pathways unknown, neoplasms can cause hypercalcaemia. Lucas (1960), describing a similar case, emphasizes that the hypercalcaemia may be a presenting feature as indeed it was in this patient. He found, like Stone and others (1961), that the hypercalcaemia was temporarily controlled with cortisone. This was not tried with this patient.

Summary

A patient is described with hypercalcaemia, hypophosphataemia and hypercalcuria associated with a pancreatic carcinoma. Although no direct correla-

tion between the presence of tumour and hypercalcaemia could be made this case is very similar to several others previously reported. The hypercalcaemia responded temporarily to sodium versenate. The parathyroids were normal at autopsy and there were no osseous metastases.

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EMETINE TOXICITY WITH PREDOMINANT NEUROMUSCULAR MANIFESTATIONS

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EMETINE, described in 1817 by Pelletier, first used by Bardsley in 1829 in dysentery, and used specifically in amoebic dysentery by Rogers, 1912, still continues to be the most widely used drug in severe amoebic dysentery and hepatitis. The generalized toxic effects of emetine as a protoplasmic poison have been well documented. Excessive dosage or, in susceptible persons, therapeutic or even subtherapeutic doses, have been known to produce a wide range of toxic effects (Sodeman, D'Antoni and Doerner, 1952).

Diarrhoea, nausea and vomiting are common. Dyspnoea, precordial pain, marked tachycardia, hypotension, even acute cardiac failure and death are the result of a toxic myocarditis (Young and Tudhope, 1926; C. Mattei, 1938; Helig and Visveswar, 1943; Dack and Molshok, 1947). Electrocardiographic changes of T wave flattening or inversion in all leads, prolongation of the P-R and Q-T intervals, and rarely changes in rhythm have been recorded (Hardgrove and Smith, 1944;

Boyd and Scherf, 1941; Klatsking and Friedman, 1948; and others in the literature).

The neuromuscular manifestations are varied, consisting of apathy, generalized weakness of muscles and hypotonia, sometimes foot-drop and rarely, atrophy of muscle groups (Manson-Bahr, 1941). Muscle weakness, aching tiredness and stiffness of skeletal muscles are also said to be part of a myositis. Young and Tudhope (1926) on histological studies of emetine-poisoned rabbits were in favour of a myositis rather than a peripheral neuritis, in explaining the motor manifestations. They did, however, find chromatolysis in the anterior horn cells of the spinal cord. Peripheral neuropathy with diffuse sensory changes does occur, but it is rare (Brown, 1935). The concentration of emetine found in the CNS after experimental intoxication is negligible (Palmer and Cottrill, 1949).

A full-blown picture of emetine intoxication is, however, rare. The case reported serves to

FIG. 1.—Electrocardiogram taken four weeks after admission to hospital, showing widespread inversion of T waves.

demonstrate all the above-mentioned features in addition to the marked neurotoxic effects of mental dullness and disorientation, nystagmus, neck rigidity, loss of tendon reflexes in association with a raised CSF protein which has hitherto not been emphasized in previous reports.

Case Report

A well-built male African was admitted to a branch hospital, complaining of diarrhoea with blood and mucus in the stools and vomiting. A stool examination showed the presence of amœbæ and he was given a seven-day course of emetine hydrochloride (gr. 1) by intramuscular injection. The diarrhoea stopped within three days of treatment, but the stools at the end of the week yet showed the presence of amœbæ and he was given a further course of emetine for three days, this being followed by emetine bismuth iodide, 1 gr. daily for a week.

During the third week of the illness the patient, who was in a reasonable state of health till now, steadily began to deteriorate. He became very weak, showed indifference to his meals and his environment and lay apathetic in a hypotonic state. He developed a watery diarrhoea during this time, and his pulse became so feeble, his blood pressure so low and his general condition so bad that he was transfused with 2 pt. of blood. The diarrhoea gradually subsided, but his general condition deteriorated, and it was found necessary to transfer him to Korle Bu General Hospital, Accra, for further investigation and treatment.

When seen he was unable to give a history, answered questions in monosyllables, was disorientated, and admitted to weakness, nausea, giddiness and palpitations, but lapsed into silence when questioned in detail.

On examination he had an athletic build, but looked very ill and toxic. He lay motionless in a flaccid hypotonic state, not unlike a person with generalized

myasthenia. He was not dehydrated nor clinically anæmic. There was no evidence of malnutrition.

