minutes but cramps persisted for an hour. Examination immediately afterwards was normal with a blood pressure of 120/70 mm Hg. Brain scan, EEG, blood urea, and serum sodium, potassium, and calcium were normal; serum magnesium was low at 0·32 mmol/l (0·78 mg/100 ml). All drugs except metolazone were continued without recurrence of symptoms. The patient recalled an episode of syncope two years previously, when not taking any drug, which lasted for "seconds." This was preceded by a leg cramp but there was no incontinence.

Discussion

These may be cases of serious adverse reaction to metolazone. The features common to both were (1) sudden onset of muscle cramps followed by collapse, impairment of consciousness, and epileptiform movements; (2) no history of epilepsy; (3) each episode closely followed small doses of metolazone; and (4) no further symptoms after withdrawal of metolazone. Gunstone *et al*[1] reported fatal seizures in a patient on metolazone and frusemide. We think this is the only reported association of metolazone therapy and convulsions. Muscle cramps alone, however, are a well-recognised effect of metolazone.[2 3]

We were unable to find severe hypotension, hypokalaemia, hypocalcaemia, or acid-base disturbances which might have provoked cramps or seizures. In case 2, however, hypomagnesaemia may have been a contributory factor. Hillenbrand and Sherlock[3] reported aggravation of hepatic encephalopathy in patients on metolazone, but this seems to have been due to hypokalaemia rather than a direct central nervous system effect. The history of previous leg cramps in both patients is interesting. It suggests enhanced neuromuscular excitation which might be further increased by a direct metolazone effect or by a metolazone-induced electrolyte flux. Pending further investigations to estimate the prevalence of similar reactions to metolazone therapy, we suggest that metolazone should be administered with caution, particularly when there is a history of muscle cramps or epilepsy.

[1] Gunstone, R, *et al*, *Postgraduate Medical Journal*, 1971, **47**, 789.
[2] Cangiano, J, *et al*, *Current Therapeutic Research*, 1974, **16**, 778.
[3] Hillenbrand, P, and Sherlock, S, *British Medical Journal*, 1971, **4**, 266.

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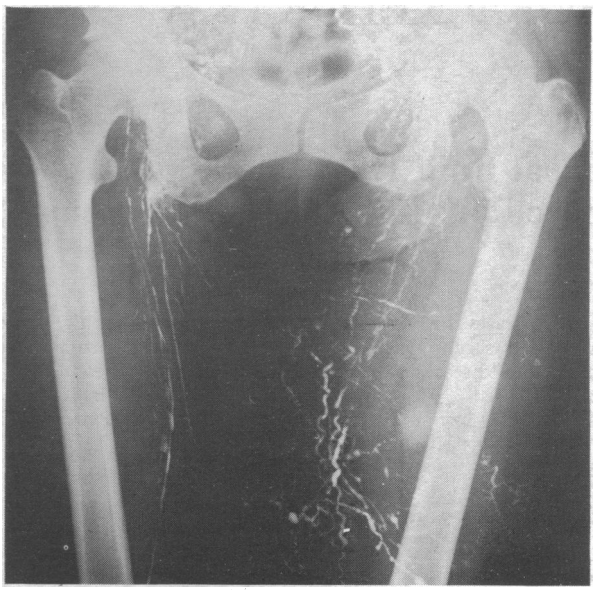
Unusual case of lymphoedema praecox

A case of lymphoedema praecox with some unusual features is reported.

Case report

A 35-year-old nulliparous woman presented with painless swelling of the whole left lower limb of 3 years' duration. She had no other symptoms and no significant or relevant medical or family history. She had not travelled outside Cyprus. She was a small, anaemic woman with obvious left lower limb oedema. The right calf was 33 cm in circumferance and the left 44 cm. There were no other abnormal physical signs and no evidence of Turner's syndrome, capillary angiomata, or other congenital anomalies.

Laboratory investigation confirmed a mild iron deficiency anaemia. Marrow biopsy showed hypercellularity but no malignant cells. Blood chemistry, liver function tests, and urine analysis were normal; hydatid complement fixation was negative; and no microfilaria were seen in the blood. *X*-ray examination of the chest and abdomen, bilateral lower limb venography, and intravenous urography were normal. Bipedal lymphography[1] showed dilated, tortuous lymphatics throughout the left lower limb (fig). There were similar dilated channels in both sides of the pelvis and the para-aortic chains to the level of L2, but the vessels below the level of the superficial inguinal nodes on the right were normal. The oily contrast medium was so slow in emptying from the dilated lymphatics that the thoracic duct could not be visualised. The abdominal lymph nodes were normal apart from fibrolipomatous deposits. The normal lymphographic appearances in the lower limb have been described by Browse[2] and in the lumbar region by Jackson.[3]



Lymphogram showing grossly dilated lymphatics of left thigh and both sides of pelvis with normal diameter vessels in right thigh.

No obstructing lesion in the upper abdomen was found on laparotomy. Lymph nodes excised were histologically normal.

Discussion

Thorough investigation failed to find a cause for the lymphoedema in this case. It may therefore be classified as primary. Primary lymphoedema is arbitrarily divided into (1) congenital; (2) praecox, occurring before age 35; and (3) tarda, starting after 35 years. It may be caused by aplasia, hypoplasia, or hyperplasia of the lymphatics.[4] In the hypoplastic group decrease in size or number of the lymphatics may be confined to a small area with proximal dilatation. Hyperplastic primary lymphoedema occurs in the absence of an obvious obstructing lesion. It may be unilateral or bilateral. The unilateral type is more common in men with no family history but often with capillary angiomata; the bilateral condition may be familial, more common in women, and associated with a variety of congenital anomalies.

Our case does not fall into either of the recognised clinical groups. Although hyperplastic lymphatics were present unilaterally in the lower limb there were bilateral changes in the abdomen and pelvis. Conventional explanations for the dilated lymphatics in these cases are thoracic duct obstruction or impedance to flow of lymph through the nodes. Competent valves in the vessels of the groin may be protecting the limb from the resistance to flow above that level. As the disease progresses bilateral oedema may develop. In acquired lymphoedema due to lymphadenectomy, radiotherapy, or inflammatory conditions dilated channels are not seen above the level of the lesions. Filariasis may be indicated by a history of visiting an endemic area, the presence of filaria in the blood, and positive filarial skin test.

[1] Dolan, P A, and Moore, A B, *American Journal of Roentgenology*, 1962, **88**, 110.
[2] Browse, N L, in *The Lymphatics: Diseases, Lymphography and Surgery*, ed J B Kinmonth. London, Edward Arnold, 1972.
[3] Jackson, B T, *Annals of the Royal College of Surgeons of England*, 1974, **54**, 3.
[4] Kinmouth, J B, *The Lymphatics: Diseases, Lymphography and Surgery*. London, Edward Arnold, 1972.

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