to support the diagnosis of brucellosis for the agglutination test was persistently negative and the patient, though improving promptly with steroid therapy, failed to improve with prolonged administration of tetracycline.

It was therefore concluded that the patient was suffering from an intrahepatic granulomatous arteriopathy of unknown aetiology. Biopsies of other organs were not performed and hence it was not known whether this was an arteriopathy confined to the hepatic vessels or whether the liver biopsy allowed the opportunity to observe a local manifestation of a generalized disease. There were no clinical features to indicate specific involvement of any other organ but the persistent and unexplained anaemia indicates that the lesion, even if localized, was accompanied by systemic effects.

The prompt response to steroid treatment in

this patient suggests, in the absence of any other obvious aetiological factors, a hypersensitivity reaction, though the arterial lesions did not resemble those described as typical of hypersensitivity states (Chure & Strauss, 1951).

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Sideropenic anaemia with reticulo-endothelial siderosis in a case of hypernephroma

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Summary

A case of sideropenic anaemia with reticulo-endothelial siderosis is described. At the time of admission the anaemia was severe and the cause was not apparent. Extensive search had to be made to reveal the neoplasm, a hypernephroma.

Introduction

Of the various types of anaemias encountered in patients with neoplastic disease, sideropenic anaemia with reticulo-endothelial siderosis is the most interesting and puzzling. According to Cartwright (1966), it is usually mild in degree and not progressive in severity, but when the anaemia is moderately severe the causal neoplasm is almost always obvious. The case reported here presented with severe anaemia long before the underlying neoplasm could be detected.

Case report

The patient, a man aged 58, a caterer by profession, was admitted with a 3 months' history of increasing tiredness, generalized weakness and

shortness of breath on exertion. He had lost approximately 1 stone of weight in the 6 months preceding admission. He had never had indigestion and his appetite had always been good. The only relevant past history was that he had contracted syphilis about 30 years before.

On examination, he appeared very anaemic, but not jaundiced. The tongue, buccal mucous membranes, nails, palms and soles of the feet appeared pale but otherwise normal. There were no palpable glands or sternal tenderness. The skin and joints were normal. The liver was just palpable, one finger breadth below the right costal margin, smooth and not tender. All the features of a hyperkinetic circulation were present, with moderate tachycardia, slightly raised JVP, hyperdynamic cardiac impulse, flow murmurs in all cardiac areas, wide pulse-pressure, warm hands and digital pulsation. The only other abnormal physical finding was the presence of Argyll Robertson pupils—evidence of neurosyphilis. Capillary fragility test, rectal examination and proctoscopy were normal.

Investigations. Hb 6.9 g/100 ml (47%), PCV 28%, MCHC 25%, ESR 47 mm/1 hr, WBC 10,000/mm³, differential count normal. Reticulocyte count 2.5%. Platelets normal. Blood film: anisocytosis, poikilocytosis, slight microcytosis and marked hypochromia. Repeated stool examination for occult blood: negative. Urine: no red cells found. Occult blood test negative. Thymol turbidity 0.5 units, SGPT <5 units, serum bilirubin 0.3 mg/100 ml, alkaline phosphatase 30 units (K.A.). Chest X-ray and ECG normal. Blood W.R. +1/160, RCPT +1/40, TPI test positive. CSF: Sugar 60 mg/100 ml protein 45 mg/100 ml 25 WBC 90% lymphocytes W.R. +1/10 RPCFT +1/5 Barium meal normal.

A provisional diagnosis of iron-deficiency anaemia was made and he was treated with iron. He also received a full course of antipsyphilitic treatment. However, bone marrow examination revealed: 'Normoblastic hyperplasia, normal leucopoiesis, with very few giant metamyelocytes, numerous megakaryocytes. Stainable intracellular iron in erythrocyte precursors virtually absent. A large excess of storage iron is present. No malignant cells are seen.'

Further investigations showed: Serum iron 15 µg/100 ml. Total iron binding capacity 156 µg/100 ml. Haptoglobin not reduced. Serum B₁₂, 245 µg/ml. Serum folate, 0.8 µg/ml. ⁵⁹Fe plasma clearance 15 min—consistent with diagnosis of secondary anaemia.

At this stage the nature of the anaemia was evident and in the absence of chronic infection and rheumatoid arthritis, the presence of an underlying neoplasm responsible for this anaemia became highly probable. Repeated clinical examinations were unhelpful. Further investigations were carried out as follows:

Barium enema showed multiple diverticula of sigmoid colon. Urine: no Bence-Jones protein detected. Serum proteins 6.3 mg/100 ml, albumin 2.1, α₁-globulin 0.8, α₂-globulin, 1.3 β-globulin, 1.1 γ-globulin, 0.8 mg/100 ml. Serum calcium 9.5 mg/100 ml, inorganic phosphate 2.6 mg/100 ml, acid phosphatase 1.2 units. Skull X-ray and repeat chest X-ray normal. Straight X-ray abdomen: osteolytic lesion of left transverse process of left lumbar vertebra.

