After three months, during which his joint pains and dyspnœa were only partially controlled, his hæmoglobin had risen to 14·7 g/100 ml and the Westergren ESR had fallen to 58 mm in 1 hour.

August 1969: The patient now showed central cyanosis on moderate effort and required further hospitalization because of increasing dyspnœa and joint pains and because he had suffered chest pains, mostly of a dull continuous type, unrelated to effort or eating but possibly influenced by changes in chest posture. Serial ECGs remained normal. Examination now showed little objective evidence of arthropathy despite the continuing widespread joint pains and stiffness. There were widespread basal crepitations and effort dyspnœa and cyanosis, evident on walking only some 10 metres. For the first four weeks in hospital he displayed a remittent pyrexia up to 39°C (102·2°F).

Radiographs of the chest showed no change from the basal patchy consolidation and reticulation seen over the previous eighteen months.

Investigations: Hb 10·9–11·6 g/100 ml, with evidence of iron deficiency, normal WBC and platelet counts. ESR (Westergren) 104–122 mm in 1 hour. Proteins: albumin 2·7, globulin 5·0 g/100 ml, with electrophoresis showing a marked excess of diffuse γ-globulin. Urea, electrolytes and blood and urine cultures all normal. LE cell phenomenon now positive and immunofluorescent ANF positive at a titre of 1:250.

Within 48 hours of increasing the daily prednisolone dosage from 7·5 to 60 mg the temperature had returned to normal and the patient was free of his joint and chest pains. Over the next ten days the prednisolone was reduced to 20 mg daily and effort dyspnœa remained his only symptom.

At this stage it was decided, because of the severe deterioration of the patient's condition over the past two years, with a very high ESR, deranged proteins and high steroid requirement, to use azathioprine which was started in a dose of 125 mg daily.

Over the past six months of outpatient follow up, the patient's progress has been maintained. He can now walk up to 800 metres comfortably and does not display effort cyanosis. It has been possible to reduce his therapy to azathioprine 100 mg and prednisolone 6 mg daily. After six months of azathioprine hæmoglobin is 13·6 g/100 ml, and WBC and platelet counts are normal; ESR 65 mm in 1 hour (Westergren); total serum proteins 7·9 g/100 ml (albumin 3·6, globulin 4·3), electrophoretic pattern normal. Blood urea and electrolyte levels remain normal.

Perhaps the most remarkable feature has been the improvement in the respiratory function tests (Dr Paul Forgacs), despite the constancy of the radiological appearances. By contrast with the tests of March 1968, the results obtained in March 1970 show improvement in FVC and carbon monoxide transfer: FVC 3, FEV 2·5 litres (predicted 3·3), VC 2·9 litres, CO transfer factor 18 ml/min per mmHg.

Discussion

There seems no doubt that this patient has fibrosing alveolitis on clinical, radiological and physiological grounds. Patients with rheumatoid disease in whom this occurs nearly always develop a high titre of circulating rheumatoid factor and usually have marked erosive change and nodule formation.

In this patient the low level and eventual absence of circulating rheumatoid factor, the absence of erosive change and of nodules even after years of progressive disease, the repeatedly positive LE cell preparations and the presence of antinuclear factor in high titre were all pointers to a diagnosis of systemic lupus erythematosus.

While pulmonary changes are fairly common in systemic lupus erythematosus they usually take the form of pleural or pneumonic episodes, often of short duration and not generally of major clinical importance; progressive incapacity from fibrosing alveolitis does not seem to be a usual complication of this disorder.

This man was a pulmonary cripple at the time that treatment with azathioprine was started; it seems reasonable to attribute to this drug the improvement in pulmonary function shown by testing and the remarkable clinical improvement that has occurred since.

Xanthomatosis, Hyperlipoproteinæmia (Type II, Fredrickson), Gout, Cardiac Infarction

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Man, aged 43

First attended hospital on 22.5.68 complaining of pain in the chest for the past few months; ECG showed evidence of posterior cardiac infarction.

