

Lesson of the Week

Sporadic disseminated histoplasmosis simulating miliary tuberculosis

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Disseminated histoplasmosis may closely resemble miliary tuberculosis in its clinical presentation.¹ In an area where infection with *Mycobacterium tuberculosis* is common the diagnosis of disseminated histoplasmosis may therefore be delayed or missed.

Case report

A 45 year old housewife presented with a one month history of progressive weight loss and abdominal swelling and intermittent fever with nocturnal sweating. She had also noticed darkened urine but her stools had been normal. Examination showed a thin, feverish patient with tachypnoea, a tachycardia of 108/min, and blood pressure 102/58 mm Hg. She also had pronounced but non-tender enlargement of liver and spleen, mild jaundice, and palpable small axillary lymph nodes. Fundoscopy showed several granulomatous choroidal lesions in both fundi.

The patient's husband had died a year before after a long illness with pulmonary tuberculosis which had been treated at a chest clinic. Also her mother had died at home five years earlier from what was thought to be tuberculous pneumonia.

Investigations showed thrombocytopenia ($70 \times 10^9/l$) with normal haemoglobin concentration and total and differential white cell counts. Her reticulocyte count was 12.5% and erythrocyte sedimentation rate 16 mm in first hour. Peripheral blood film showed slight hypochromia with normocytes, occasional normoblasts, and myelocytes. Bone marrow aspirate and biopsy showed normal erythropoiesis with increased immature megakaryocytes and a slight increase in reticulin only. There was no evidence of myelofibrosis, and no acid-fast bacilli or fungi were seen on staining with Gomori's methenamine silver. Serum protein concentration was 51 g/l (albumin 29 g), bilirubin concentration 44.8 $\mu\text{mol/l}$ (2.6 mg/100 ml), and alkaline phosphatase activity 243 U/l; serum transaminase activities were normal. Serum electrolyte values were normal except for sodium (125 mmol(mEq)/l). Serial blood sugar estimations ranged from 8.6 to 16.7 mmol/l (155 to 300 mg/100 ml). The Mantoux test produced no reaction with 1 and 5 tuberculin units. Radiography of the chest showed diffuse pulmonary miliary shadows with scattered nodular lesions (fig 1). A working diagnosis of miliary tuberculosis with underlying diabetes mellitus was made and treatment begun with streptomycin 1 g, rifampicin 450 mg, isoniazid 300 mg, and ethambutol 1.5 g daily.

Despite treatment the patient became weak and apathetic and remained feverish. Three weeks after admission she suddenly became drowsy, very dyspnoeic, and hypotensive (blood pressure 90/60 mm Hg). No other signs were found. Serum urea concentration had risen

Acute disseminated histoplasmosis resembles miliary tuberculosis. This may be overlooked in an urban area endemic for tuberculosis

to 16 mmol/l (96 mg/100 ml), sodium fallen to 118 mmol/l, and chloride and potassium concentrations were 92 and 4.5 mmol(mEq)/l respectively. A provisional diagnosis of acute adrenal failure was made and treatment instituted with hydrocortisone. This promptly corrected the hypotension and hyponatraemia but the patient remained drowsy.

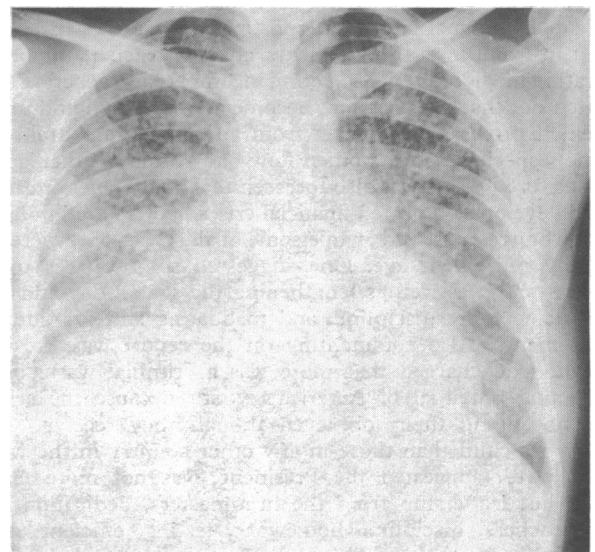


FIG 1—Chest radiograph on admission showing diffuse miliary pulmonary shadows and larger nodular opacities.

A repeat platelet count showed a drop to $5 \times 10^9/l$. An intracranial bleed was suspected but computerised tomographic scan of the brain showed no abnormality. Lumbar puncture yielded clear cerebrospinal fluid containing protein 6.5 g/l, glucose 11.1 mmol/l (200 mg/100 ml), but no cells and no acid-fast bacilli. Arterial blood gas values were oxygen pressure 6.4 kPa (48 mm Hg), carbon dioxide pressure 2.5 kPa (19 mm Hg), standard bicarbonate concentration 16.2 mmol(mEq)/l, and pH 7.4. Conscious level deepened, and a day later the patient died.

Full postmortem examination was not carried out but percutaneous biopsy specimens of liver and spleen showed reticuloendothelial cells packed with *Histoplasma capsulatum*, which was also recovered on culture (figs 2, 3). Subsequent investigation of the patient's four children showed normal chest x ray appearances, and complement fixing antibodies to histoplasma were not detected.

