accompanying with PDN is often refer to as numbness, tingling pain, or augmented due to touch. It may also be labelled as electrical, burning, or stabbing with paraesthesia, deep aching and hyperesthesia. The pain is classically more at night-time. PDN characteristically progresses in the lower legs and feet. Allodynia (excruciating sensations to mild stimuli) and hyperalgesia (augmented sensitivity to painful sensations) may also develop.[78]

Warning sign of nerve impairment may comprise:[9]

- Tingling and numbness, or pain in the toes, arms, legs feet and hands
- hands and feet muscle wasting
- Nausea, or vomiting
- Constipation or diarrhoea
- Faintness or dizziness due to postural hypotension
- Urinary problems
- Erectile dysfunction in men or vaginal dryness in women
- weakness

Approximately, 20% of all diabetic persons and about a third of individuals with DPN are suffer from painful symptoms like tingling, burning (paraesthesia or 'pins and needles'), shooting or stabbing.[1011]

III. Diabetic Peripheral Neuropathy Pathophysiology

The diabetic peripheral neuropathy pathophysiology still not fully understood. A few studies have shown that the ideal way to avert or deferral diabetic peripheral neuropathy is a close control of glycaemia.[12] Numerous theories of pathogenesis have been distinguished in the aetiology of DN such as: [13]

- Oxidative-nitrosative stress
- Neuroinflammation
- Mitochondrial dysfunction
- Bioenergetic crisis
- Axon-glia interactions
- Demyelination

Some recent studies have demonstrated that nearly 30% of diabetic patients are influenced by distal symmetric polyneuropathy. In T1DM patient, the EURODIAB prospective complications study found a prevalence rate of 28% for distal symmetrical polyneuropathy.[14]

Theories concerning the numerous aetiologies of diabetic neuropathy comprise:[15]

- Nerve fibers injury by metabolic disorder.
- Insufficiency of nerve and blood vessels
- Impaired autoimmune
- Deficient of neurohormonal growth factor

Nevertheless, Current studies have demonstrated that both metabolic interactions and vascular factors are included at all steps of DPN.[16]Neuropathic pain mechanisms can be summarized in following table:[17]

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Peripheral mechanisms	Central mechanisms
Alterations in sodium channel distribution and expression Alterations in calcium channel distribution and expression Changed neuropeptide expression Sympathetic sprouting Peripheral sensitization Changed peripheral circulation Axonal atrophy, degeneration or regeneration Small fibres injury Glycaemic flux	Central sensitization Aβ-fibre sprouting into lamina II of the dorsal horn Decreased inhibition via descending pathways

The risk factors of autonomic neuropathy and distal symmetric polyneuropathy:[18]

- Length of diabetes
- High blood glucose
- Arterial hypertension
- Peripheral artery disease (PAD)
- Mönckeberg's medial sclerosis
- Diabetic nephropathy and retinopathy
- Depression
- Truncal obesity
- Hypercholesterolemia
- Nicotine and/or alcohol misuse
- sedentary lifestyle
- Demographic factors (height, age, weight)

IV. Classification of Neuropathy

The different types of diabetic neuropathy (DN) can be grouped as follows:[19]

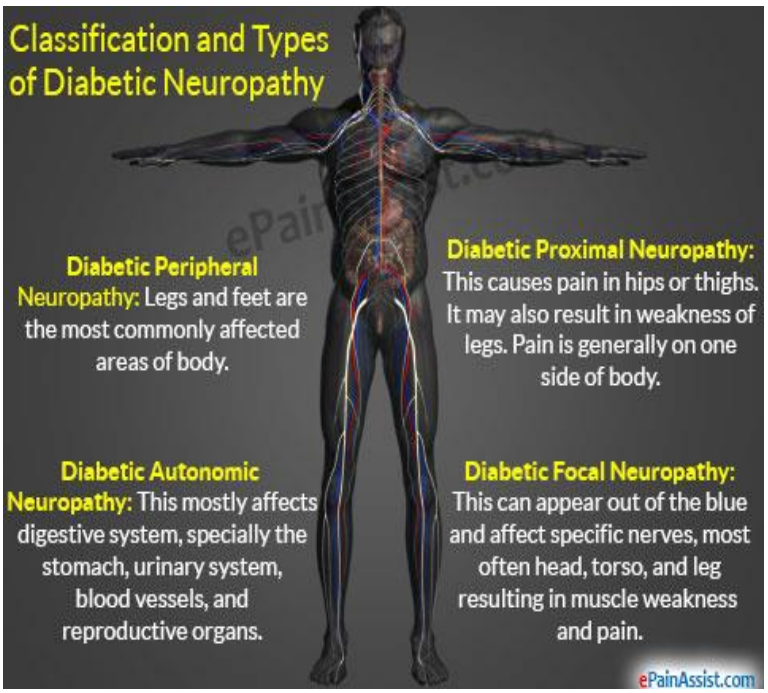
1. Anatomical distribution
   - Proximal or distal
   - Symmetric or asymmetric
   - Focal or multifocal or diffuse
2. Clinical course
   - Acute
   - Sub acute
   - Chronic
3. Characteristic main features
   - Aching or non-aching
   - Sensory
   - Motor, or autonomic
   - Pathophysiology

