patients whose carcinomas responded completely or partially to tamoxifen and who developed dermatomyositis or polymyositis within three months of tumour regression.

Case reports

Dermatomyositis, polymyositis, or polymyositis-systemic sclerosis overlap syndrome were diagnosed as definite by the criteria of Bohan *et al.*² Results of investigations are shown in the table. In all our cases muscle biopsies gave results compatible with inflammatory polymyositis and tumour recurrences were confirmed histologically.

Case 1—A 50-year-old woman had a left mastectomy in 1972. In September 1976 she developed a mass in the right supraclavicular fossa and enlarged mediastinal nodes. The recurrent tumour responded completely to radiotherapy and six courses of combination chemotherapy. In June 1979 tumour recurred in the left supraclavicular fossa. Tamoxifen 10 mg twice daily was started, and by August the nodes had completely regressed but she had developed muscle aches and stiffness. In September she had swelling of both arms, proximal muscle weakness, and the characteristic rash of dermatomyositis. She was treated with prednisolone 60 mg daily and tamoxifen was stopped. Dermatomyositis progressed rapidly, however, and she died. Necropsy showed bronchopneumonia and dermatomyositis but no evidence of carcinoma of the breast.

Case 2—A 46-year-old woman had a right lumpectomy and postoperative radiotherapy for breast carcinoma in 1973. In April 1977 she had a right axillary recurrence. Tamoxifen 10 mg twice daily was given and the nodes regressed completely, but over the next three months she developed general muscle weakness, dysphagia, Raynaud's phenomenon, and increased skin pigmentation and induration. Tamoxifen was stopped in January 1979. The weakness improved after three weeks but progressed again when tamoxifen was restarted. Tamoxifen was again stopped, but the weakness did not improve. In July a tumour recurrence in the right breast was excised. She developed perioral telangiectasia. In October she was treated with prednisolone 30 mg daily and methotrexate 15 mg by mouth weekly. Her strength gradually improved.

Case 3—A 60-year-old woman presented in September 1979 with a mass in the left supraclavicular fossa. Biopsy showed a poorly differentiated mucus-secreting adenocarcinoma. Chest radiography showed probable secondary deposits in the left lower lobe. Tamoxifen 10 mg twice daily was given for presumed secondary carcinoma from an undetected breast primary. By January the nodes had partially regressed (from 4×3 to 2×2 cm), with no change on the chest x-ray picture. Three months later she developed aches in her knees, elbows, and hands. In July she had a scaly pruritic rash on her fingers and aches in her thighs. In September she had dysphagia, proximal muscle weakness, cardiomegaly with left bundle-branch block, and the characteristic rash of dermatomyositis. Tamoxifen was stopped. She was given prednisolone 60 mg/day, with initial improvement in muscle weakness, but she died from progressive dermatomyositis in December. Necropsy showed a necrotic mucus-secreting adenocarcinoma in the lung, but the primary site was unknown. Dermatomyositis was confirmed.

Investigations in three patients with dermatomyositis or polymyositis associated with malignancy

Investigation	Case No		
	1	2	3
Creatinine phosphokinase (normal <50 IU/l)	580	145	2146
Alanine transaminase (normal <17 IU/l)	77	21	45
RA latex test	Negative	Positive	Negative
Anti-double-stranded DNA antibody (normal <28×10 ³ units/l)	10	7	Not done
Erythrocyte sedimentation rate (mm in first hour)	104	63	47
Electromyography	Not done	Negative	Not done
Muscle biopsy	Negative	Negative	Negative
Cine swallow	Neuromuscular inco-ordination	Dilated, inert	Dilated, inert
Antinuclear factor	Negative	Positive	Negative
		Speckled nucleolar 1/60	
Electron microscopy	Endothelial microtubular particles	Not done	Not done
Immune complexes (normal (IgG) <100 mg/l)	Not done	71.9	153.6
C3 (normal range 840-1652 mg/l)	Not done	1921	1559
Lymphocyte count	2.13×10 ⁹ /l	1.9×10 ⁹ /l	2.7×10 ⁹ /l

Comment

The cause of dermatomyositis is unknown. Possible mechanisms include autoantibodies³ and cell-mediated reactions to muscle.⁴ Viral-like endothelial microtubular particles have also been seen on electron microscopy,⁵ as in case 1.

Tamoxifen may possibly interact with cell components—for ex-

ample, oestrogen receptors—that on release from dying cells induce an immunological cross-reaction with similar components in connective tissue.

Although tamoxifen was stopped in all the patients, two died from dermatomyositis before complete clearance of tamoxifen could be expected, because of the long plasma half life. If patients develop muscle aches and pains while receiving tamoxifen consideration should be given to the possibility of myositis rather than assuming the symptoms to be non-specific or signs of bone metastases.

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Hormone replacement treatment and benign intracranial hypertension

Benign intracranial hypertension is an uncommon condition associated with many drugs, including oral contraceptives. I report the first case of benign intracranial hypertension associated with hormone replacement treatment.

Case report

A 58-year-old woman was admitted to hospital with constant headache of eight days' duration, dizziness, vomiting, deteriorating visual acuity with transient obscurations, and generalised weakness. Intermittent headaches of increasing frequency and severity over the past three years had correlated chronologically with the start of hormone replacement treatment with Menophas (mestranol and norethisterone).

