

Practice Changing Continuing Education: A Critical Review of Neurological Complications in Acute Pancreatitis

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ABSTRACT

This uncommon syndrome of pancreatic encephalopathy was first described in 1923. A manifestation of multiple organ dysfunction syndromes, generally occurs in the early stage of severe acute pancreatitis and carries high mortality of up to 57% and more. The syndrome must be distinguished from Wernicke encephalopathy, which may follow as a part of neurological complications in the last or recovery phase of acute pancreatitis, and occurs as a result of long fasting, hyperemesis and total parenteral nutrition without thiamine. Poorly recognized by clinicians, a large dose of vitamin B1 is effective in the management of Wernicke encephalopathy. In view of above the present review draws attention to the challenging and lesser recognized complications of acute pancreatitis and briefly dwells on their pathogenesis and management.

Keywords: Acute pancreatitis, Metabolic encephalopathy, Pancreatic encephalopathy, Wernicke encephalopathy.

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INTRODUCTION

Derived from the Greek language, encephalopathy means the suffering of the brain. Acute encephalopathy usually manifests as a confusional state or delirium. A common cause of encephalopathy is metabolic encephalopathy, a term first coined by Kinnier Wilson. This encompasses features of cerebral dysfunction that are induced by systemic factors. This is most often seen in hospitals (5–40%) and more commonly in intensive care units (11–80%). The feature may start with minor and subtle cognitive dysfunctions and may be severe including delirium, coma, and even death. It results in frequent neurological

consultations for altered sensorium with no structural lesions and their management.¹

Most metabolic encephalopathies are due to drug effect, withdrawal, or interaction with other drugs. Metabolite abnormalities, nutritional deficiency, and toxin exposure are among the other common causes. Symptoms are more frequently seen in elderly, debilitated, and patients with visual or auditory impairment.¹

One of the less common causes of metabolic encephalopathy is pancreatic encephalopathy.¹

DISCUSSION

Pancreatic encephalopathy was described by Lowell in 1923. The abnormalities of mental status that defined pancreatic encephalopathy were first described in 1941.² The condition is seen in association with severe acute pancreatitis and is classified into pancreatic encephalopathy of early stage and late stage.³ The early stage of pancreatic encephalopathy is seen in patients with acute pancreatitis within 15 days (usually 2–5 days) after acute pancreatitis. Many consider it to be a part of septic encephalopathy, but different pathophysiology does not suggest so.^{3,4} The late stage of pancreatic encephalopathy, known to occur after 2 weeks or during convalescence, results from the loss of Vitamin B1 and is more commonly known as the Wernicke's encephalopathy.³

Clinical Features

Clinically it is similar to other encephalopathies. There however seems to be no correlation between the severity of pancreatitis and incidence of this condition.⁴ It usually presents early in the disease and shows many neuropsychiatric manifestations including altered sensorium, confusion, agitation, seizures, speech disorders, and hallucinations.⁵ Short intervals of the lucid period are interspersed in these neuropsychiatric phases. There is a cyclic progression with remission and relapses.⁶ The patients may have features of an upper motor neuron lesion, but these are not always present.⁵ These signs include rigidity involving all four limbs, myalgias, and hyperreflexia.⁶ Asterix has been associated with the disease.⁵

Pathogenesis

In the early stage, the pancreatic enzymes enter the circulation. Phospholipase A2 converts encephalin and lecithin

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into highly cytotoxic hemolytic forms that damage the blood-brain barrier and also leads to vasogenic edema, demyelination, and neuronal damage (cell membrane and mitochondria). Intracerebral edema results secondary to increased intracerebral vascular permeability caused by platelet-activating factor.^{3,4,7}

The inflammatory cytokines (in particular, tumor necrosis factor- α , interleukin-6 (IL-6, IL-8, and IL-1 β) involved in acute pancreatitis cause hypotension, hypoxia, and fat embolism, which may contribute to the delirium.^{4,7} Swelling of the neurons and cerebral stroma may cause myelin cell degeneration and worsen with time.⁷ This a cytokine storm, in association with the entry of pancreatic enzymes into the central nervous system by the damage of the blood-brain barrier and hemodynamic dysfunctions usually associated with acute pancreatitis, forms the multifactorial basis of the pathogenesis of this encephalopathy.^{5,7}

The late stage of the pancreatic encephalopathy results due to low levels of Vitamin B1. Vitamin B1 deficiency causes decreased activity of transketolase. This precludes the oxygenation of pyruvic acid in the tricarboxylic acid cycle.^{3,7} This, in turn, leads to loss of recognition of function. This Wernicke's encephalopathy was described in 1881 by Carl Wernicke, who designated it as "polioencephalitis hemorrhagica superioris."^{2,7} If the diagnosis of pancreatic encephalopathy and Wernicke's encephalopathy is to be cleared, diagnostic treatment may be attempted by administering 100 mg Vitamin B1 parenterally daily. On treatment, the latter would improve.²

Laboratory Data

Routine blood investigations may be inadequate. In the presence of lack of reliable investigations, abnormal sugar curves may provide a clue to the diagnosis if the patient has psychotic symptoms such as anxiety neurosis and melancholia.⁸ Cerebrospinal fluid shows a raised lipase level, but this is rarely tested.⁴ Patchy white matter lesions are known in the condition, but the neuroradiology may be normal.⁵ These patchy white matter signal abnormalities may be seen in magnetic resonance imaging in the cerebral white matter and may resemble multiple sclerosis. Electroencephalogram changes are nonspecific and are not in correlation with the treatment or the course of pancreatitis.² Most commonly, a slowing of the waves is seen.⁹ Histological examination of the brain tissues show perivascular demyelination and diffuse petechiae.⁶ The diagnosis is mainly one of the exclusions, and other causes of metabolic encephalopathy need to be ruled out.⁵

Treatment

There is no specific treatment for this condition except for supportive care and thiamine.⁴ LMW heparin, tumor necrosis factor α , and resveratrol are all being studied for their preventive and protective roles.¹⁰⁻¹² With proper treatment, recovery is uneventful among patients below 40 years of age and may have sequel-like cerebral infarction in elderly, especially those above 60 years of age.² If recognition and treatment are delayed, there may be a devastating neurological outcome.⁹

Pancreatic encephalopathy carries a high mortality. The causes of death include shock, ketoacidosis, and multiorgan dysfunction syndrome. On autopsy, the patient's show pinpoint hemorrhages in multiple areas of the brain such as the hypothalamus, thalamus, and mammillary bodies.²

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