include phaeochromocytoma since recognition of the condition and treatment with adrenergic-blocking agents may be life saving.

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Departments of Medicine and Pathology, Kantonsspital Basel, CH-4031 Basel, Switzerland

U KELLER, MD, resident in internal medicine
Th MALL, MD, resident in internal medicine
M WALTER, MD, resident in internal medicine
O BERTEL, MD, resident in internal medicine
J M MIHATSCH, MD, resident in pathology
R RITZ, MD, director of intensive care unit

Malignant mesothelioma and gas-mask assemblers

Since the relation between malignant mesothelioma and asbestos exposure was first described in 1960¹ there have been several studies of groups exposed to asbestos. Jones² reported the incidence of mesothelioma at three factories which assembled service respirators containing blue asbestos and charcoal fibres during the second world war. To date, 50 workers at these factories have developed a mesothelioma. Apparently there are no reports of mesothelioma after the assembly of gas masks in the first world war. We describe one such patient, who assembled masks in the 1914-18 war, and another case in a man who was briefly employed at a mask assembly plant in Leyland, Lancashire, in the second world war.

Case reports

Case 1—An 83-year-old widow had been well until three months before presentation, when she developed dull right-sided chest pain. Three weeks before admission she had fallen and become progressively breathless, and hence came to hospital. The only finding was a large left-sided pleural effusion, which was confirmed by the chest x-ray film. Heavily blood stained fluid (3.5 l) was aspirated by continuous suction. Cytological appearances suggested a mesothelioma and pleural biopsy confirmed this. The effusion recurred and was tapped on two further occasions. Thoracoscopy was performed and further biopsies taken (again confirming malignant mesothelioma) followed by pleurodesis with iodised talc.

She had been a housewife except during the first world war, when she had assembled gas masks at a factory in SE London. The early gas masks were filled with cloth fibres, but with the deployment of poison gas in the Battle of Ypres in 1915 there was an urgent need for adequate protection. Several types of filters were devised and for six months in late 1915 Service respirators with asbestos filters were assembled by Baldwin Bros Ltd (Munitions Department Memorandum of the War Office, 1916) where she had worked.

Case 2—A 62-year-old lorry driver who had had a transitional cell carcinoma of the bladder treated in 1971 had remained well until November 1977, when he complained of dull right-sided chest pain and a non-productive cough. The straight chest x-ray film was unremarkable but the lateral film showed a mass lying deep to the sternum. Tomography showed no invasion of the sternum. The mass was biopsied and the histological findings were diagnostic of malignant mesothelioma.

He had worked as a lorry driver but had never serviced his own vehicle. Nevertheless, during the second world war he had collected gas masks from a factory in Leyland, Lancashire, and for three months had assembled the filters for the masks. He had no other history of exposure to asbestos and there was therefore a 37-year latency before symptoms developed.

Comment

These cases reinforce the suggestion by Elmers and Simpson³ that mesothelioma must be considered in anyone with a pleural lesion of

insidious onset. The latent period between exposure and presentation is remarkably constant in several large series at 42 years ($\pm$ SD13 years).⁴ The first patient developed a mesothelioma 63 years after exposure, which equals or even exceeds the latent period described.⁵ The association between gas-mask assembly in the first world war and mesothelioma has not been described, possibly because other patients with a shorter latency would have died before mesothelioma was regarded as a malignant entity. The second case typifies those described by Jones in gas-mask assemblers who have been exposed to blue asbestos, and he has reported the incidence of mesothelioma at this particular factory.² These cases illustrate the importance of taking a detailed history.

We thank Dr C L Joiner and Dr G W Scott for allowing us to report patients under their care and the staff of the Imperial War Museum for their help.

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Guy's Hospital, London SE1 9RT

D B JEFFERYS, BSC, MB, junior medical registrar
J A VALE, MB, MRCP, senior medical registrar

Recurrent pleural effusion in Waldenström's macroglobulinaemia

Primary disease of the pleura or pulmonary parenchyma in Waldenström's macroglobulinaemia (WM) is uncommon¹ and may be the predominant manifestation.² We report a patient presenting with recurrent pleural effusion; this unusual mode of presentation led to delay in recognising the underlying disorder.

