Barium swallow showing contracted left cricopharyngeus (arrowed) obstructing flow on this side and barium passing down on right side.

has been divided. There has been some debate about the innervation of the cricopharyngeus. Asherson² states that the recurrent laryngeal nerve is responsible and blames "achalasia of the cricopharyngeal sphincter" on trauma to recurrent laryngeal nerves.³ None of the patients described, however, had symptomatic dysphagia.

More recent work,⁴ including dissections, has failed to support this view and suggests that the cricopharyngeus is innervated unilaterally by the pharyngeal branch of the vagus via the pharyngeal plexus. The active side will push barium into the paralysed and therefore atonic side of the pharynx.¹ The failure of relaxation or incoordination of cricopharyngeus on the denervated side causes formation of a pocket and thus the appearances of achalasia of the cricopharyngeus.

Some improvement was achieved in this patient's swallowing by performing cricopharyngeal myotomy and subsequent dilation. He was then able to take a reasonable diet and maintain a somewhat reduced weight. Further surgical interference was not attempted.

I wish to thank Dr Stuart Field and Mr Alan Ardouin for their help and Mr Michael Williams for permission to report this case.

¹ Seaman, William B, *Alimentary Tract Roentgenology*, ed A R Margulis and H J Burnhenn, Saint Louis, The C V Mosby Company, 1967.

² Asherson, N, *Proceedings of the Royal Society of Medicine*, 1962, **55**, 117.

³ Asherson, N, *Journal of Laryngology*, 1950, **64**, 747.

⁴ Lund, W S, and Ardran, G M, *Annals of Otolaryngology and Rhinology*, 1964, **73**, 599.

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Erythema nodosum and brucellosis

Erythema nodosum is a distinct clinical entity which may be an important cutaneous sign of systemic disease. Its uniform appearance gives no indication of the underlying cause nor does the characteristic histopathology.¹ It is thought to represent a hypersensitivity phenomenon² but not the classic Arthus type; its close association with conditions having delayed hypersensitivity suggests a cell-mediated mechanism.³ The commonest cause of erythema nodosum in Britain

up to 20 years ago was primary tuberculosis, but is now probably sarcoidosis; whereas in the USA streptococcal pharyngitis is the predominant cause on the east coast and coccidioidomycosis in the west.³ Other recognised associations include drug hypersensitivity, leprosy, and ulcerative colitis. An association between erythema nodosum and brucellosis has not been recorded in the past 10 years and is not mentioned in the standard textbooks of medicine. The following case history is reported because of the importance of diagnosing brucellosis, for which there is effective treatment.

Case report

A 38-year-old man was admitted to hospital in January 1974 with pain which started four weeks previously in the ankles and knees and spread to spine, hips, wrists, and hands. He had had drenching night sweats for 10 days. Five days before admission he developed typical erythema nodosum on the front of both legs below the knees. The only drug he had taken was two tablets of naproxen prescribed a few days earlier. His occupation involved metal weighing, principally gold and silver but also brass, nickel, and bronze. He had had no contact with livestock or unpasteurised milk, nor had he recently left the city. He had a low-grade fever but was otherwise fit. The typical rash on the legs was accompanied by swelling of soft tissues around the joints. He continued to have night sweats and fever over the next few days.

The results of investigations showed: haemoglobin 13.2 g/dl, white cell count $7 \times 10^9/l$ ($7000/mm^3$), and erythrocyte sedimentation rate (ESR) 40 mm in 1 hour; chest radiograph and liver function were normal; Mantoux test reaction (1/1000) was negative; sheep red cell agglutination test result was normal; and he was negative for antinuclear factor; *Brucella abortus* agglutination titre $> 1/3200$. He was treated for six weeks with tetracycline and all his symptoms and signs disappeared. The ESR fell to normal and the *Br abortus* agglutination titre was $< 1/25$ at the end of treatment and six months later when he appeared fit.

Comment

Brucellosis is still endemic in Britain and may be difficult to diagnose unless suspected. It should be considered in patients with erythema nodosum in whom the usual investigations do not reveal the underlying cause.

¹ Cecil-Loeb Textbook of Medicine, ed P B Beeson and W McDermott, 13th edn, p 846. Philadelphia, Saunders 1971.

