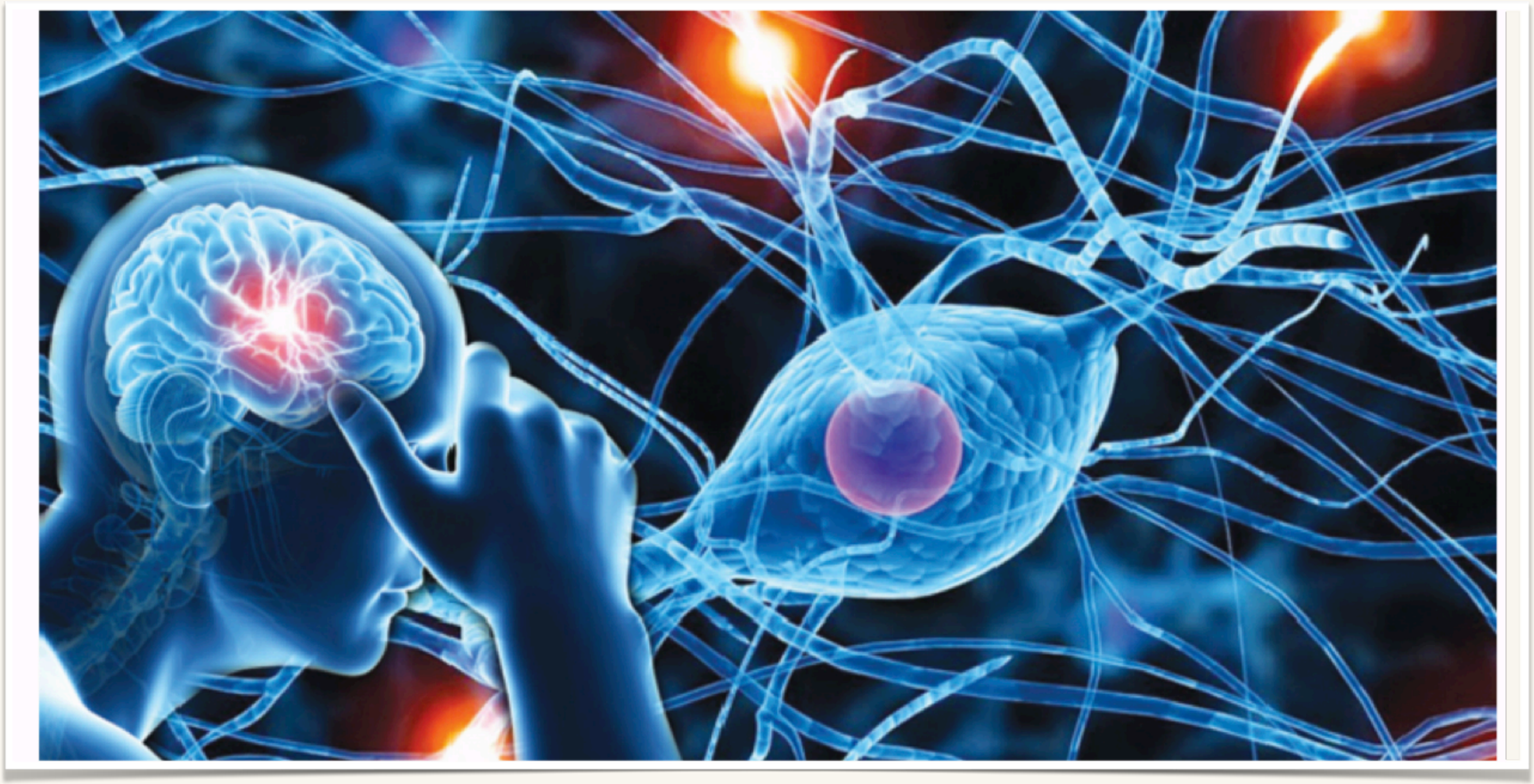

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Diabetes mellitus & the nervous system

