The Uncommon Syndrome of Pancreatic Encephalopathy

Saumya H Mittal, Salony Mittal[1], Tuhina Govil[2]

Departments of Neurology and [1]Pathology, KMC Hospital, Mangalore, Karnataka, India, [2]Detroit Medical Centre, Children's Hospital of Michigan, Detroit, Michigan, USA

Abstract

Even though first described in 1923, the syndrome of pancreatic encephalopathy is an uncommon complication of acute pancreatitis. A multiple organ dysfunction syndrome, it generally occurs in early stage of severe acute pancreatitis and carries a 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 restoration stage 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. The present article draws attention to the two lesser recognized complications of acute pancreatitis and briefly dwells on their pathogenesis and management.

Key words: Acute pancreatitis, metabolic encephalopathy, pancreatic encephalopathy

Introduction

Derived from the Greek language, encephalopathy literally means 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%). 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 a 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 lucid period are interspersed in these neuropsychiatric phases. There is a cyclic progression with remission and relapses.[6] The

Access this article online

Quick Response Code:

Website: www.astrocyte.in

DOI: 10.4103/2349-0977.191047

Address for correspondence: Dr. Saumya H Mittal, Department of Neurology, KMC Hospital, Mangalore, Karnataka, India. E-Mail: saumyamittal1@gmail.com

How to cite this article: Mittal SH, Mittal S, Govil T. The uncommon syndrome of pancreatic encephalopathy. Astrocyte 2016;2:185-6.

patients may have features of a upper motor neuron lesion, but these are not always present.[5] These signs include rigidity involving all 4 limbs, myalgias, and hyperreflexia.[6] Asterixis has been associated with the disease.[5]

Pathogenesis

In the early stage, the pancreatic enzymes enter the circulation. Phospholipase A2 converts encephalin and lecithin 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-1β) involved in acute pancreatitis cause hypotension, hypoxia, and fat embolism, which may contribute to the delirium.[4,7] Oxygen-free radicals cause cerebral injury. Swelling of the neurons and cerebral stroma may cause myelin cell degeneration and worsen with time.[7] This 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 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 malmetabolism 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 neuroradioimaging 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 supportive care and thiamine.[4] 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 devastating neurological outcome.[9] Pancreatic encephalopathy carries a high mortality. The causes of death include shock, ketoacidosis, and multiorgan dysfunction syndrome. On autopsy, the patients show pinpoint hemorrhages in multiple areas of brain such as hypothalamus, thalamus, and mammillary bodies.[2]

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. Katramados A, Varelas P. Encephalopathy. In: Torbey M, editor. Neurocritical Care. Cambridge: Cambridge University Press; 2010. p. 220-6.
2. Sun GH, Yang YS, Liu QS, Cheng LF, Huang XS. Pancreatic encephalopathy and Wernicke encephalopathy in association with acute pancreatitis: A clinical study. World J Gastroenterol 2006;12:4224-7.
3. Ding X, Liu CA, Gong JP, Li SW. Pancreatic encephalopathy in 24 patients with severe acute pancreatitis. Hepatobiliary Pancreat Dis Int 2004;3:608-11.
4. Weathers AL, Lewis SL. Rare and unusual... or are they? Less commonly diagnosed encephalopathies associated with systemic disease. Semin Neurol 2009;29:136-53.
5. Sharma V, Sharma R, Rana SS, Bhasin DK. Pancreatic encephalopathy: An unusual cause of asterixis. JOP 2014;15:383-4.
6. Sharf B, Bental E. Pancreatic encephalopathy. J Neurol Neurosurg Psychiatry 1971;34:357-61.
7. Zhang XP, Tian H. Pathogenesis of pancreatic encephalopathy in severe acute pancreatitis. Hepatobiliary Pancreat Dis Int 2007;6:134-40.
8. Rothermich NO, Von Haam E. Pancreatic encephalopathy. J Clin Endocrinol Metab 1941;1:872-81.
9. Ramanathan RS, Ahluwalia T. Acute necrotizing pancreatitis leading to pancreatic encephalopathy in a patient undergoing long-term continuous ambulatory peritoneal dialysis. J Acad Med Sci 2012;2:85-7.