SHORT REPORTS

Oldest case of sarcoidosis in the world

Acute sarcoidosis in an octogenarian is rare. In this case bone-marrow trephine biopsy uncovered an unsuspected diagnosis.

Case report

An 81-year-old spinster presented with a six-month history of anorexia, weight loss of 6.35 kg, and lower abdominal distension which was always relieved by an episode of diarrhoea. The only other symptoms were night sweats and nocturnal leg cramps, both of which had lasted for one month. Her history included Bell's palsy at the age of 70, a severe epistaxis requiring hospital admission when she was 79, and longstanding congestive cardiac failure, which had been controlled by digoxin and diuretics. These were her only medications.

On examination she had no fever, there were palpable mobile lymph glands in both axillae and both inguinal regions, her liver was enlarged 3 cm below the costal margin, but her spleen was not palpable. She had a persisting partial right facial nerve palsy. Chest x-ray examination showed bilateral hilar lymphadenopathy. The result of the Mantoux test was negative with 10 IU of purified protein derivative. Haemoglobin concentration was 12.5 g/dl; mean cell volume 81 fl; white blood count $10.9 \times 10^9/l$, with a slight lymphocytosis; erythrocyte sedimentation rate 84 mm in the first hour; urea and electrolytes normal. Serum aspartate aminotransferase activity was transiently raised up to 31 IU but returned to normal without changes in the electrocardiogram. Serum protein concentration was 95 g/l, and electrophoresis showed decreased α_2 -globulin with increased gammaglobulin. Serum and 24-hour urinary calcium concentrations were normal. Results of respiratory function tests were as follows: forced vital capacity 1.5 l, forced expiratory volume in 1 s 1.0 l, transfer factor reduced at 2.0 mmol/min/kPa (6.0 ml/min/mm Hg) (predicted value 6.4 mmol/min/kPa (19.0 ml/min/mm Hg)). Ophthalmological examination, including slit-lamp inspection and lacrimal gland secretion, showed no abnormality. X-ray examinations of the hands and feet showed them to be within normal limits for age. Tissue for histological examination was obtained in the first instance by Jamshidi trephine bone-marrow biopsy. This showed scanty normal marrow elements with depleted iron stores and multiple non-caseating granulomas (see figure). Sections of a biopsied axillary lymph node showed multiple small non-caseating epithelioid and giant-cell granulomas. The result of the Kveim test (Colindale K19 type 1 lot 9) was strongly positive on histological examination.

Comment

The patient was found to have peripheral lymphadenopathy and bilateral hilar lymphadenopathy. The symptoms of night sweats led to a suspicion of a lymphoma, and we performed a marrow biopsy to save her from undergoing general anaesthetic for a lymph-node

Tissue from trephine bone-marrow biopsy showing scanty normal marrow elements and multiple non-caseating granulomas. Haematoxylin and eosin $\times 200$ (original magnification).

biopsy. This showed non-caseating granulomas. A full investigation for sarcoidosis followed.

Acute sarcoidosis was diagnosed by the finding of multiple system disease with non-caseating epithelioid and giant-cell granulomas, along with a positive Kveim test and negative tuberculin test.

We believe that this is the oldest patient with acute sarcoidosis ever reported. Population surveys and large series of cases of sarcoidosis¹ have shown a peak incidence in adults aged 20 to 40 years. Most cases reported outside this age group have been below the age of 15,² and cases presenting after 70 years are extremely rare, although Haugh³ has described the clinical course and necropsy findings in an octogenarian with chronic sarcoidosis of 30 years' duration.

Within a period of six weeks our patient's symptoms had resolved, although results of a chest x-ray examination at six months had not altered. Clinical examination showed spontaneous resolution of the peripheral lymphadenopathy, and the patient continues to improve. Corticosteroid treatment was not given.

¹ Douglas AC. Sarcoidosis in Scotland. *Am Rev Respir Dis* 1961;**84**, suppl: 143-7.

² Siltzbach LE, Grundberg CM. Childhood sarcoidosis—a study of 18 patients. *N Engl J Med* 1968;**279**:1239-45.

³ Hauch EW. Sarcoidosis in the aged—a report of a case. *Geriatrics* 1954;**9**: 334-6.

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Levodopa dosage and ventilatory function in Parkinson's disease

Ventilatory function is impaired in many patients with Parkinson's disease. This is apparently due to the disease itself and may relate to its severity.¹ Mehta *et al* reported that simple tests showed improved ventilatory function when patients with Parkinson's disease were treated with levodopa² and suggested that measurement of ventilatory function might provide an objective index response to treatment. We examined the relation between the clinical signs of Parkinson's disease and various tests of respiratory function in patients receiving varying doses of levodopa in a double-blind randomised trial.