Case report

A 66-year-old Chinese man presented in September 1975 with a chronic cough for six months and progressive exertional dyspnoea for three months. He denied having fever, chest pain, haemoptysis, weight loss, weakness, or contact with tuberculosis. He had stopped smoking 10 years before. Chest x-ray film showed a right pleural effusion. Mantoux test using 1 TU PPD gave 14 mm induration. Sputum smears and cultures gave negative results for tubercle bacilli. Pleural aspiration showed straw-coloured fluid containing 70 g/l of protein, some lymphocytes, but no malignant cells. Pleural biopsy was unsuccessful. Tuberculous pleurisy was diagnosed and he was given streptomycin, isoniazid, and ethambutol. He developed bilateral effusion in December 1975. Despite the addition of prednisolone, pleural fluid re-accumulated rapidly over the months necessitating further aspirations. Fluid examination showed lymphocytes and histiocytes but no malignant cells; protein concentration varied from 50 g/l to 109 g/l. A pleural biopsy specimen in May 1976 showed focal collections of lymphocytes.

Laboratory investigations in March 1976 showed: haemoglobin 9.4 g/dl; white cell count $5.5 \times 10^9/l$ ($5500/mm^3$); platelet count $175 \times 10^9/l$ ($175\,000/mm^3$); reticulocyte count 1.0%. Erythrocyte sedimentation rate (Westergren) 132 mm in first hour. Proteinuria 0.55 g/24 h to 1.1 g/24 h was present. Total serum protein concentration was 103 g/l; serum albumin 25 g/l; serum globulin 78 g/l; serum gammaglobulin 45 g/l. Serum electrophoresis showed a monoclonal peak in the gamma region. Serum immunoglobulin concentrations were IgM 45.5 g/l; IgG 10.0 g/l; IgA 1.92 g/l. The results of Sia test, for serum cryoglobulins, and of urine for Bence Jones protein were negative. Pleural fluid immunoglobulin concentrations were: IgM >72 g/l; IgA nil; IgG 7.2 g/l. Marrow examination showed a slight increase of plasma cells and lymphocytes. Skeletal survey was normal. Results of estimating concentrations of blood urea, serum electrolytes, and serum calcium and phosphate, and liver function tests were normal. Rheumatoid factor, LE cells, and antinuclear factor were not present.

At this stage the possibility of WM was considered. Clinically he looked wasted and weighed 50 kg. He had no finger clubbing, bleeding tendency, visual disturbance, or neurological abnormality. The liver, spleen, and lymph nodes were not enlarged. Fundi showed slight venous distension. Anti-

tuberculous drugs were discontinued and he was started on chlorambucil 4-6 mg daily for six months followed by 2 mg daily. He was also given a red cell transfusion and a 10-week course of prednisolone. He responded with a weight gain of 5 kg within four months, resorption of pleural fluid, and fall of serum IgM to 6 g/l in February 1978.

Comment

The features of WM are fatigue, weakness, anaemia, bleeding, hyperviscosity syndrome, and enlargement of the liver, spleen, and lymph nodes.¹ Nevertheless, WM may have predominantly pulmonary manifestations in the absence of some or most of the features listed above. Winterbauer *et al*² reviewed 15 such cases which showed the following radiological features: pleural effusion, diffuse pulmonary infiltration, hilar enlargement, and tumour-like opacities. Out of the six cases with pleural effusion, two were not associated with any parenchymal lesions, as was the case in our patient. While respiratory symptoms, anaemia, and weight loss were present, the main characteristic features of this disorder were absent in our patient. The high concentration of IgM in the pleural fluid indicated that IgM-producing lymphocytes were present in the pleura. Waldenström's macroglobulinaemia should be considered in any elderly patient with a high erythrocyte sedimentation rate, recurrent pleural effusion, and a protein content of more than 50 g/l. This disorder, though rare, is treatable and is compatible with many years of survival.

We thank the Medical Superintendent, Tan Tock Seng Hospital, Singapore, for permission to report this case.

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Department of Medicine (II), Tan Tock Seng Hospital, Singapore 11

S K TEO, MB, MRCP, senior registrar

S K LEE, MB, FRCP, senior physician and head

Response of "idiopathic" recurrent angioneurotic oedema to tranexamic acid

Recurrent episodes of angioneurotic oedema without any obvious allergic basis or identifiable precipitating causes present a not uncommon clinical problem, often difficult to manage. The episodes of oedema may cause considerable embarrassment and threaten obstruction to the airway. A well-recognised but rare cause for such attacks of spontaneous oedema is hereditary angioneurotic oedema, due to a genetically determined defect in the inhibitor to the activated first component of complement, C1 esterase inhibitor.^{1 2} The symptoms of hereditary angioneurotic oedema are controlled by synthetic inhibitors, which act primarily as inhibitors of plasmin, though they also affect other systems. These are epsilon aminocaproic acid,³ and more recently its cyclic analogue tranexamic acid.⁴

We have recently seen two women with recurrent attacks of spontaneous oedema not due to hereditary angioneurotic oedema but responding dramatically to tranexamic acid.

