Central pontine myelinolysis

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Summary

This appears to be the first report of a case of central pontine myelinolysis associated with chronic alcoholism and liver cirrhosis in the United Kingdom. The pathological features and theories of aetiology are briefly discussed.

Introduction

Central pontine myelinolysis (CPM) in alcoholics and malnourished patients was first described by Adams, Victor and Mancall in 1959. This commonly fatal demyelinating process that involves the pons almost exclusively, is of unknown aetiology. In the majority of the published cases, CPM was associated with chronic alcoholism, malnutrition and electrolyte abnormalities, particularly hyponatraemia. Other factors implicated in this disease have included toxins, chronic debilitation, cerebral ischaemia, infection and immunological injury. Of about 175 cases published in the literature, only 4 were reported from the United Kingdom (Adams, 1962; Tomlinson, Pierides and Bradley, 1976). The first case of CPM associated with chronic alcoholism and liver cirrhosis in this country is now described.

Case report

A 60-year-old woman had been admitted to hospital on several occasions for treatment of chronic alcoholism. Her immediate relatives stated that she had drunk approximately half a bottle of gin each day for several years. Five months before death she was admitted to Hope Hospital, Salford, because of prolonged anorexia. On physical examination she was dehydrated and markedly jaundiced but with no palmar erythema or spider naevi. There was no significant abnormality in the chest or cardiovascular system. The liver was firm and palpable approximately 12 cm below the costal margin. The spleen was not palpable and there were no signs of ascites. Rectal examination revealed no abnormality. There were no gross neurological abnormalities.

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Investigations carried out included: Hb 8.8 g/dl; MCHC 31.7 g/dl; WBC $14.6 \times 10^9/l$ (80% neutrophils); platelets $221 \times 10^9/l$ and a peripheral blood film showed moderate macrocytosis and toxic granulations of neutrophils. Serum chloride, bicarbonate, sodium, potassium, urea and glucose were normal. Albumin 33 g/l (normal range 36-52); calcium 2.02 mmol/l (2.1-2.6); phosphate 0.28 mmol/l (0.65-1.62); total bilirubin 36 $\mu\text{mol/l}$ (3-17); alkaline phosphatase 23 KAu./ml (3-13); SGPT 43 Sigma Frankel (SF) u./ml (5-35); SGOT 133 SFu./ml (8-40); and LDH 662 Berger Broida u./ml (0-400); serum iron 4.5 $\mu\text{mol/l}$ (10.7-32.1) and total iron binding capacity 54 $\mu\text{mol/l}$ (45-70). Tests for occult blood in faeces were negative. Urine showed an active urinary tract infection with a coliform organism. IgG, IgM and IgA were normal. Test for hepatitis antigen was negative. Alpha-feto protein was < one mg % and blood cultures were negative. Chest X-ray and ECG showed no abnormality. Serum folate and vitamin B₁₂ were normal. Ultra-sound liver scan showed diffuse hepatic enlargement. She was rehydrated and treated with cyanocobalamin, folic acid, Parentro-vite and nalidixic acid for urinary tract infection.

Her condition improved and she was discharged 4 weeks after admission. She continued to drink and failed to keep 2 out-patient appointments. After being ill for some time she was found collapsed in bed at home and pronounced dead upon arrival at hospital.

The post-mortem was performed approximately 40 hr after death. The body was that of a moderately well nourished, normally developed middle-aged female. There was no jaundice. The brain weighed 1230 g and showed no external abnormality. The meninges and venous sinuses were normal. The arteries at the base of the brain showed no significant atheroma. Serial coronal sections of the cerebral hemispheres showed slight cortical atrophy, otherwise there was no significant abnormality. The pons contained a central soft grey granular area approximately 1.5 cm in maximum transverse diameter and 1 cm in maximum dorso-ventral dimension. The heart weighed 260 g and was unremarkable. The

lungs showed slight oedema and congestion. The liver weighed 1910 g and showed micro-nodular cirrhosis and marked fatty change. All other organs were essentially unremarkable.

Histological examination showed a fairly well circumscribed area of demyelination in the central

FIG. 1. Transverse section through the pons showing a slightly irregular but sharply demarcated central area of demyelination. (Loyez stain for myelin $\times 3.8$.)

part of the pons (Fig. 1). Oligodendroglial cells were markedly reduced in number and several foamy macrophages were present. Within the area of demyelination numerous neurones and axons remained intact. An occasional small focus of recent haemorrhage was present; however, the blood vessels were patent and showed only some enlargement of the endothelial cells. Towards the periphery of the lesion there was slight astrocyte proliferation. There was no inflammatory cellular infiltration. Sections from other parts of the brain showed no significant histological abnormality. The liver showed micro-nodular cirrhosis of alcoholic type.

Discussion

Central pontine myelinolysis was first described from 4 patients by Adams *et al.* in 1959, during the

course of studying the neuropathology of alcoholism. The lesion was localized in the central rostral part of the pons and consisted of a single sharply outlined focus of myelin destruction. Quadriplegia and pseudobulbar palsies were the main clinical findings. Only about 175 cases have been reported in the literature, the majority of which were middle-aged subjects, although the disease has been described in all age groups including children under the age of 10 years (Bhagavan, Wagner and Juanteguy, 1976).

Central pontine myelinolysis is usually a post-mortem diagnosis, although in occasional cases the disease has been diagnosed clinically and 2 patients have survived with minimal neurological damage after treatment of intercurrent illnesses (Wiederholt *et al.*, 1977).