Examination showed her to be distressed and obese with bilateral papilloedema, mild paresis of the lateral recti, and intact visual fields on confrontation testing. Full investigations including chest radiography, haematological and biochemical screening, and barium series of the gastrointestinal tract showed no abnormality apart from mild diverticular disease of the colon. An isotope brain scan gave normal results and a computed tomogram showed ventricles of normal size. Lumbar puncture yielded clear colourless cerebrospinal fluid under increased pressure (greater than 300 mm cerebrospinal fluid) with normal protein and cell contents.

Benign intracranial hypertension was diagnosed. Hormone replacement treatment was stopped, and she was treated with dexamethasone and later tapering doses of oral prednisolone. This resulted in prompt cessation of headaches, restoration of normal vision, and gradual clearance of papilloedema. She was maintained on decreasing doses of prednisolone over the subsequent six months; on withdrawal there was no recurrence of papilloedema.

Comment

Hormone replacement is widely used in the treatment of acute menopausal symptoms, and the duration of treatment has become increasingly prolonged in many instances for various reasons, including potential prevention of osteoporosis.¹ Conventional combined oral contraceptives have been reported in rare instances to cause benign intracranial hypertension.^{2,3} The occurrence with hormone replacement treatment is, however, surprising in view of the pseudo-physiological nature of the dosage, which in the case of Menophas would account for less than 20% of that of the oestrogen and proges-

terone used in the common combined oral contraceptive preparations estimated over a 28-day cycle.

Obese middle-aged women appear prone to develop this rare condition,⁴ and this risk would appear compounded by prolonged hormone replacement treatment, as in this case. Careful repeated fundoscopic examination is thus mandatory in evaluating persistent headaches in patients taking hormone replacement treatment, as delayed diagnosis and treatment may result in long-term visual impairment.⁵

Both the manufacturers of Menophase, Syntex Pharmaceuticals Limited, and the National Drugs Advisory Board in Dublin have been informed about the case. The latter body communicates with the Committee on Safety of Medicines and the World Health Organisation, who state that they have no record of similar cases.

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Zinc deficiency due to alcoholic cirrhosis mimicking acrodermatitis enteropathica

Zinc deficiency has been established as the cause of acrodermatitis enteropathica, an autosomal recessive disorder of zinc metabolism. The clinical features of acrodermatitis enteropathica may also be seen in acquired disorders of zinc deficiency. We describe a patient in whom the cause of zinc deficiency was alcoholic cirrhosis and malnutrition.

Case report

A 33-year-old woman was admitted to hospital in March 1981 with a history of loss of appetite, abdominal pain, and swelling. On examination she was thin and emaciated and showed signs of liver disease with jaundice, spider naevi, hepatomegaly, ascites, and oedema of the legs. She was evasive about her alcohol intake, but her family confirmed that she had been a heavy drinker, particularly during the past two years. Alcoholic liver disease was diagnosed. After admission she had episodes of gastrointestinal bleeding due to oesophageal varices, which were shown at endoscopy. Initial treatment included a low-sodium, low-protein diet and oral neomycin, lactulose, and diuretics. She required blood transfusion on three occasions.

By May tests of liver function showed improvement but she remained emaciated and malnourished, weighing 35 kg. Parenteral feeding was attempted but was abandoned after nine days as she removed the subclavian line. Nasogastric feeding was not tolerated because of discomfort due to the nasogastric tube. She continued to be fed by mouth with supplements of folate and vitamins. Her general condition showed slow improvement, but she remained anorexic and suffered repeated episodes of nausea and vomiting, and her weight did not increase above 38 kg.

In July she developed typical lesions of acrodermatitis enteropathica around the nose, the angles of the mouth (figure), and in the perineum. There was a similar eruption over the elbows, knees, and dorsal aspect of the fingers.

Zinc deficiency was considered to be likely. Serum zinc concentration was 9.0 µmol/l (58.8 µg/100 ml) (normal 12.7-20.2 µmol/l (83-132 µg/100 ml)), and plasma albumin concentration was 26 g/l (normal 30-50 g/l). Treatment was started with zinc sulphate 220 mg thrice daily by mouth, and within one week the eruption had disappeared. In addition a sacral pressure sore that had been present before the onset of the rash started to heal. She died suddenly in August. At necropsy the cause of death was shown to be micro-nodular cirrhosis of the liver.

Erosive, erythematous eruption around nose and at angles of mouth before treatment.

Comment

An abnormality of zinc metabolism in alcoholic liver disease was first reported in 1957.¹ The mechanism is unknown. Hyperzincuria is reported as a constant feature in hepatic cirrhosis but is not thought to be the cause of low plasma zinc concentrations.² Low plasma zinc concentrations in cirrhosis may reflect the low plasma concentrations of albumin or other zinc-binding proteins. A true decreased zinc content in hepatic tissue has, however, been shown in patients with alcoholic liver diseases.³

Poor nutrition may contribute to zinc deficiency in alcoholics, and spirits and beer have a low zinc content. Malnutrition was certainly a factor in our patient. Long-term diuretic treatment causes increased urinary zinc excretion⁴ and in this case may have been a contributory factor.

The skin features of zinc deficiency were pronounced in our patient, the well-demarcated, erosive, erythematous eruption of the face, perineum, and extensor surfaces of the limbs and fingers being characteristic. Other cutaneous features of zinc deficiency that may occur include asteatotic eczema, alopecia, thin lustreless hair, nail dystrophy, and chronic paronychia.⁵

A single measurement of plasma or serum zinc concentration is not a good indicator of total body zinc stores. This patient's response to treatment, however, suggests that she indeed had acute zinc deficiency. This case appears to support the view that the best indicator of zinc deficiency is the response to treatment.

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