Bronchial carcinoma presenting as autoimmune haemolytic anaemia

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Summary

A 68-year-old man presented with autoimmune haemolytic anaemia. Investigation revealed underlying bronchial carcinoma. A positive direct Coombs' test failed to revert to negative after removal of the primary tumour. This suggested the presence of metastases which was subsequently shown. The possible significance and origin of the autoantibody is discussed.

Introduction

Autoimmune haemolytic anaemia (AIHA) is a well recognized complication of lymphoid neoplasia but it has been recorded in only 4 cases of bronchial carcinoma (Ellis and Westerman, 1965; Horne and McAnally, 1978; Najafi and Guzman, 1979). All developed AIHA more than 12 months after diagnosis in association with advanced metastatic disease. The authors now report what they believe to be the first case of bronchial carcinoma presenting as AIHA.

Case report

A 68-year-old retired caretaker was admitted to hospital complaining of increasing breathlessness on exertion for 2 weeks. He was previously well, smoked 10 cigarettes a day and had not taken any drugs. Clinical examination revealed pallor and a spleen palpable 5 cm below the left costal border. Laboratory investigations showed: Hb 7.4 g/dl; MCV 112 fl; reticulocyte count 55%; ESR (Westergren) 138 mm/hr; serum bilirubin 28 μ mol/l; LDH 560 u./l (normal range 240-525 u./l; HBD 388 u./l (normal range 50-290 u./l); haptoglobin not detected; IgG 21.1 g/l (normal range 8-18 g/l); and normal IgA, IgM, serum B₁₂ and folate. The blood film showed small spherocytes and a *Treponema pallidum* haemagglutination test was negative. Direct Coombs' test was strongly positive with IgG and

C3d on the red cells but direct and elution panels failed to show red cell antigen specificity.

Bone marrow examination showed erythroid hyperplasia but no evidence of malignancy. Chest X-ray showed ill-defined shadowing in the right mid-zone and lymphangiography was negative. Treatment with oral prednisolone 60 mg daily was started and 10 days later Hb had risen to 11.8 g/dl and reticulocyte count fallen to 25%. Bronchoscopy showed no abnormality macroscopically but a blind biopsy of the right upper bronchial mucosa revealed squamous carcinoma. Serum calcium and liver function tests were normal so prednisolone was stopped and the upper middle lobes of the right lung were resected. At operation a piece of the tumour was freeze-dried and sections stained directly with fluorescein isothionate conjugated sheep anti-human IgG. When examined under a fluorescent microscope, strongly positive staining was seen in the tumour.

Two units of blood were transfused at operation and, 2 weeks later, Hb was stable at 11.0 g/dl with a reticulocyte count of 2%. Serum bilirubin, LDH and HBD were normal and haptoglobin had risen to 3 g/l (normal range 1-3 g/l). Direct Coombs' test remained positive and was again positive 3 weeks later. This suggested occult tumour, and radioisotope bone and liver scans were performed which strongly suggested metastases. This patient was alive on no treatment 5 months postoperatively, there was no evidence of haemolysis but the direct Coombs' test was still positive.

Discussion

At presentation the findings suggested underlying lymphoid neoplasia and, because of the rare association with AIHA, the authors were surprised when the biopsy showed bronchial carcinoma. Prednisolone appeared to control auto-haemolysis

pre-operatively but was not required after surgery when presumably the concentration of IgG on the red cells decreased. The positive direct Coombs' test 2 weeks postoperatively might have been expected owing to the persistence of autoimmune IgG synthesized pre-operatively. Its failure then to revert to negative suggests the IgG was a marker reflecting the persistence of occult tumour, which was subsequently shown.

The presence of IgG in the tumour is interesting. All classes of immunoglobulin have been demonstrated in bronchial carcinomas (Gerstl, Eng and Bigbee, 1977) and, although the significance is unknown, it possibly represents an attempt at tumour rejection. Presumably in this patient the IgG directed against the tumour also recognized antigens on red cells, resulting in AIHA. A second possibility is that the tumour synthesized the IgG which had red cell specificity. A recent report of a benign bronchial tumour producing IgG with red cell antigen specificity (Burmester *et al.*, 1980) supports this. The origin of the autoimmune IgG in the present patient is unresolved but it appeared,

as do most markers of ectodermal tumours, in the presence of a large tumour mass.

Acknowledgments

We thank Dr S. B. Cohen for permission to report this case and Dr C. H. Vickers for his help with the immunofluorescence.

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