Patients, methods, and results

Three men and three women with Parkinson's disease aged 62-78 agreed to participate in the study, which was approved by the area health authority ethical committee. They were already being treated with levodopa and carbidopa in combination, Sinemet, which had been titrated before the study to an optimal dose as judged by clinical response. The mean levodopa dose was 316.7 mg/day combined with 31.7 mg of carbidopa. The study periods each lasted three weeks, during which the patients received in double-blind fashion and randomised order doses of levodopa that were respectively 30% more, 30% less, or the same as their previous "optimum" dose. The daily total number of tablets was constant throughout the study, the tablets were individually packaged, and, when appropriate, placebo tablets were included to maintain the double-blind design. The mean doses of levodopa in each phase were 216.7 mg, 416.7 mg, and 316.7 mg with appropriate doses of carbidopa.

Assessments at the end of each treatment phase consisted of a clinical symptom and sign score,³ lying and standing pulse rate and blood pressure, self-scored visual analogue scale, and pulmonary function tests. The pulmonary function tests included peak flow rate, forced expiratory volume in one second, vital capacity, maximum voluntary ventilation, and measurement of maximum inspiratory and expiratory pressures. The patients were all trained in the performance of the pulmonary function tests before the formal study and were selected on the basis of an ability to co-operate with the tests.

Decreasing the levodopa dosage resulted in a significant impairment in the clinical rating scale of Parkinsonian signs. The mean score with standard treatment was $19.5 (\pm \text{SEM } 2.35)$ and on the reduced dose $22.7 (\pm 3.42)$ ($p < 0.05$) (table). Increasing the dose produced no significant improvement in rating, although two patients experienced dyskinesia. There was no significant change in any other measurement. In particular, respiratory function did not change (table). The peak flow rate and maximum voluntary ventilation were significantly lower ($p < 0.05$ and $p < 0.02$ respectively) than values predicted using the patients' age, sex, and height* (table). There were no significant differences from the predicted value in forced expiratory volume in one second or vital capacity. The maximum pressure values during inspiration and expiration were probably low, though there are no appropriate control data for patients of this age.

Mean ($\pm$ SEM) summed scores of clinical signs of Parkinsonism and results of respiratory function tests at three dosages of levodopa. Also shown are mean predicted values⁴ based on patients' age and height

	Values at:			Predicted value
	Standard dose	Increased dose	Reduced dose	
Summed clinical sign score	19.5 ± 2.35	19.3 ± 2.8	$22.7 \pm 3.42^*$	
Maximum voluntary ventilation (l/min)	55.3 ± 8.9	63.8 ± 10.1	58.5 ± 10.8	95.1^*
Peak flow rate (l/min)	246.0 ± 30.3	237.0 ± 30.4	251.5 ± 41.6	405.5^{**}
Forced expiratory ventilation in one second	1.5 ± 0.21	1.6 ± 0.32	1.6 ± 0.27	1.9
Vital capacity (l)	2.33 ± 0.33	2.28 ± 0.31	2.36 ± 0.33	2.6
Maximum inspiratory pressure (kPa)	-5.75 ± 1.55	-4.28 ± 1.21	-5.98 ± 1.27	
Maximum expiratory pressure (kPa)	7.23 ± 1.22	6.66 ± 0.83	6.78 ± 1.15	

Compared to results during standard treatment: * $p < 0.05$; ** $p < 0.02$.

Comment

Improvement in maximum voluntary ventilation,⁶ peak flow rate, and forced expiratory volume in one second² has been reported after levodopa treatment has been started in patients with Parkinson's disease. We therefore wished to establish whether the assessment of respiratory function in patients with Parkinson's disease would be of use as a simple index of optimal therapeutic response. The patients studied were receiving fairly low doses of levodopa, which raises the possibility that they might have had a mild form of Parkinson's disease. Nevertheless, there was still evidence of ventilatory impairment as indicated by a low maximum voluntary ventilation and peak flow rate. Despite significant deterioration in the clinical rating scale when the dose of levodopa was reduced, however, there was no significant change in any of the respiratory function tests. Maximum voluntary ventilation and peak flow rate are more effort dependent than spirometric variables, and presumably the low values in Parkinson's disease reflect muscle disorders, perhaps akinesia in particular.

Our findings suggest that the use of respiratory function tests as an independent measure of the efficacy of drugs in Parkinson's disease does not seem to be helpful.

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¹ Nev HC, Connolly JJ, Schwertley FW, Ladwig HA, Brody AW. Obstructive, respiratory dysfunction in parkinsonian patients. *Am Rev Respir Dis* 1967;95:33-47.

² Mehta AD, Wright WB, Kirkby BJ. Ventilatory function in Parkinson's disease. *Br Med J* 1978;ii:1456-7.

³ Calne DB, Reid JL, Vakil SD, et al. Idiopathic Parkinsonism treated with an extracerebral decarboxylase inhibitor in combination with levodopa. *Br Med J* 1971;iii:729-32.

⁴ Cotes JE. *Lung function assessment and application in medicare*. 4th ed. Oxford: Blackwell Scientific, 1979:369-70.

⁵ Langer H, Woolf CR. Changes in pulmonary function Parkinson's syndrome after treatment with L-dopa. *Am Rev Respir Dis* 1971;104:440-42.

