LEAD ENCEPHALOPATHY — REPORT OF TWO CASES

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SYNOPSIS

Two cases of lead encephalopathy are described in this paper. Industrial lead poisoning more rarely affects the brain and can present as pseudotumour cerebri or psychosis.

Numerous investigations for confirmation of the diagnosis are elaborated. Treatment with calcium versene in both cases was met with improvement.

INTRODUCTION

Lead poisoning is still a frequent industrial hazard. In smaller industries, where there is low or no surveillance for signs of toxicity, the toxic condition may be overlooked. Lead is a versatile metal. Its use is ubiquitous in most types of engineering. It is present in grease paints used by actresses[4], as well as in petrol as an additive in the form of tetraethyl lead. Soon after the introduction of the latter in 1923, there were 149 cases of encephalopathy with eleven deaths among the works within an 18 month period[5].

Lead intoxication affects principally the neurological system, the alimentary tract, the kidneys, the cardiovascular system and the haematopoietic system. Neurologically, it involves in combination or individually, muscles, peripheral nerves ('lead palsy') and more rarely the brain ('lead encephalopathy'). We describe here two cases which presented as Pseudotumour Cerebri and Psychosis, respectively. These cases also illustrate the point that routine tests of confirmation have numerous pitfalls, which, if not corrected, may lead to an inaccurate diagnosis and treatment.

Case 1

T.M.H., a 26 year old Chinese man, was born in China. He emigrated to Malaya 11 years ago. Apart from an episode of febrile illness at the age of 5 years, he had maintained good health. Since arriving in Malaya, he had been working in his brother's bicycle-repair shop. Three years ago, his family noticed that he had frequent attacks of syncope while at work. These attacks were intermittent, with no fixed periodicity in time. Frequency of attacks varied from 2 per day to 1 per every few months. At the onset of the attack, which was always sudden, his limbs turned rigid. This was followed by left-turning of his head. Tonic and clonic movements of the limbs were not seen. Neither was there turning of the body nor raising of the arms as seen in an adversive seizure. During the episode, he remained continent of urine and faeces. Salivation was not excessive. Eyes were opened and appeared fixed at infinity. Half an hour later, he would wake spontaneously to continue at his job. During this period, he had, at various times, consulted neurosurgical and medical units in Malaya, as well as another medical unit in Singapore. At each consultation, he was diagnosed and treated as Idiopathic Epilepsy.

On 5.10.71, he was admitted to another medical unit, diagnosed as Brain Tumour. The chief complaints were frequent attacks of giddiness and postprandial vomiting for the preceding three weeks. Headache was not a feature. There was slight improvement ten days prior to admission. However, this was to deteriorate again two weeks later. On 11.10.71, the day before he was transferred to this Unit, (for neurosurgical management) he was irrational and complained of increasing blurring of vision.

On examination, his general condition was poor. Pallor and jaundice were present. Pulse rate was 84 per minute. Blood pressure was recorded at 110 mm.Hg. systolic, 80 mm.Hg. diastolic. There was no abnormality in the chest or abdomen. Neurological examination revealed a confused young man who was having frequent spasms of his trunk and limbs. His pupils were unequal in size,— the right being larger and less reactive than the left. Funduscopy showed bilateral, severe papilloedema. His visual acuity was poor. There was paralysis of the right Occulomotor Nerve and bilateral Abducent Nerves. Limb hypertonus was present with excellent muscle power. Modalities of sensation were normal, as were the reflexes. The plantar response was downgoing on both sides.

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Investigations performed at an earlier date revealed normal cerebrospinal fluid and an anaemia, which was haemolytic in nature. A smear of the peripheral blood and showed stippling of the RBC (See Figs. 1*a* and 1*b*). Brain scanning and Echogram were performed. Neither showed any evidence of a space-occupying lesion. These suggested a chronically intoxicated state, most likely due to lead.

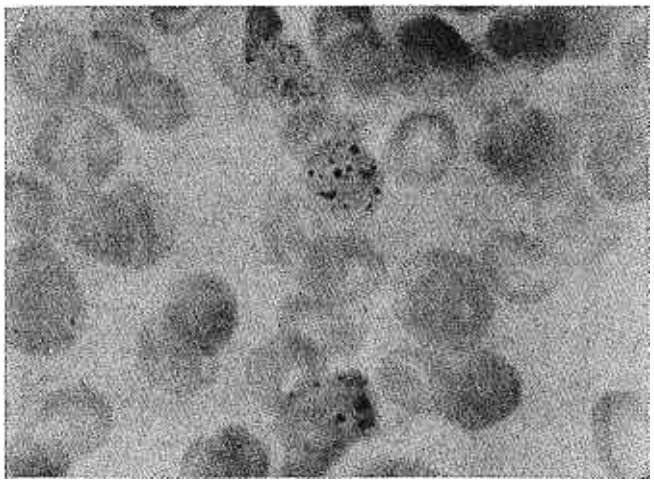

Fig. 1(*a*)