At this time he was found to have painless swellings of the tendo achillis, with tenderness and swellings over the tibial tuberosities. There were nodules in the extensor tendons of the left middle finger. These swellings had been present for many years without symptoms. Other investigations: serum cholesterol 860, serum uric acid 6·1 mg/100 ml. X-rays of hands and ankles normal.

He was treated with clofibrate (Atromid-S) 250 mg twice a day. This produced little change in the cholesterol level so the clofibrate dosage was increased to 500 mg three times daily. He now complained of increasing pain in the ankles and on 21.1.69 he developed acute redness and swelling of the right foot. The appearance of the foot seemed typical of gout; serum uric acid 7·4 mg/100 ml.

The symptoms and signs were rapidly controlled by indomethacin 25 mg four times a day, and there have been no further attacks of this type. On subsequent occasions the serum uric acid has not risen above 6·4 mg/100 ml. 20.6.69: total serum lipids 930, serum cholesterol 300 mg/100 ml. The serum appeared quite clear. A lipoprotein electrophoretic pattern showed normal α-lipoproteins, increased β-lipoproteins, with normal prebeta-lipoproteins and a normal chylomicron area. 5.2.69: Total cholesterol 413, triglycerides 82·2 (normal), phospholipids 322 mg/100 ml.

These clinical and lipoprotein findings are consistent with hyperlipoproteinæmia Type II (Fredrickson *et al.* 1967).

Progress: Treatment was continued with clofibrate and indomethacin and the xanthomata have decreased in size, but he still gets attacks of pain in the chest which are relieved by trinitrin. The serum cholesterol level did not change greatly and cholestyramine 4 g daily was given but the patient did not tolerate this drug. On one occasion when clofibrate was discontinued for 14 days the pain in his ankles became worse but there was no recurrence of the acute swelling.

His three children have been investigated and two appear to be affected.

Discussion

Although the serum uric acid level in this patient was not usually raised, on one occasion he had an attack of gout with a raised serum uric acid and this seemed to be precipitated by an increase in the dose of clofibrate and later there was a return of pain when the clofibrate was stopped.

The relationship between hypercholesterolæmia and hyperuricæmia has been investigated on several occasions without any firm agreement being reached by various authors.

Harris-Jones (1957) considered that hypercholesterolæmia had an effect on uric acid metabolism and Borrie (1969) states that hyperuricæmia is common in hyperlipoproteinæmia Type II (Fredrickson *et al.* 1967). However, Jensen *et al.* (1966), studying a Danish family with hypercholesterolæmia, found no evidence of a general increase in uric acid level. Mishkel (1967) agreed with this view. Berkowitz (1964) considered that hyperuricæmia occurred only in the presence of a high triglyceride level which is not a feature of Type II cases, and which was not present in this case.

Harris-Jones (1957) considered that cholesterol-lowering agents might affect the uric acid level and felt that these should be studied, and Trevaks & Howell (1965) showed that clofibrate had a mild uricosuric effect without causing a sustained fall in serum uric acid. It may have been this effect which occurred in this case, but it should also be remembered that a transient and migratory type of arthritis may occur in familial hypercholesterolæmia without gout (Khachadurian 1968). The exact relationship between these various conditions remains to be elucidated.

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Whipple's Disease

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A labourer at a milk depot, aged 61, presented in 1963 with an acute inflammatory arthritis involving wrists, elbows, knees and ankles and was admitted to St Thomas's Hospital. All investigations were negative and his arthritis settled spontaneously in three weeks. He has had no further joint symptoms since.

He presented again at King's College Hospital in November 1969 with a history of persistent diarrhœa which had started abruptly four months before. He had lost 11 kg in ten weeks.

On examination: Skin showed increased pigmentation; blood pressure 130/65; no other abnormality apart from limitation of wrist movement.

Investigations revealed evidence of small bowel malabsorption. The jejunal biopsy showed blunting of villi, dilatation of lymphatics, foamy histiocytes in the submucosa with periodic-acid-Schiff-positive inclusions, these features being diagnostic of Whipple's disease. X-rays of hands