Intravenous pyelography revealed that the left pelvicalyceal system was displaced downwards and the upper pole calyces were displaced and dilated. The appearance was suggestive of renal carcinoma. Selective renal angiography also showed that the upper pole of the left kidney was occupied by a mass of tumour vessels. The appearance was very suggestive of renal tumour.

When the patient was subjected to operation,

a large vascular tumour, occupying the upper half of the left kidney and invading along the pedicle, aorta and lumbar vertebrae was found. The tumour could not be removed completely. Histology showed adenocarcinoma of the kidney.

The immediate post-operative period was uneventful. Two weeks after operation the haemoglobin rose to 12.7 g/100 ml (87%) and serum iron up to 195 µg/100 ml, PCV and MCHC were 39% and 33%, respectively. He was treated with a course of deep X-ray therapy, but about 4 weeks later his condition deteriorated again due to widespread metastases to the lungs and bones and he ultimately died. Necropsy showed extensive metastases to the lungs, the opposite kidney and to the vertebrae.

Discussion

In neoplastic disease various types of anaemias may be encountered: myelophthisic anaemia with extensive bone-marrow metastases (Rundles & Jonson, 1949); true iron deficiency anaemia with low storage iron due to chronic blood loss from an ulcerating tumour; overt haemolytic anaemia (Tedeschi & Cannicelli, 1948); sideroblastic anaemia—all have been found in tumour-bearing hosts. Another well-documented type of anaemia may occur in patients suffering from neoplastic disease. This is characterized by low serum iron, reduced total iron-binding capacity, low saturation of transferrin, normal or slightly increased erythropoiesis in bone marrow and excess of storage iron in the reticulo-endothelial system. As this same type of anaemia may occur in various other disorders like chronic infection, rheumatoid arthritis, rheumatic fever, collagen diseases, fractures and severe tissue injuries, dermatological conditions, etc., it has been variously known as 'chronic simple anaemia', 'anaemia of chronic disorders', 'anaemia of infection' and 'anaemia of malignancy'. But we preferred the term 'sideropenic anaemia with reticulo-endothelial siderosis', as suggested by Cartwright (1966), as it states most of the important diagnostic features of the anaemia.

Severe anaemia is a frequent finding in lymphomas and leukaemias. In carcinomas and other neoplasms, though mild to moderate anaemia is common, severe anaemia to the extent with which our patient presented (haemoglobin 6.9 g/100 ml, PCV 28% and MCHC 25%), is not very common. In the series of Shen & Homburger (1951), out of 193 patients with advanced carcinomas, 116 cases had anaemia and of those only 19% had haemoglobin below 55%. In the series of Samuels & Bierman (1956), with normal haemoglobin defined as 12.2 g/100 ml,

two patients with carcinomas had an average haemoglobin of 10.2 g/100 ml. In the series of Miller *et al.* (1956), only 13% of the patients had PCV between 25 and 29%, 2% between 20 and 24% and 2% below 24%. Most of the patients had very advanced carcinoma.

The patient under discussion presented with severe anaemia without apparent cause, and, like others reported in the literature, failed to improve after iron therapy. In these cases, as there is already excess of storage iron, iron administration does not produce any haematological response. However, in some patients with cancer, absence of iron in bone marrow reticulo-endothelial cells has been observed and only these patients are likely to improve with iron therapy. Hence it is important to know the state of storage iron in bone marrow before any iron therapy is instituted in patients with neoplastic disease.

It is thought that the degree of reduction of serum iron in neoplastic disease probably depends on the extent of the metastases. In the series of Clark Griffith *et al.* (1965), very low serum iron was found only in those cases who had widespread metastases. In the case reported here, although the serum iron was only 15 µg/100 ml pre-operative investigations did not show evidence of widespread metastases and on surgical exploration the tumour was found to be large but only invading locally the transverse processes of the lumbar vertebrae. It appears that the degree of reduction of serum iron depends on the total mass of tumour cells—whether wide-spread or contained in a single large tumour.

Although the pathogenesis of this type of anaemia is still not clear, it is known that erythrocyte survival time is reduced and the bone marrow fails to correct the anaemia; there is also a failure of iron-release from reticulo-endothelial cells. How neoplasms bring about these changes is not yet clearly understood. But whatever the mechanism might be, it is known that if the underlying disorder is alleviated the anaemia improves and the haematological response is observed. Even incomplete removal of

the tumour in this case was followed by a rise of haemoglobin to 87% and of serum iron to 195 µg/100 ml.

From the large number of communications in the literature, mostly devoted to elucidating the mechanism of this type of anaemia, we were unable to find a case where such a degree of anaemia was the only presenting feature for a long time before the underlying neoplasm could be detected.

The purpose of this communication is to emphasize the fact that when this type of anaemia presents as a diagnostic problem, extensive search for neoplasm should be carried out and is likely to give the answer.

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