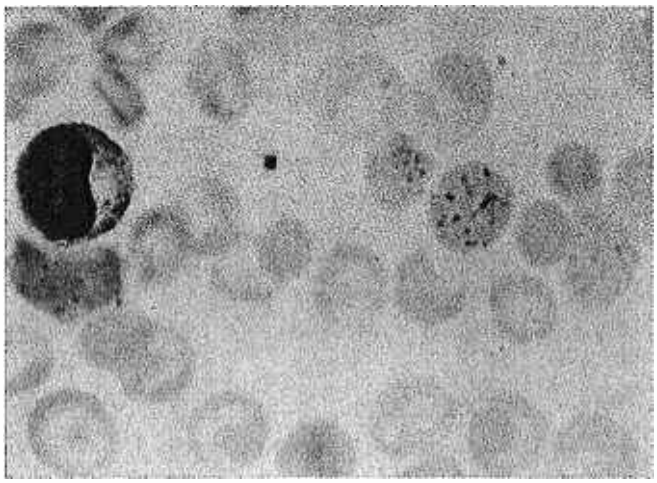

Fig. 1(*b*)

Peripheral blood films showing stippling of the red cells.

During his first day in our ward, his conscious state deteriorated further. He was lapsing in and out of consciousness. A swinging fever was also present. At this juncture, a brain tumour could not be excluded. An emergency carotid angiogram was carried out—only to reveal a normal cerebral vasculature and oral Dexamethasone 3mg. qds. was initiated. A pint of blood was given to correct the anaemia.

Two days later, he showed signs of improvement. The temperature returned to normal, and remained so for the rest of his hospitalization period. One week after his transfer, all drugs were discontinued. By this time, he was fully alert, cooperative and rational. His memory for past and recent events was good. Papilloedema of both optic discs slowly resolved, as did the nerve palsies, jaundice and haemolysis.

During this time, supportive evidence of chronic lead intoxication was actively pursued. Confirmation of the diagnosis came late, because of the intermittent nature of the illness. In the first week, repeated blood films made of the peripheral blood only served to confirm an anaemia with a high reticulocyte count (between 6% to 22%). There was no basophilic stippling of the RBC. Corproporphyrin was detected in the urine on two occasions. However, an estimation of a 24-hour urine collection revealed a lead content of 0·05 parts per million (Normal up to 0·1 part per million). Subsequently, Acute Intermittent Porphyria was considered and excluded. A repeat examination of the cerebrospinal fluid, at this time, showed it to be normal, but under low pressure (20 mm.CSF). Intermittent obstruction of cerebrospinal fluid circulation was considered. Probably the obstruction was at the Aqueduct or the third Ventricle. While this was being considered, the bone marrow aspirates as well as smears of the peripheral blood were sent to the haematologist for assessment. These were reported as "Marked macronormoblastic hyperplasia. Punctuate basophilia very prominent in erythroid series. Granulopoiesis is normal. Megakaryocytes are normal. Iron stores are increased. Siderotic granules prominent in erythroid series. No ring sideroblasts. Peripheral smear—RBC show marked hypochromia. Moderate aniso and poikilocytosis. Polyshromasia is prominent. Coarse punctuate basophilia prominent. WBC and platelets normal." We then collected his urine over 72 hours, and sent it for lead estimation. This time, the specimen of 8 litres (he had plenty of fluids to drink) was found to contain 1·7 mg. of lead i.e. 0·21 parts per million. This confirmed our diagnosis of lead poisoning.

A course of calcium versene (Calcium EDTA) was given over five days. This was delivered in a slow intravenous infusion twice a day. On the first day, 500 mg. CaEDTA in 250 c.c. of 5% dextrose was given twice. No complication developed. On subsequent days, he received the full dosage of 2 gm. CaEDTA daily. During therapy, urinary excretion of lead averaged 0·59 parts per million. After a total of seven weeks of hospitalization, he was discharged and returned to Malaya (West Malaysia). When we reviewed him again in our Outpatient Department, we found that he was still having occasional lapses in his conscious state.

These were milder and lasted only 15 minutes, when compared to those he had prior to treatment. These were subsequently controlled by Zarontin (Ethoxusimide) 250 mg. qds. When last seen in mid-1972, he was free of fits. Although he denied

any contact with lead in his job, he was advised to change his employment.

Case 2

W.S.L., is a 27 year old Chinese male. He had been working as a petrol kiosk attendant for two years. One year after commencing work, he was found to display abnormal traits in his behaviour. He was duly examined and warded in Woodbridge Psychiatic Hospital for a month. Subsequently, he was treated as an outpatient in the Psychiatic Clinics. On 17.7.72, he was admitted to our Medical Unit. The history was one month of anorexia, one week of yellowness in his eyes and fever, three days of vomiting black fluids and the passage of soft, black stools. There was also a history of ingesting Chinese medicines after the onset of vomiting. Urine colour was dark brown. Examination revealed a very ill young man. He was very pale and jaundiced. Temperature was 101°F. His musculature, however, was well preserved. Funduscopy did not detect any abnormality. Hepatosplenomegaly was absent. Apart from being dull and unco-operative, no neurological deficit was evident. Investigations showed:

Haemoglobin—3·3 gm.%

Total white cell count—34,800 /c. mm.

