Haemolytic anaemia with hypernephroma

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Summary
A case is reported of Coombs' positive haemolytic anaemia associated with hypernephroma. The anaemia regressed on removal of the tumour but returned when secondary deposits developed.

Introduction
Although Coombs' positive haemolytic anaemia is fairly common in neoplastic diseases of the lymphoreticular system it occurs only rarely with solid tumours, usually dermoid cysts or teratoma of the ovaries (Dacie, 1967). Spira and Lynch (1979) have recently described 4 cases of this type of anaemia associated with carcinoma and found 12 other cases in the literature. Two of these patients had a hypernephroma: this report documents a further case.

Case report
A previously fit 57-year-old woman was admitted to hospital for investigation of pyrexia and anaemia. Over the preceding 9 months she had experienced increasing dyspnoea, lassitude, malaise and had lost 6-4 kg in weight. Her only medication had been iron tablets. On examination she looked anaemic and an ill-defined mass was felt in the left hypochondrium which was thought to be the spleen. A fluctuating pyrexia was noted.

On admission to hospital her Hb was 6-8 g/dl with a normocytic normochromic film and 14% reticulocytes. Bilirubin was marginally elevated at 22 μmol/l and LDH was elevated at 307 u/l. Urine was negative for urobilinogen on ward testing and serum haptoglobin levels were raised. The direct Coombs' test at presentation was positive with broad spectrum antihuman globulin (+) and anticomplement (+++) but negative with anti-IgG. The serum gave non-specific reactions with enzyme-treated red cells and weakly by saline agglutination at 16°C. The strength of reactions were consistent with there being a cold antibody present, but in the absence of detectable IgG on the red cell surface elution was not possible.

Blood cultures, urine cultures and serology for viruses and Mycoplasma were negative. Plasma electrophoresis failed to show a myeloma band and was consistent with inflammation. A plain abdominal X-ray showed a large left kidney which in retrospect must have been the palpable mass in the left hypochondrium. IVP demonstrated a large space-occupying lesion in the lower pole.

Steroids were given in an attempt to suppress haemolysis and the patient was transfused 4 units of blood in preparation for nephrectomy. There was considerable difficulty in obtaining compatible blood and this transfusion produced brisk haemolysis with jaundice. Nevertheless, nephrectomy was performed without complication, and the tumour proved to be a solid clear cell carcinoma. After the operation her Hb rose and she became apleyrexial; steroids were discontinued and 2 months later her Hb was normal and Coombs' test negative (see Fig. 1).

She remained well for a year but anaemia returned as pulmonary secondaries became evident. The Hb dropped to 4-3 g/dl with 11% reticulocytes and raised serum bilirubin and urine urobilinogen. Despite blood transfusion and steroids she died 17 months following the nephrectomy. The direct Coombs' test became weakly positive again shortly before she died but only with anti-complement 3d (+++). Weak reactions were obtained with enzyme-treated cells.

Discussion
Although red cell survival was not studied in this patient, there was good presumptive evidence of haemolysis with reticulocytosis, hyperbilirubinaemia, a hyperactive but normal narrow and a rapidly falling Hb. The haptoglobin levels were either within normal limits or in excess for the whole duration of the illness indicating predominantly extra-vascular haemolysis. Raised haptoglobin levels are sometimes seen in association with neoplasm. Removal of the tumour cured the anaemia but recurrence was associated with further haemolysis so there can be little doubt that the two were related.

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The pathogenesis of haemolytic anaemia in these circumstances is uncertain; possibilities include coating of the red cells by antibodies produced by the tumour, and host production of antibodies to an antigen common or similar to the tumour and host erythrocytes. The patient was not on steroids for long enough confidently to evaluate their effect, but there was no obvious benefit.

Acknowledgment
We thank Dr J. H. Dadds and Mr G. F. Abercrombie for allowing us to report their case.

References
Hypernephroma.

G. W. Bradley and M. Harvey

*Postgrad Med J* 1981 57: 46-47
doi: 10.1136/pgmj.57.663.46

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