² Samter, M, *Immunological Diseases*, ch 28, 29. London, Churchill Livingstone, 1971.

³ Sherman, W B, *Hypersensitivity, Mechanisms and Management*, p 370. Philadelphia, W B, Saunders, 1968.

⁴ James, D Geraint, *British Medical Journal*, 1961, **1**, 853.

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Extramedullary plasmacytomas, renal failure, and intermittent haemodialysis

Chronic renal failure in multiple myeloma is associated with a poor prognosis, and treatment by dialysis rarely prolongs life.¹ Extramedullary plasmacytomas, however, may be associated with prolonged survival, and we have been unable to find any report of renal failure complicating the disease. We describe here a patient with extramedullary plasmacytomas who developed irreversible renal failure and who was maintained on regular dialysis.

Case report

A 56-year-old plumber was admitted to hospital in October 1974 with a four-month history of bilateral loin pain, nocturia, weight loss, and feeling unwell. He was pale with periorbital oedema, and had tenderness in his right

loin. His initially raised blood pressure soon returned to normal, and no other abnormal features were noted on physical examination. Investigations showed: haemoglobin 10.7 g/dl; leucocytes $6.8 \times 10^9/l$; platelets $169 \times 10^9/l$; sternal marrow, active haemopoiesis with no increase in plasma cells; blood urea 34 mmol/l (204 mg/100 ml); serum creatinine 1350 $\mu\text{mol/l}$ (15 mg/100 ml); serum potassium 7.1 mmol/l (7.1 mEq/l); serum albumin 3.4 g/l; creatinine clearance 1 ml/min; and 24-hour urine output 150 ml. Serum electrophoresis in cellulose acetate was normal but immunoelectrophoresis of plasma and urine showed free kappa light chains. There was mild immunoparesis (IgA 63×10^3 IU/l; IgG 81×10^3 IU/l; IgM 64×10^3 IU/l), and the serum complement (C3) was 1.58 g/l. Radiography showed a soft-tissue mass embracing the bodies of the eighth to tenth thoracic vertebrae. Bronchoscopy, mediastinoscopy, barium swallow, and skeletal survey were non-contributory. At thoracotomy two tumours were found in the posterior mediastinum. Histologically there was dense plasma cell infiltration with many binucleate and multinucleate cells. High-dose intravenous pyelography with nephrotomography showed poorly functioning, normal sized kidneys. Ascending ureterograms were normal. Renal biopsy showed the characteristic histology of a myeloma kidney, with brittle, laminated casts and tubules surrounded by multinucleate giant cells.

The patient was maintained on haemodialysis twice a week using a hollow fibre dialyser. At the time of writing he had survived for 14 months. During that time he had had more than 100 dialyses, an initial three-week course of radiotherapy to the mediastinum (total dose 3070 rads), five courses of melphalan 5 mg daily for not longer than seven days, infrequent blood transfusions, and the routine management of chronic renal failure. Although his weight had decreased from 81 to 58 kg, his general condition was satisfactory apart from some transient subcutaneous swellings, particularly at the site of the arteriovenous fistula. Blood pressure remained normal. Lately fragmented erythrocytes appeared in the peripheral blood but coagulation studies showed no evidence of intravascular coagulation. Recent skeletal survey showed no lytic lesions or generalised decalcification, and bone marrow biopsy of the posterior iliac crest showed active haemopoiesis with no increase in plasma cells. Free kappa light chains were detected in the serum on five occasions and the mild immunoparesis persisted.

Discussion

The plasmacytomas appeared to be confined to the posterior mediastinum with no evidence of bone marrow disease. Probably the kappa light chains were being produced by the abnormal plasma cells, though no immunofluorescence studies were carried out on the biopsy tissue,² and the light chains had precipitated in the renal tubules, causing widespread tubular obstruction and terminal renal failure.³ The contribution of the antimitotic treatment to survival was uncertain.

Although haemodialysis in such a case is questionable, we wish to emphasise that this man survived with relative wellbeing for over a year in the presence of a malignancy causing terminal renal failure.

¹ Report on the First Myelomatosis Trial, *British Journal of Haematology*, 1973, 24, 123.