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Comment

This case shows several interesting features and illustrates how a sporadic case of disseminated histoplasmosis might occur in an urban area endemic for *M tuberculosis* and pose a difficult differential diagnosis. This may not be suspected clinically or radiologically. Acute disseminated histoplasmosis is an uncommon presentation of the disease in adults.¹ It is always regarded as indicative of some breach in the host immunological defence mechanism, the nature of which may not be obvious, such as diabetes mellitus in this case.

Another unusual feature was the choroidal lesions, which could

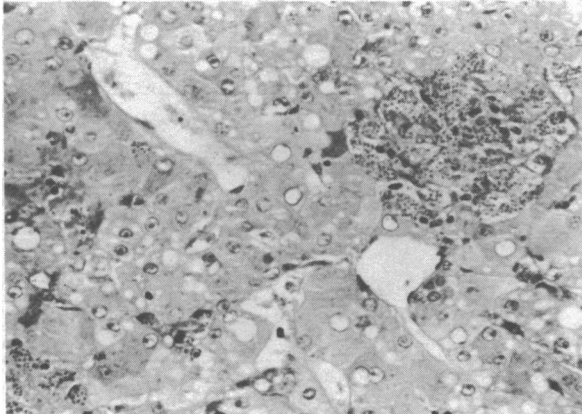


FIG 2—Biopsy specimen of liver showing organisms in Kupffer cells in sinusoids. Haematoxylin and eosin $\times 640$ (original magnification).

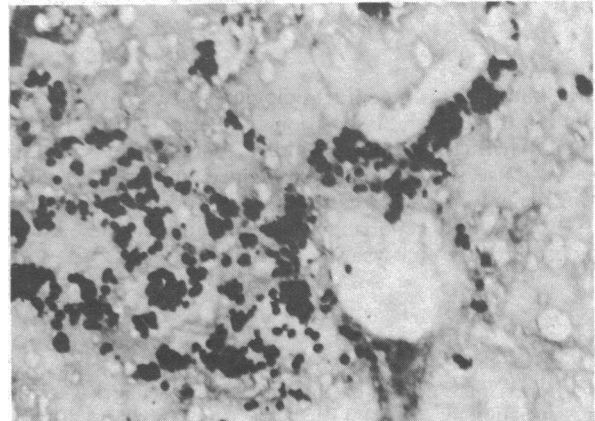


FIG 3—Biopsy specimen of liver stained with Gomori's methenamine silver. Organisms shown darkly stained. $\times 640$ (original magnification).

not be differentiated from choroidal tubercles. Ocular lesions in patients with established histoplasmosis are rare, though various choroidal lesions have been associated with a positive histoplasmin skin test result in endemic areas.² Although there was no mycological proof in our patient, the progressive proliferation of the ocular lesions strongly suggested the aetiology. The bone marrow findings were also interesting. Firstly, the marrow showed increased numbers of megakaryocytes, contrary to the usual finding of reduced numbers in all cases reported by other authors.¹ This supports the hypothesis that the severe thrombocytopenia was due to a peripheral immunological reaction of the

organism with platelets.³ Secondly, silver stains of the trephine biopsy specimen were negative, though in one well studied series⁴ this investigation was diagnostic in all cases examined.

The hyponatraemia, which was corrected by corticosteroid, suggested that acute adrenal failure probably occurred in our patient, though no endocrine studies were carried out.

The diagnosis of histoplasmosis was delayed as the patient had a strong family history of tuberculosis and lived in an area where the disease is common. This emphasises the importance of eliminating causes other than tuberculosis in patients presenting with military shadows in the chest radiograph, even in areas where tuberculosis is endemic.

References

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A patient in her early 50s has type IIa hypercholesterolaemia which has responded to a low cholesterol diet. She has stopped menstruating and is bothered by sweats and an anxiety state, which is relieved by a mild tranquilliser. Is hormone replacement therapy likely to be of any value?

Yes. Natural oestrogen therapy will not only relieve the sweats but should also exert further beneficial effects on the lipid profile. Type IIa hypercholesterolaemia is usually primary—that is, idiopathic—and has been associated with an increased risk of premature coronary artery disease. Until recently the mainstay of treatment was dietary restriction of cholesterol and saturated fatty acids. It is now known, however, that in postmenopausal women natural oestrogen therapy exerts beneficial effects by decreasing the serum low density lipoprotein cholesterol concentration and raising the high density lipoprotein cholesterol level. The high:low density lipoprotein ratio is favourably increased and the atherogenic potential of this lipid abnormality is likely to be reduced. Synthetic oestrogens, such as ethinyloestradiol, have more wide ranging effects, including raising triglyceride levels,

and so are best avoided. Thus type IIa hypercholesterolaemia should not be regarded as a contraindication to exogenous oestrogen therapy. Such treatment will also abolish night sweats, thereby improving sleep patterns, and will reduce anxiety if this is due to oestrogen deficiency. Because of the small risk of endometrial carcinoma a progestogen should be added to the oestrogen therapy for at least 12 days each month. Certain types of progestogens, such as the nonsteroid derivatives, may depress high density lipoprotein cholesterol levels, whereas other progestogens, such as the derivatives of progesterone, do not. A derivative of progesterone is to be preferred in this patient, and a suitable preparation and dosage would be dydrogesterone, 20 mg daily.—M I WHITEHEAD, consultant gynaecologist, London.

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