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Effect of long-term treatment with beta-blocking drugs on plasma lipids and lipoproteins

Recent studies have shown that beta-blockers increase plasma concentrations of triglycerides and urate and reduce concentrations of high-density lipoprotein (HDL)-cholesterol.^{1,2} As the treatment has lasted only two to 12 months in most of these studies, we investigated whether a similar effect could be shown in patients with essential hypertension³ who had been treated with beta-blockers for an average of 54 months, (range 8-79) before the study.

Patients, methods, and results

Fifty-one patients were taking beta-blockers: 47 were treated with propranolol (160-480 mg/day), two with atenolol (100 mg/day) and two with metoprolol (200 mg/day). Twenty-five men and 16 women (80% of the group) also received hydroflumethiazide (50 mg/day), which had been given for a similar period of time. Forty-two patients who were not on beta-blockers served as controls; they were taking methyldopa (750-2000 mg/day), clonidine (0.075-0.450 mg/day), and prazosin (1.5-6.0 mg/day). Twenty-one of these men and 13 women (81% of the group) also received 50 mg hydroflumethiazide per day. The controls had been treated for a similar length of time to the patients taking beta-blockers. As diuretics also affect plasma concentrations,⁴ the values in seven patients treated with beta-blockers either alone or combined with hydralazine were also compared with those in seven age-matched untreated hypertensive patients. All patients had been fasting for 12 hours before blood samples were drawn and had omitted their morning medication. Weight and height were also recorded and the relative weight calculated. Plasma triglyceride and total cholesterol concentrations were measured enzymatically (Boehringer Mannheim). HDL-cholesterol was measured after precipitation of low density (LD) and very low density (VLDL) lipoproteins from plasma with MgCl_2 and dextran sulphate.⁵ Urate concentrations were measured enzymatically.⁶

There were no significant (unpaired t test) differences in any of the investigated values between the groups. HDL-cholesterol tended to be lower in men treated with beta-blockers, whereas the opposite was seen in women treated with beta-blockers and in patients on beta-blockers who were not taking diuretics. Triglyceride values tended to be higher in men on beta-blockers and patients on beta-blockers not taking diuretics. As can be seen from the t values, these trends were far from significant. Urate concentrations correlated positively with triglyceride values ($r = 0.62$; $p < 0.0001$) and negatively with HDL-cholesterol values ($r = -0.44$; $p < 0.0001$).

Comment

The reason why this study failed to show that long-term treatment with beta-blockers has an effect on plasma lipid and urate concentra-

Plasma lipids and urate and relative weights in patients on long-term beta-blocker treatment and controls with essential hypertension (values are means $\pm$ SD)

	On beta-blockers*	Not on beta-blockers	t Values
Men			
No	31	26	
Mean age (and range) yrs	57 (41-71)	58 (41-70)	0.17
HDL-cholesterol (mmol/l)	1.12 ± 0.38	1.20 ± 0.30	0.89
Total cholesterol (mmol/l)	6.53 ± 1.33	6.40 ± 0.84	0.50
Total triglycerides (mmol/l)	2.42 ± 0.95	1.93 ± 1.65	0.08
Urate ($\mu\text{mol/l}$)	427 ± 138	445 ± 198	0.42
Relative weight (kg/m^2)	28 ± 4	28 ± 3	0.82
Women			
No	20	16	
Mean age (and range) yrs	56 (42-69)	56 (42-67)	0.19
HDL-cholesterol (mmol/l)	1.46 ± 0.28	1.28 ± 0.29	1.85
Total cholesterol (mmol/l)	7.41 ± 1.29	7.17 ± 1.22	0.58
Total triglycerides (mmol/l)	2.03 ± 1.07	2.09 ± 1.16	0.42
Urate ($\mu\text{mol/l}$)	373 ± 108	360 ± 105	0.36
Relative weight (kg/m^2)	29 ± 5	28 ± 5	0.48
Not on diuretics†			
No	7	7	
Male:female	3:4	3:4	
Mean age (and range) yrs	49 (31-60)	50 (32-63)	0.42
HDL-cholesterol (mmol/l)	1.26 ± 0.41	1.21 ± 0.26	0.40
Total cholesterol (mmol/l)	6.86 ± 1.22	6.76 ± 1.01	0.16
Total triglycerides (mmol/l)	2.09 ± 1.13	1.60 ± 0.95	0.89
Urate ($\mu\text{mol/l}$)	388 ± 121	392 ± 96	0.07
Relative weight (kg/m^2)	31 ± 7	29 ± 7	0.52

*Mean duration of treatment ($\pm$ SD) was 52 ± 16 months (range 8-72 months) for men and 55 ± 11 months (range 35-79 months) for women.

†Patients treated with beta-blockers either alone or combined with hydralazine v untreated patients.

Conversion: SI to traditional units—Cholesterol: 1 mmol/l $\approx$ 39 mg/100 ml. Triglycerides: 1 mmol/l $\approx$ 89 mg/100 ml. Urate: 1 $\mu\text{mol/l}$ $\approx$ 0.0168 mg/100 ml.