Fundi normal. Pupils equal, central and reactive to light and accommodation. Bilateral ptosis prominent, nystagmus present; ocular movements, however, full and equal. Apart from a generalized weakness of the facial muscles and of the muscles of mastication, the other cranial nerves were normal.

There was marked weakness of all movements at all joints of both upper and lower limbs, the weakness being somewhat more peripheral than central and the left knee and ankle being weaker than the right. Deep reflexes were absent in both upper and lower limbs. In contrast with the marked hypotonia of all muscles he had well-established neck rigidity, but Kernig's sign was absent. Sensation normal for touch, pain and temperature. Posterior column sensation diminished on both lower limbs. Light percussion with a tendon hammer on the muscles brought out a sustained, localized, firm contractile swelling at the site of stimulation.

Pulse feeble, 120/min., blood pressure 90/60 mm. Hg. The apex beat of the heart was in the 5th interspace mid-clavicular line; a well-established protodiastolic gallop rhythm was heard. There were no murmurs. There was no evidence of cardiac failure. The lungs were clear, clinically and radiologically. The heart contours were normal.

The abdomen was soft and pliable, a thickened colon was palpable in the left iliac fossa. Liver and spleen were not palpable. In view of his neurological signs it was thought wise to exclude a primary neurological condition and a lumbar puncture was done.

Investigations

Hb 78% (11.4 g./100 ml.). ESR 50 mm./hour. WBC 6,450, polymorphs 57%, lymphocytes 40%, eosinophils 3%. Urine: albumin trace, few pus cells, and epithelial cells seen. Faeces: no amœbæ, ova or cysts seen. Round worm ova present. Serum sodium 148

mEq./l., potassium 4.8 mEq./l., chloride 92.2 mEq./l. Blood urea 24 mg./100 ml. Liver function tests normal. CSF: proteins 70 mg./100 ml., sugar 62 mg./100 ml., chlorides 673 mg./100 ml. Globulin (Nonne Apelt) positive. Cells: 2 lymphocytes/100 ml. ECG rate 120/min. PR interval 0.12 sec.

There was universal T-wave inversion with the S-T segment elevated in V₂, V₃, S-T depression in V₄, V₅, V₆, V₇, the ECG being consistent with widespread myocardial damage.

Course and Treatment

He was treated with strict bed rest, 2 pt. of 5% dextrose on the first day and thereafter with a nourishing easily digestible low-residue diet. His tachycardia gradually improved, a rate of 80/min. being recorded on 31.3.62 (three weeks later). Triple rhythm persisted for five weeks. ECG taken four weeks later continued to show (Fig. 1) persistent T-wave changes. His mental state improved remarkably, he became more communicative and talked and laughed with his bed mates. The weakness gradually disappeared with the return of deep reflexes to normal in four weeks. The nystagmus and neck rigidity were not noticed at the end of three weeks. By the second week he had desquamation of the skin of his palms and soles of the feet, which was complete in four weeks.

Discussion

A review of the literature reveals a wide range of opinion as to the relative incidence of toxicity; e.g. 8 out of 535 cases, and these subjects had received a total of 70 to 130 gr. (Manson-Bahr, 1941). Brown recorded an incidence of 0.54% in those having received 0.54 g. or less. Several fatalities in those not exceeding the therapeutic maximum of 0.64 g. (10 gr.) are reported by Helig and Viswasar, 1943 and an incidence of 30 to 90% by Klatskin and

Friedman, 1948. One could conclude that a great deal of individual susceptibility does exist (Sodeman and others, 1953). In recent years there has been a trend to regard the toxic effects of emetine to have been much over exaggerated (Adams, 1960; Woodruff, 1959).

The case recorded received 0.6 g. of emetine hydrochloride and 0.42 g. of emetine bismuth iodide. Considering that all the emetine bismuth iodide need necessarily not have been absorbed from the gut, the exceeded dose is not much more than the considered maximum of 0.72 g. for emetine hydrochloride alone (Adams, 1960). The rare but susceptible case does exist and only careful observation for toxic effects can forestall a catastrophe. It would be wise to restrict the dosage of emetine hydrochloride to 0.64 g. (10 gr.) in one single course or to use emetine bismuth iodide for a maximum of 1.26 g., avoiding their use concurrently or as an immediate follow-up of the former with the latter.

Summary

The toxic effects of emetine as a protoplasmic poison are reviewed. A case is reported with a full-blown picture of emetine intoxication, with predominant neurological features. The statement that the toxic effects of emetine are much exaggerated is briefly discussed. The relevant literature is reviewed.

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