Case histories

Case 1—A 24-year-old married woman had had intermittent attacks of angioneurotic oedema for about five years, but these had been particularly troublesome in the previous 18 months, occurring almost every day. The distribution of the oedema was widespread, occurring on her arms and legs and face and trunk, and varying in size from small lumps a few centimetres in diameter to large areas affecting part of a limb or a side of her face. Neither she nor her family had any history of allergy, and her attacks were unrelated to food or seasons or time of day or obvious environmental factors. The results of skin tests to allergens were negative, and those of other immunological studies are summarised in the table. The concentration of C1 esterase inhibitor (measured both immunochemically and functionally) and other complement components, measured on several occasions, was always within normal limits, even during an acute attack on two separate occasions. The patient was asked to keep a diary of her attacks for three weeks, during which she recorded an average of two to three separate swellings each day. She was given a trial of tranexamic acid, 1 g three times daily, and the effect was dramatic. The attacks ceased completely and the dose was gradually reduced to 0.5 g twice daily, on which she has been maintained symptom-free for 3 months.

Case 2—A 36-year-old married woman had had symptoms for about eight months; these consisted of episodes of swelling particularly of the face, tongue, and pharynx, although swellings were also widespread over her body. She suffered from hay fever in the summer, but the angioneurotic oedema occurred well after the hay fever had subsided, and was without obvious precipitating cause. At presentation her swellings had been occurring almost every day. Her serum showed no abnormalities of the complement system (table) or of her C1 esterase inhibitor concentration, and her serum IgE concentration was within normal limits. As the patient and her husband were becoming very apprehensive at the frequency and site of attacks, she was started on tranexamic acid, 1 g four times daily. Again, there was a dramatic effect, the attacks ceasing altogether. Her maintenance dose is now being reduced.

Comment

The clinical response in these two patients to tranexamic acid was striking. It strongly supports the view that the lability of effector mechanisms, and the "threshold" at which they react, vary from time to time, and may be an important factor in contributing to symptomatic illness, affecting the level of response to specific "trigger" stimuli. Presumably these two patients developed a low threshold of their kinin-release mechanisms, perhaps owing to an acquired defect of an uncharacterised inhibitor for which tranexamic acid substituted. The threshold would undoubtedly also be affected by the balance of circulating adrenal and "stress" hormones, perhaps being lowered at times of psychological and physical stress.

We conclude that patients with this syndrome of "idiopathic" recurrent angioneurotic oedema for which there is no clear allergic or familial basis, and which is not controlled by antihistamines, should be offered a trial of tranexamic acid.

Correspondence to Dr R A Thompson, Regional Immunology Laboratory, East Birmingham Hospital, Bordesley Green East, Birmingham B9 5ST.

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Regional Immunology Laboratory and Department of Medicine, East Birmingham Hospital, Birmingham B9 5ST

R A THOMPSON, MRCP, MRCPATH, consultant immunologist

D D FELIX-DAVIES, MD, FRCP, consultant physician

Immunological values in two patients with angioneurotic oedema (normal ranges are given in parentheses)

Case No	CH ₅₀ U/ml (25-45)	C1 esterase inhibitor		C3 g/l (0.75-1.7)	C4 g/l (0.14-0.54)	IgG g/l (6.00-16.00)	IgA g/l (0.90-4.50)	IgM g/l (0.40-1.80)	IgE U/ml (50-500)
		g/l (0.18-0.26)	Functional activity (75-130) % standard						
1	29	0.19	80	1.15	0.30	12.60	2.50	1.35	100
	31*	0.21	90	2.10	0.48				
	30*	0.20	100	1.35	0.24				
2	40	0.25	120	1.80	0.45	8.85	2.05	1.10	430
	40*	0.30	140	2.05	0.50				

*Specimen taken during an attack—that is, when a localised swelling was present.