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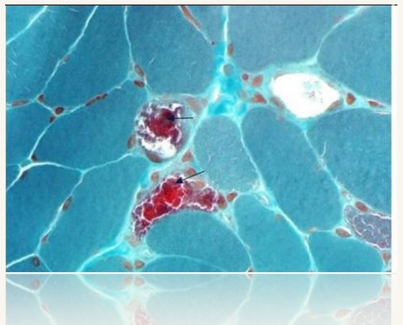
Introduction

A wide variety of disturbances affecting the central and peripheral nervous systems, either directly or indirectly, may be encountered in patients with diabetes mellitus. This short selective review concentrates on recent progress in the delineation of the clinical features of the neurological syndromes related to diabetes and their management. It will deal, sequentially, with the classification of diabetes, a listing of some genetic disorders that may be accompanied by diabetes, the consequences of acute metabolic decompensation, and somatic and autonomic neuropathies, cerebrovascular disease, certain infections that have a particular association with diabetes and, finally, congenital malformations.

Genetic disorder Associated with DM

Genetic disorder

Mitochondrial disorder
MELAS



Mitochondrial related diabetes usually presents at between 30 and 40 years of age and is due more to impaired insulin secretion than insulin resistance.[4] Some patients come to need insulin treatment and some can even develop diabetic ketoacidosis. As well as deafness, other neuromuscular features are sometimes seen in diabetic patients with this mutation: some may have a myopathy (with ragged red fibres) and a group of five patients with insulin induced painful neuropathy has been described with the 3243 mutation.[5] The prevalence of complications seems similar to that among diabetic patients without this mutation, so that meticulous control of diabetes in this condition is just as important as in others.

Diabetes & nervous system

Genetic disorder

FRIEDREICH'S ATAXIA

Friedreich's ataxia is an autosomal recessive spinocerebellar degeneration that has recently been shown to be due to an intronic GAA repeat expansion on chromosome 9q[6] resulting in a defect in its gene product frataxin. The function of frataxin is unknown but there is evidence that it is a mitochondrial protein[7] and that its deficiency leads to abnormal energy metabolism.[8] Between 10% and 20% of patients with Friedreich's ataxia develop diabetes.[9] This always begins after the onset of the neurological symptoms and is insulin dependent. Ketoacidosis may occur

Genetic disorder

WOLFRAM SYNDROME

Wolfram syndrome is a rare recessively inherited form of insulin dependent diabetes (type 1) associated with diabetes insipidus, optic atrophy causing blindness and deafness (hence DID-MOAD syndrome). Although best known as an endocrine disorder, the clinical features are predominantly neurological and include late onset cerebellar ataxia, psychiatric disturbances, anosmia, apnoeic episodes, and startle myoclonus. Its course is one of gradual decline and premature death. The exact genetic defect is not known but there is evidence of linkage to chromosome 4, and evidence for a mitochondrial defect has also been presented.

Acute Metabolic Decompensation

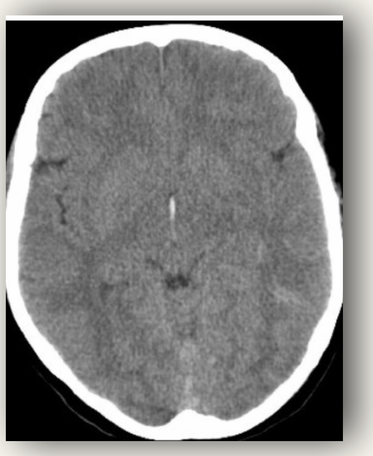
Acute Metabolic Decompensation

Hyperosmolar Encephalopathy

The level of consciousness is related to the degree of hyperosmolality. Patients are not infrequently stuporose, and sometimes unconscious. Focal or generalised seizures sometimes occur and very rarely dystonic movements are witnessed. These neurological features resolve completely when the metabolic state has returned to normal.

Acute Metabolic Decompensation

Cerebral Edema



Cerebral oedema is a well known but rare and potentially fatal complication of diabetic ketoacidosis, which occurs during apparently successful treatment. Children are particularly vulnerable and some 1% to 2% may develop clinically apparent cerebral oedema during treatment. The exact cause is uncertain but electrolyte exchanges in and out of cells with a net influx of sodium into the cells might be responsible.[11] Cerebral oedema usually occurs within 8 to 24 hours after starting treatment with intravenous fluids and insulin. Excessively rapid correction of hyperosmolality or the use of hypotonic saline are thought to be precipitating factors. Patients who have shown every sign of recovery then unexpectedly decline. Those who show clinical signs of raised intracranial pressure or cerebral herniation are unlikely to recover. The use of mannitol or dexamethasone is advocated but evidence of their effectiveness is lacking.

