pressure was 145/105 mm Hg. One year later she complained of episodic headaches, chest pain, palpitations, and blanching of the hands. Urinary catecholamine and vanillylmandelic acid concentrations were normal. For the next three years she had recurrent abdominal pains and episodes of anxiety associated with pallor. In January 1977 she was given propranolol 40 mg twice daily for hypertension. Several weeks later she attended another hospital with acute pulmonary oedema. Her presenting blood pressure was 130/90 mm Hg. She also had symptoms similar to the previous paroxysms. Urinary catecholamine concentrations were high.

When first seen at the Royal Melbourne Hospital, her blood pressure was 110/80 mm Hg. This rose to 190/130 mm Hg on firm palpation of the right loin. She was placed on both alpha- and beta-adrenergic blocking agents. Arteriography showed a rounded mass medial to the right kidney. At exploration a pheochromocytoma 5 cm in diameter was excised. Although her blood pressure was unstable intraoperatively her postoperative course was relatively uneventful. She has since remained normotensive on no medication.

Comment

The pulmonary oedema in these patients shortly after starting treatment with propranolol may have resulted from interruption of the beta-adrenergic drive to the heart associated with vasoconstriction mediated by unopposed alpha-adrenergic stimulation. The ECG and enzyme evidence in case 1 suggests that myocardial necrosis, a recognised complication of catecholamine excess, may have contributed to the acute pulmonary oedema. Neither patient's blood pressure was raised when they reached hospital, although this may have reflected their impaired cardiac output. While a causal relationship between beta-adrenergic blockade and precipitation of pulmonary oedema cannot be proved in either case, the sequence of events is suggestive in both. The events described support the contention that beta-adrenergic blockers should not be used before alpha-adrenergic blockade in patients suspected of having pheochromocytomas.

¹ Melman, K L, in *Textbook of Endocrinology*, ed R H Williams, 5th edn, p 313. Philadelphia, W B Saunders and Co, 1974.

² Thomas, D J B, et al, *British Medical Journal*, 1977, **1**, 688.

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Rheumatoid arthritis: C-reactive protein and erythrocyte sedimentation rate during initial treatment

Patients with rheumatoid arthritis (RA) are generally treated first with aspirin or other non-steroid anti-inflammatory drugs. The usual view, to which we subscribed when suggesting a systematic approach to treatment,¹ is that many patients will not need additional drug treatment and that a period of observation will identify them. We now re-examine this view.

Patients, methods, and results

There were 76 patients, 52 women and 24 men, with definite or classical RA (American Rheumatism Association criteria). Their mean age was 55.2 and mean duration of RA 5.6 years; 57 had positive Rose-Waaler tests. They were all newly referred patients who were being treated with aspirin, indomethacin, or ibuprofen. No patient had had gold, corticosteroids, penicillamine, antimalarial, or cytotoxic drugs. Serum C-reactive protein concentration (CRP) was measured by radial immunodiffusion using commercially available standards (Hoechst), which gives values about half those previously reported by us.² Erythrocyte sedimentation rate (ESR) was measured by the Westergren method. Student's *t* tests for paired variants were applied to the results.

At the first consultation serum CRP ranged from 0-328 mg/l, mean 63 mg/l; ESR from 5-161 mm in 1 h, mean 57.7 mm in 1 h. After 12 weeks

Relation between serum CRP at first attendance and 12 weeks later. Hatched area denotes values falling to <20 mg/l.

mean serum CRP had fallen by 8.5 ± 5.0 mg/l and mean ESR by 3.8 ± 2.7 mm in 1 h. The differences were not significant. The differences between the initial values for serum CRP and values at 12 weeks in individual patients show (fig) that when CRP was initially above 100 mg/l it had usually fallen; with lower initial values serum CRP rose or fell in roughly equal numbers of patients. There were only 10 patients whose serum CRP fell from above 20 mg/l to that figure or below. The results for ESR were similar, though the tendency for higher initial values to fall was less obvious than with CRP. There were only eight patients whose ESR fell from above 30 mm in 1 h to below that figure.

Comment

In 76 patients with RA, probably representative of any group of newly referred patients being treated with aspirin-type drugs only, there were no significant changes in mean serum CRP or ESR in the first 12 weeks. The result was unexpected. Although neither aspirin nor indomethacin influence these measurements³ we had assumed that spontaneous remissions in a proportion of patients, perhaps one-third, would have a demonstrable effect on the group as a whole. If we are correct in asserting that serum CRP and ESR levels reflect the progress of RA,² and that values for serum CRP above 20 mg/l or for ESR above 30 mm in 1 h indicate detectable radiographic deterioration,⁴ we must assume that most of the patients referred to us had progressive disease when first seen and that the position had not significantly altered after 12 weeks. Thus the policy of using aspirin or other non-steroid anti-inflammatory drugs to relieve symptoms and allowing three months to observe progress did identify about 10% of patients satisfactorily controlled. For most of them, however, it only unnecessarily delayed consideration of more active treatment. We suggest that treatment with drugs such as gold, capable of lowering acute-phase protein levels⁵ and thus likely to alter the course of the disease by reducing the rate of radiological progression, should usually be begun soon after the first consultation if serum CRP and ESR values are substantially raised.

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¹ Constable, T J, et al, *Lancet*, 1975, **1**, 1176.

² McConkey, B, Crockson, R A, and Crockson, A P, *Quarterly Journal of Medicine*, 1972, **41**, 115.

³ McConkey, B, et al, *Quarterly Journal of Medicine*, 1973, **42**, 785.

⁴ Amos, R A, et al, *British Medical Journal*, 1977, **1**, 195.

⁵ McConkey, B, et al, *Rheumatology and Rehabilitation*, 1976, **15**, 230.

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