The most characteristic type of diabetic neuropathy is chronic distal symmetric polyneuropathy which account for around 75% of DNs and it was classified into typical or atypical according to their existence.20

There are four categories of diabetic neuropathy: [7 21]

- Peripheral neuropathy (moreover termed distal polyneuropathy and diabetic nerve pain)
- Proximal neuropathy (also named diabetic amyotrophy) can cause muscle weakness
- Autonomic neuropathy
- Focal neuropathy (also named mononeuropathy) it disturbs one precise nerve

Classification demonstrated in below diagram



Studies have revealed that reasonable intensity walking may not prompt augmented jeopardy of foot ulcers or re ulceration in peripheral neuropathic persons.[22] Autonomic neuropathy is also clearly connected with cardiovascular disease in diabetic's individuals.[23]

Essential Differential Diagnoses includes: [17]

- Medicines (such as cytostatic drugs)
- Toxins, metals(suchas alcohol)
- Kidney disorders
- Deficient Vitamin B (B1, B6, B12)
- Tumours, paraproteinemias
- Infections (such as Lyme disease ,HIV)
- Vasculitides
- Inherited neuropathies
- Endocrine illnesses (acromegaly, hypothyroidism)
- Immune neuropathies
- Impingement syndromes.

Diagnosis by exclusion should be based on laboratory test such as

- (CBC) Complete blood count
- Creatinine
- Vitamin B12
- Erythrocyte sedimentation rate (ESR)
- Alanine aminotransferase (ALAT)
- Thyroid-stimulating hormone (*TSH*)
- Gamma GT
- Folic acid
- immunoelectrophoresis.

V. Treatment for Neuropathic pain: [24]

1st drugs

- Tricyclic antidepressants (nortriptyline, amitriptyline, imipramine)
- Anticonvulsants (pregabalin, carbamazepine, gabapentin)
- SNRIs (venlafaxine, duloxetine)
- Topical Lidocaine

2nd drugs

- Tramadol
- Opioids (fentanyl, morphine)

3rd drugs

- Others anticonvulsants (topiramate, lamotrigine)
- NMDA (N-Methyl-D-aspartate) antagonists (memantine)
- Topical capsaicin
- GABAB (Gamma-aminobutyric acid B) receptor agonists [baclofen]
- SSRI

VI. Conclusion

The exact mechanisms creating DSP are unknown, yet are without a doubt depend on a number of factors and involve pathological changes due to reduced typical levels of blood glucose, the utmost noticeable of which includes augmented creation of free radicals due to hyperglycaemia-stimulated oxidative stress. The main demonstrated management that successfully defers the start or development of DSP is tight glycaemic control. However, DSP sooner or later precede in many diabetic's individuals in spite of good glycaemic control. Diabetes makes persons vulnerable to focal peripheral neuropathies including single nerves and nerve roots. The most recurrently affected cranial nerve is the oculomotor nerve which appears as incomplete oculomotor nerve palsy with pupillary sparing. Moreover, problem such as a unilateral truncal (thoracic) radiculopathy, display with acute abdominal or chest pain. Diabetes also leads to other peripheral nerve entrapments such as, median, ulnar, lateral femoral cutaneous, radial, and plantar nerves.[25]Despite the fact that it stays unsubstantiated whether tight glycaemic control can turn around pre-existing autonomic and peripheral nervous system injury brought on by type 1 diabetes, the sooner we perform intensive treatment, the more successfully we counteract future complications, involving neuropathy.[26]

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