Polymorphs 90%, lymphocyte 7%, monocyte 3%

Platelet count—230,000/c. mm.

Reticulocyte count 15%

Erythrocyte Sedimentation Rate—30 mm. in 1 hour.

A peripheral blood smear was not done because of a technical fault. Urine microscopy was normal with no bile, urobilin or Urobilinogen being detected.

Serum electrolytes were normal. Bl. urea was 168 mg.%. Glucose-6-phosphate dehydrogenase was present. Haemoglobin electrophoresis showed normal HbA was present. Septicaemia was excluded by virtue of negative blood cultures on 9 febrile occasions. Leptospirosis and Typhoid were excluded by Serology. Bone marrow aspirated from the sternum was reported as normal when performed on the 8th day of admission. Direct Coombs' Test was negative. Meanwhile, urine collected over 24 hours was examined for lead. This was present in 0·3 p.p.m. However, corproporphyrin was not detected in two early morning specimens. Nonetheless, he was given EDTA treatment, as was given to T.M.H. During the five-day treatment, 24-hours collections of urine was performed on three days. The lead content in these were 0·3 p.p.m., 0·3 p.p.m., 0·09 p.p.m. His haematological condition improved. However, he remained dull and unco-operative. Occasionally, he would become violent and would speak to himself. On 18.8.72, he was transferred to Woodbridge Hospital for further management.

DISCUSSION

Lead is a cumulative poison which is excreted slowly and intermittently. In the encephalopathic state, symptoms may develop suddenly after chronic exposure, as shown in both our cases. However, preceding signs of ill-health may pass unnoticed. Encephalopathy occurs chiefly in children and is manifested by recurrent epileptiform seizures, mania, delirium and coma. Other features are diplopia, stippling of retina[6], progressive dimness of vision, intense papilloedema and various nerve palsies that may simulate brain tumour. Other eye signs of moderate intoxication are optic neuritis, oedema of disc, ocular muscle paralysis, ptosis, and central vision disturbance.

Pathologically, the brain is oedematous, and neurones are likewise affected with glial cell proliferation. The symptoms are attributable to the inhibition of the intracellular enzyme systems. Opinion is expressed that this is the result of the combination of the metal with sulphydryl groups[1]. This would explain the occurrence of encephalopathy in those whose cerebral spinal fluid is not under increased pressure as evident in both our cases. However, should cerebral oedema set in, as a result of cellular injury, the brain is further taxed and this could result in death of the patient.

The management of patients is two-fold:

1. To treat the seizure and to reduce possible cerebral oedema.
2. To remove the lead from the body stores—namely bone, liver, blood, kidneys, spleen, lungs, brain in that order of decreasing concentration.[2]

The seizures are treated on their merit. We use Phenobarbitone and Epaneutin for grand mal epilepsy, while Petit Mal attacks are controlled by Zarontin (Ethosuximide). When cerebral oedema is deemed present, Dexamethasone and Frusemide are administered. Mannitol is an alternative. There is no place for surgical decompression. 'Deleading' the patient went through many changes. Early physicians attempted to drive lead into the bones during the acute episode. In 1941, the first efforts to remove lead by chelation were described[3]. Kety *et al* used sodium citrate. Subsequently, BAL (2,3—dimercapto propanol) was used. It was shown that BAL removed lead bound to the sulphydryl groups of the enzymes, hence reversing the lead effect on

the cellular systems. However, the toxic side effects caused by BAL soon cause it to be surpassed by Calcium Disodium Versene (CaEDTA). This is now the drug of choice. A possible complication is the intensification of the encephalopathy if the initial tissue concentration of lead is high, causing sudden mobilization of large amounts of lead, some of which may enter the brain. Some advocate, in adults, the use of combined therapy with BAL, CaEDTA followed by oral penicillanine. This is probably of use in the patients with persistently high blood levels (exceeding 100 mg. of lead per 100 cm. of blood) after the initial course of therapy with CaEDTA. The risk of symptomatic relapses is considerably higher at this blood level. Oral Penicillamine may be used, in place of CaEDTA, in mildly asymptomatic cases. In a dosage of 1 to 1·5 Gm. daily for 3 to 5 days, urinary excretion of lead is increased, (smaller amounts of lead are removed with the faeces and perspiration). Penicillamine administered orally saves the patient from painful parenteral injections.

The mortality and morbidity of lead poisoning is difficult to assess, as many 'poisoned' individuals are asymptomatic. The early recognition and prevention in people at risk is the only method of controlling this disease which is becoming more widespread as industries increase. Those who do survive encephalopathy have some residual mental deterioration, visual defect, nerve palsy and epilepsy.

ACKNOWLEDGEMENTS

We wish to thank Dr. Lee Yong Kiat, Head Medical Unit, Thomson Road General Hospital for permission to publish the cases. We are also grateful to Dr. Feng Pao Hsii and Dr. Loong Si Chin for their encouragement and all the doctors of the Unit for their assistance. Our thanks are also due to Dr. Ong Yong Wan for her assistance in the haematological investigations.

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