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CASE REPORT

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Pancreatic encephalopathy: a 7-year follow-up case report and review of the literature

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Abstract Pancreatic encephalopathy is a rare complication of acute pancreatitis. Clinical features include focal neurological signs and acute onset of dementia. This picture can fluctuate over time: cyclic progression with remission and relapses has been described. We present the case of a 43-year-old man who, after an acute episode of pancreatitis, experienced five relapses, with alternating focal signs. The patient has improved, but cognitive impairment persists after a 7-year follow-up.

Key words Pancreatic encephalopathy • Pancreatitis • Metabolic dementia

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Introduction

Pancreatic encelopathy, an uncommon sequela of acute pancreatic infection, was first described in 1941 by Rothermich and Von Haam [1] and later by Vogel [2]. It is characterised by a pattern of neurological signs and symptoms that may occur during the first two weeks of acute pancreatitis, irrespective of its aetiology (e.g. gallbladder or biliary tract stones, alcoholism). It can arise abruptly with convulsions, amaurosis (due to an acute optic neuritis or to haemorragic retinopathy), paresis of one or more limbs, dysarthria, or it can have a gradual onset with behavioural changes, psychomotor agitation, disorientation to time, space and person, and visual and auditory hallucinations on a state of clouded consciousness that can lead to coma [3, 4]. These symptoms can fluctuate over a period of hours or days.

We report our observations over 7 years of a patient with pancreatic encephalopathy.

Case report

A 43-year-old man, with a history of gallbladder stones, experienced an acute episode of pancreatitis. He recovered in one month, but upon stopping a low fat diet he had a relapse. Ultrasound and computed tomography (CT) revealed a pancreatic abscess, removed two months later, and he improved again. Upon stopping total intravenous nutrition, a third episode of increased blood amylase (590 IU/l; normal values, 100–300 IU/l) induced a rapidly clouded consciousness with disorientation to time, space and family members and auditory hallucinations, gradually leading to coma. Blood analysis (including cell count, electrolytes and metabolic parameters) as well as brain CT were normal. The patient recovered from coma in two days, when he came under our observation.

On admission, neurological examination showed dysphonia, dysarthria, facies figèe, auditory and visual impairment,

vertical nystagmus, right-sided paresis, bilateral dysmetria and severe cerebellar ataxia (he could not stand or walk without assistance). Fundus examination disclosed a smal haemorragic spot along the edge of the left macula. Neuropsychological assessment revealed disorientation to time, space and person, short attention span (with inability to focus on a specific stimulus to perform a task), and memory and language impairment (Table 1). Cerebrospinal fluid (CSF) was normal, except for hyperglycorrachia (250 mg/dl), apparently unrelated to the pancreatitis. A diffuse slowing of background activity, with theta waves recorded over all the regions of the scalp, was detected at electroencephalography (EEG). CT and magnetic resonance imaging of the brain (MRI) were normal. Within one week, blood amylase levels returned to normal (210 IU).

After 10 days of treatment with intravenous corticoids, somatostatin, H2 antagonist, pancreatic enzyme and low-fat diet, some of the focal signs and symptoms improved. In particular, dysarthria, nystagmus and auditory hallucinations disappeared, but the gradual reduction of corticoids induced another acute increase of blood amylase (510 IU/l) and a consequent worsening of the patient's conditions.

Six months later, most of the neurological signs and symptoms had disappeared. Persisted cerebellar ataxia and right-sided paresis made the patient still unable to walk without the use of a cane. He still complained of hearing loss. Neuropsychological evaluation (Table 1) showed improved cognitive functions, but a persistent apathy and absent-minded aspect impaired social and work ability. Visual evoked potentials were normal, but auditory evoked potentials, somatosensory and motor evoked potentials were altered (possibly due to damage of the central pathways). In particular, brainstem auditory evoked potentials (BAEPs) showed increased latency of component III, increased latency and dispersion of IV-V complex and increased III-V interval. Somatosensory evoked potentials (SEPs) registered from median nerve showed increased latency of N20 and increased central conduction time (CCT), prevalent on the right side. SEPs from the tibial nerve showed increased latency and dispersion of P40, N50 an P60. Motor evoked potentials (MEPs) recorded from the abductor pollicis longus showed increased threshold and CCT, prevalent on the right side.

Second MRI examination of the brain showed a moderate degree of cortical and subcortical atrophy.

Five years later, after constant physical rehabilitation, the patient came for a follow-up visit. He still walked with the use of a cane. Mild cerebellar ataxia persisted, but the right-sided paresis had disappeared, leaving a prevalence of the right deep tendon reflexes. Hearing function was normal. Cognitive functions were normal, except for a persistent reduction in verbal fluency (Table 1). The patient was still unable to work because of an abulic-apathetic state. All evoked potentials remained altered.