Acute Metabolic Decompensation

Hypoglycaemia

Early warning:	Shaking, trembling
	Sweating
	Tingling in lips and tongue
	Hunger
	Palpitations
	Headache (occasionally)
Neuroglycopenia:	
Mild	Impaired cognitive dysfunction
	Mild diplopia
	Dysarthria
More advanced	Confusion
	Change of behaviour
	Truculence
	Naughtiness in children
Unconsciousness	Restlessness with sweating
	Seizures, especially in children
	Hemiplegia, especially in elderly patients (but rare)

Neuropathies of DM

Neuropathies of DM

Various different neuropathy syndromes may be encountered in patients with diabetes (table 3), this probably reflecting a range of underlying disease mechanisms. These syndromes can occur in isolation or in combination.

Neuropathies are common in both type 1 and type 2 diabetes and there are no major structural differences in the pathology of the nerves in the two diabetes types. However, there are some important clinical distinctions. Thus symptomatic autonomic neuropathic syndromes almost invariably occur in established long duration type 1 diabetic patients in middle age. By contrast the reversible mononeuropathies occur much more often in older men with type 2 diabetes. There are no known reasons for these clinical differences.

Classification of the diabetic neuropathies

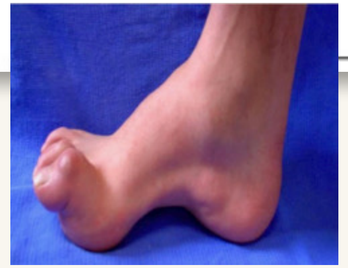
Hyperglycaemic neuropathy
Generalised neuropathies
Sensorimotor polyneuropathy
Acute painful sensory neuropathy
Autonomic neuropathy
Focal and multifocal neuropathies
Cranial neuropathies
Thoracolumbar radiculoneuropathy
Focal limb neuropathies {including compression and entrapment neuropathies}
Proximal diabetic neuropathy
Superimposed chronic inflammatory demyelinating polyneuropathy

Neuropathies of DM

- Polyneuropathy
- Neuropathic osteoarthropathy
- Autonomic neuropathy
- Focal neuropathy.
- Cranial neuropathies:4-3-6

Clinical features of autonomic neuropathy

	Clinical syndromes	*Other abnormalities*	
Cardiovascular	Orthostatic hypotension	High peripheral blood flow	
	Neuropathic oedema	Tachycardia	
		Rigidity/calcification of arteries	
Sudomotor	Nocturnal sweating		
	Gustatory sweating		
	Dry feet		
Genitourinary	Impotence		
	Neurogenic bladder		
Gastrointestinal	Diarrhoea	Oesophageal motility	impaired
	Gastroparesis	Gall bladder emptying	impaired
Respiratory	Arrests	? Sleep apnoea	
	? Sudden deaths	Cough reflex reduced	
Skeletal	Charcot arthropathy	Foot bone density reduced	
Eye	Iritis	Pupillary responses impaired	
		Pupil size reduced	
Neuroendocrine		Catecholamines	
		Glucagon	reduced
		Pancreatic polypeptide	reduced