² Levi, D F, Williams, R C, and Lindstrom, F D, *American Journal of Medicine*, 1968, 44, 922.

³ Zlotnick, A, and Rosenmann, E, *Archives of Internal Medicine*, 1975, 135, 40.

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Combination of clonidine and sotalol in hypertension

Clonidine is a sympathetic inhibitor with central site of action. Various clinical trials have shown its antihypertensive efficacy. But there is a large incidence of side effects during treatment. In a comparative trial on 30 hypertensive patients who were treated first with methyl dopa, then clonidine, methyl dopa caused side effects in 11 patients and clonidine in 23.¹

The therapeutic value of beta-adrenergic receptor blockade in the treatment of hypertension has been documented. Sotalol is, like propranolol, a beta-adrenergic blocker which does not have any intrinsic beta-adrenergic stimulating action. Clinical investigations have shown the good antihypertensive effect of sotalol.²⁻⁴ Side effects were relatively infrequent and mild in these investigations. According to Prichard and Boakes² sotalol produces a fall in blood pressure comparable to that produced by methyl dopa. Beta-blockers given in combination with conventional antihypertensive drugs generally give satisfactory results. On theoretical grounds, however, the hypertensive crisis which may follow, if clonidine is withdrawn rapidly, could well be aggravated by the presence of a beta-blocker.⁵

Patients, methods, and results

As I have seen no reports of interaction between clonidine and beta-blockers, I have studied six elderly hypertensive patients who were admitted with severe or moderate hemiplegia produced by stroke. Microscopical examination of CSF showed blood in five of the six patients in the acute phase. Antihypertensive treatment was started with clonidine in three patients and sotalol in three patients. The dosage of clonidine was 0.15 mg three times daily and that of sotalol 80 mg twice daily. In three patients antagonism between clonidine and sotalol was evident. This produced a marked rise in blood pressure, the peak of which occurred six to seven days after the combination treatment started. Blood pressure reversed during single treatment in approximately the same time. In two patients blood pressure was lower during combination treatment than in one of them on clonidine or the other on sotalol as a single treatment. Blood pressure did not change in one patient when he changed from sotalol to combination of sotalol and clonidine (see table). For the sake of control four additional patients with uncomplicated high blood pressures were studied. In three patients the blood pressure was raised during combination treatment. In one patient the blood pressure was not markedly affected when clonidine was replaced with combination treatment (see table).

Systolic/diastolic lying blood pressures (average levels in each place of treatment) before, during, and after treatment with combination of clonidine and sotalol

Patients	Sex	Age	Without anti-hypertensive drugs	Treatment			
				Clonidine	Sotalol	Combination	Same drugs as before combination
Patients with stroke							
1	F	58	180/130	150/100		200/120	170/110
2	M	71	170/100	150/90		200/110	130/80
3	F	76	210/100	160/80		120/70	165/90
4	F	64	200/120		180/100	200/130	150/90
5	M	69	190/120		170/90	180/90	170/100
6	F	76	190/120		185/115	140/100	160/100
Patients with uncomplicated hypertension							
7	M	50	230/140	150/110		170/130	150/120
8	M	41	210/130	190/120		180/120	180/120
9	F	56	240/140		160/120	230/140	160/120
10	F	60	190/120		190/110	230/120	190/110

Discussion

An antagonistic effect between clonidine and sotalol could be observed in six of 10 hypertensive patients. The same phenomenon occurred both in patients who had suffered recent cerebral damage and in patients with uncomplicated hypertension. The mechanism of the blood pressure elevation is still unknown. I think that the combination of clonidine and beta-blockers should be avoided until their interactions have been investigated thoroughly.

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² Prichard, B N C, and Boakes, A J, in *Proceedings of International Symposium of Advances in Beta-adrenergic Blocking Therapy*, ed A G Smart. Rome, 1974.

³ Ruikka, I, Lehtonen, A, and Saarimaa, H, in *Proceedings of International Symposium of Advances in Beta-adrenergic Blocking Therapy*, ed A G Smart. Rome, 1974.

⁴ Sundquist, H, Anttila, M, and Arstila, M, *Clinical Pharmacology and Therapeutics*, 1974, 16, 465.

⁵ Zacest, R, *Drugs*, 1974, 8, 408.

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