The aetiology of CPM is unknown. In a review of 78 cases the disease was found to be associated with cirrhosis or severe fatty change of the liver (54%); pneumonia and upper respiratory tract infection (40%); malnutrition, cachexia and weight loss (38%); neoplasms including leukaemias (20%); ulceration and bleeding from the gastrointestinal tract (19%); Wernicke's encephalopathy (19%); Wilson's disease (8%); diabetes mellitus (5%); pancreatic diseases (5%); obesity (4%); burns (4%); and subdural and subarachnoid haemorrhage (4%) (Bhagavan *et al.*, 1976). Other associated conditions included pulmonary emboli and infarctions, suppurative bacterial and meningo-encephalitis, mumps, scleroderma and hypertension. Drugs, particularly antibiotics, steroids and diuretics have been incriminated. Although in approximately 60% of all cases a history of alcohol abuse is present (De Reuck *et al.*, 1975), it is unlikely that this disease is caused solely by excessive alcohol intake, as other lesions of the central nervous system that are generally attributed to alcohol ingestion have not been consistently present in cases of CPM. Wernicke's disease was present in less than 20% of the reported cases, and pontine demyelination has not so far been observed in Marchiafava-Bignami disease. An immunopathological process has been suggested by Seitelberger (1974) in view of the finding of a significant plasmocellular infiltration in areas of recent focal changes. In 1975, De Reuck *et al.*, in studying the arterial blood supply of CPM, suggested that among the associated disorders, oligoemic shock combined with a local decrease in the blood flow in the basilar artery was the most important cause of this pathological entity. Other possible aetiological factors considered in the pathogenesis of CPM have included vitamin deficiency especially thiamine deficiency and electrolyte imbalance such as hyponatraemia, which occurred in approximately 61% of cases (Burcar, Norenberg and Yarnell, 1977), abnormal copper metabolism (Bhagavan *et al.*, 1976).

and lack of an unidentified metabolic factor (Adams, 1962).

Recently, ultrastructural studies of CPM have revealed the presence of intramyelinic vacuoles at the periphery of the lesion, suggesting that the pathogenesis of CPM might include a phase of intramyelinic oedema with subsequent rupture of the distended myelin sheath (Powers and McKeever, 1976), although the pathogenetic mechanism of the oedematous change in the myelin remains unknown.

Central pontine myelinolysis is most frequently a solitary lesion involving the pons, although other parts of the brain were also involved in 12 reported cases (Wright, Laureno and Victor, 1979). It has been suggested that the oligodendroglial cells at the areas affected are more susceptible to noxious influences than are myelin-producing cells elsewhere in the brain (Sima and Bradvik, 1976; Tomlinson *et al.*, 1976).

Although the majority of the reported cases were alcoholics and malnourished, none of the 4 previously reported cases from the United Kingdom had a history of alcohol abuse. Three were females aged between 31 and 57 years and one was a 7-year-old boy. All 4 cases had gross electrolyte disturbances, particularly hyponatraemia associated with vomiting. The present patient was a known alcoholic and had been admitted to hospital for chronic alcoholism on several occasions. Unfortunately, as the patient died at home, no investigations were performed immediately before death. In view of the frequent association of vomiting with alcoholism it is likely that the suggestion of electrolyte imbalance as an aetiological factor in CPM is important.

It has been suggested that the scarcity and lack of detailed study of chronic alcoholism and malnutrition in the United Kingdom may partly explain the relative absence of CPM in the British literature (Tomlinson *et al.*, 1976).

Central pontine myelinolysis is obviously a rare

disease; however, it is likely that the lesion is much commoner than the number of the reported cases in the literature suggests. This is probably due to the fact that the disease has not yet been widely recognized and in some cases the lesion can be very small and easily missed on naked eye examination. A greater awareness of the occurrence of this lesion would lead to its more frequent clinical diagnosis and possible treatment.

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References

- ADAMS, J.H. (1962) Central pontine myelinolysis. In: *4th International Congress of Neuropathology*, Vol. 3, p. 303. Georg Thieme Verlag, Stuttgart.
- ADAMS, R.D., VICTOR, M. & MANCALL, L.E. (1959) Central pontine myelinolysis. *Archives of Neurology and Psychiatry*, **81**, 154.
- BHAGAVAN, B.S., WAGNER, J.A. & JUANTEGUY, J. (1976) Central pontine myelinolysis and medullary myelinolysis. *Archives of Pathology and Laboratory Medicine*, **100**, 246.
- BURCAR, P.J., NORENBURG, M.D. & YARNELL, P.R. (1977) Hyponatremia and central pontine myelinolysis. *Neurology*, **27**, 223.
- DE REUCK, J., VANDER ECKEN, H., THIERY, E. & CREVITS, L. (1975) Central pontine myelinolysis and its arterial blood supply. *Acta neurologica et psychiatrica belgica*, **75**, 192.
- POWERS, J.M. & MCKEEVER, P.E. (1976) Central pontine myelinolysis. An ultrastructural and elemental study. *Journal of the Neurological Sciences*, **29**, 65.
- SEITELBERGER, F. (1974) Central pontine myelinolysis. *Neuropathologia polska*, **12**, 247.
- SIMA, A. & BRADVIK, B. (1976) Central pontine myelinolysis. *Acta pathologica et microbiologica scandinavica*, Series A, **84**, 73.
- TOMLINSON, B.E., PIERIDES, A.M. & BRADLEY, W.G. (1976) Central pontine myelinolysis. *Quarterly Journal of Medicine*, New Series, **XLV**, 179, 373.
- WIEDERHOLT, W.C., KOBAYASHI, R.M., STOCKARD, J.J. & ROSSITER, V.S. (1977) Central pontine myelinolysis. *Archives of Neurology*, **34**, 220.
- WRIGHT, D.G., LAURENO, R. & VICTOR, M. (1979) Pontine and extra pontine myelinolysis. *Brain*, **102**, 361.