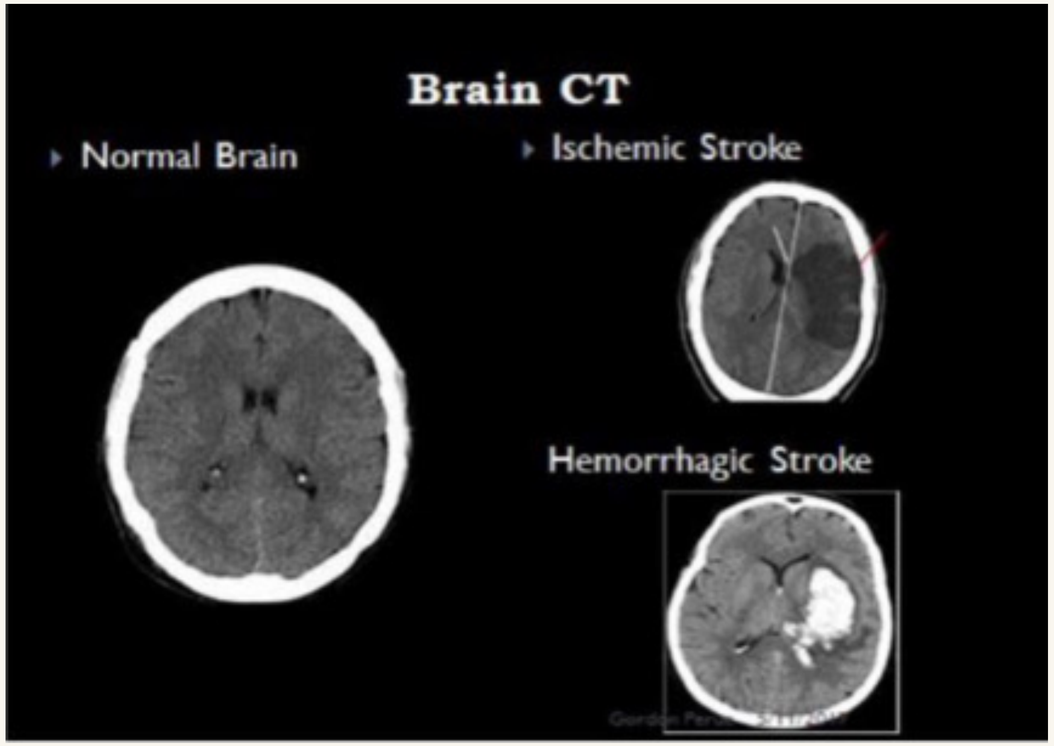


Neuropathies of DM

- Pathophysiology:Vasa nervouam
- Control diabetic
- Gabapantin,CBZ,pergabalin,nerve block

Diabetes & nervous system

Cerebrovascular disease



Alzheimer's diseases

The neurocognitive changes seen in diabetic patients have been associated with changes in the white and gray matter volume. These changes are particularly seen in those with long-standing hyperglycemia, early-onset disease, or recurrent episodes of severe hyperglycemia. Studies have shown a decreased volume of gray matter in the thalamus, temporal lobes, parahippocampal gyrus, insular cortex, and angular gyrus. These regions are associated with memory, attention, and language processing [ ]. These patients were shown to have high levels of HbA1C as well. Some structures like the cerebellum and occipital gyrus showed increased gray matter density possibly to compensate for the early retinal changes seen in diabetic pa-

first region of the brain to be affected due to any kind of stress, whether it be in response to any diet, environmental factors, endocrine changes, or metabolic changes. Neuronal loss in the hippocampus is related to oxidative stress. Within the hippocampus, the most affected areas are the dentate gyrus and cornu ammunis (CA3). There is reduced dendritic spine density, synaptic proteins, and also an increase in the apoptotic markers as a result of DM. It also affects hippocampal neurogenesis (generation of new neuronal cells). Imaging shows a decreased volume of the hippocampus and electrophysiological studies reveal a reduction in long-term potentiation. This causes a decline in learning, memory, and affective expression [ ]

On the other hand, cognitive decline and dementia seen in diabetes are also attributed to white matter disease. Patients with T2DM are more prone to dementia than T1DM due to associated metabolic risk factors like hypertension, obesity, and hyperlipidemia [ ]. The white matter disease appears as

with DM have a 65% higher chance of developing AD [ ]. The cause of this is insulin resistance, imbalance in insulin growth factors, and damage to blood vessels. [ ]

Involuntary movement disorders

Huntington's disease (HD)
tardive dyskinesia
tremor
Parkinson's disease

Infection

Phagocytic function
Meningitis,epidural abscess
Rhinocerebral mucormycosis
Malignant external otitis

Thanks for attention

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