Six years later, he was able to stand and to walk without any support, and the only persisting symptom was apathy, associated with an absent-minded aspect, still responsible for his inability to conduct a normal style of life.

Seven years later, the patient was re-admitted in our ward because of a relapse. The previous week, he had complained of abdominal pain. At that time, blood analysis showed a new increase of amylase (460 IU). On neurological examination, he could not walk without bilateral support because of cerebellar ataxia associated with right hemiparesis and vertical nystagmus. The signs and symptoms disappeared two days later. Brain MRI, neuropsychological examination and blood analysis did not show new signs of abnormality. Two weeks later, on a repeated blood analysis, amylase values were normal (110 IU).

Table 1 Scores on neuropsychological tests at admission and during follow-up

Neuropsychological tests (range of scores)	Admission	6 months	5 years	7 years	Normal scores
MMSE (0–30)	19	25	29	29	≥24
Prose memory (1–4)	0	2	2	2	≥1
Digit cancellation (1–4)	0	2	3	3	≥1
Token test (1–4)	3	4	4	4	≥1
RCPM (1–4)	2	2	2	2	≥1
Verbal fluency (1–4)	1	2	0	0	≥1

MMSE, mini-mental state examination; *RCPM*, Raven Coloured Progressive Matrices

Discussion

Pancreatic encephalopathy is characterised by a pattern of neurological signs and symptoms, tipically fluctuating over time, with remission and relapses. Diagnosis depends on the criteria followed and on whether or not other underlyng conditions can be excluded [5]. Pallis and Lewis [6] suggested to exclude all the situations that can mimic this syndrome, such as electrolyte imbalance, hypo- or hyperglycaemia, diabetic acidosis, hypo- or hyper-calcaemia, hyperrosmolarity syndrome, renal or hepatic failure, cerebral vascular insufficiency and delirium tremens, all conditions that can follow pancreatitis.

In our patient, there was no history of alcoholism. Haematological parameters were normal, as were blood and CSF analyses for common infections. In our opinion, hyperglycorrachia could not be responsible for the clinical picture. This finding can be explained as a consequence of a transient hyperglycaemia, common in pancreatic disease [7], not detected at the time of laboratory test analysis.

The close relationship between the increases in blood amylase and the oscillating neurological picture, worsened after the fourth and fifth (7 years later) increases in blood amylase, and always improved after its reduction, let us believe that the patient had pancreatic encephalopathy.

Some of the signs and symptoms recovered in few days (e.g. dysarthria, nystagmus, hallucinations and disorientation), and some others in few years (e.g. motor skills and cognitive functions), but a persistent cognitive impairment (reduced verbal fluency, absent-mindedness, apathy and loss of willing abilities) made the patient unable to return to work and enjoy social life. This seems to be the result of a persistent diffuse damage of the brain and not a transient condition related to metabolic disequilibrium.

Moreover, while the previous brain CT and MRI examinations did not disclose any focal signs of abnormality, and this could explain the fluctuation of some signs and symptoms of the neurological picture, the 6-month MRI examination showed diffuse (cortical and subcortical) brain atrophy and evoked potentials confirmed that a scattered pathological damage of the CNS persisted.

We believe that this persistent neurological damage responsible for the clinical picture, detected also by auditory, somatosensory and motor evoked potentials, neuropsychological evaluation and MRI, is the consequence of diffuse and non-selective brain lesion that led to extensive neuronal loss, shown by cortical and subcortical atrophy on neuroimaging.

The pathogenesis of this condition is still unclear. According to one of the most reliable hypotheses [2, 8], the presence of pancreatic enzymes in the blood stream alter the blood-brain barrier and damage scattered areas throughout the cerebrum, brainstem and cerebellum. Vogel obtained a similar picture by injecting hog pancreatic lipase into rabbit brain [2]. The resulted demyelinated areas may correspond to the patchy white matter lesions observed by Boon et al. [9] on MR images and found at autopsy by Guardia and Bilbao [10]. Another proposed mechanism is the passage of fat emboli in the blood stream, especially in cases of cytosteatonecrosis, that damage many organs including the brain.

Sommario *L'encefalopatia pancreatica è una rara complicanza della pancreatite acuta. L'esordio spesso è improvviso ed è caratterizzato da segni neurologici focali spesso associati ad una demenza ad esordio acuto. Tuttavia tale quadro clinico può oscillare nel giro di qualche ora o di pochi giorni, per cui è frequente l'alternarsi di fasi di remissione e riesacerbazione. Nel nostro caso, dopo tre ricadute con segni focali alternanti, è residuato un deterioramento cognitivo, solo parzialmente migliorato in 7 anni di follow up.*

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