Pernicious anaemia among Arabs in Kuwait

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SYNOPSIS Addisonian pernicious anaemia is believed to be very rare in Arabs. Three cases are reported. Two were Jordanians of Palestinian origin and one an Egyptian. All had the typical peripheral macrocytosis, a frankly megaloblastic bone marrow, and a Schilling test result in the range of pernicious anaemia. All three improved remarkably on vitamin B₁₂ therapy and have maintained a normal haemoglobin level. There was no evidence of gastric carcinoma in any of these cases.

Since the first description of pernicious anaemia by Thomas Addison of Guy's Hospital in 1855 till quite recently it was thought to be a disease of patients of European descent, particularly of the fair Nordic races, and rare in Asiatic or Negro people (Friedlander, 1934). This observation is now being questioned (Wintrobe, 1967). There are few reports of Addisonian pernicious anaemia amongst Arabs. Jalil and Demarchi (1952) reported only two cases over the period of three years in Iraq and even then their report did not include serum vitamin B₁₂ and folate levels or Schilling tests. Fawdry (1955), from Aden, reported a syndrome with splenomegaly, anaemia, hepatomegaly, and sometimes macrocytosis, but he did not report any cases of pernicious anaemia. However, it seems that cases are probably being overlooked or at least not reported. The three cases of pernicious anaemia we found occurred amongst 55 cases of macrocytic anaemia, including the anaemia of pregnancy, seen in Arabs by one of us (S.A.A.) during the period 1967 to 1969.

Method and Material

Routine haematological examinations were carried out according to the methods described

by Dacie and Lewis (1968). Haemoglobin was estimated as cyanmethaemoglobin using a lysed whole blood standard (Diagnostic Reagent Ltd, England).

Peripheral films were stained with Leishman's stain. The serum B₁₂ was estimated using *Euglena gracilis* and serum folate by the *Lactobacillus casei* method.

An augmented histamine test meal examination was carried out on the three cases as described by Kay (1953). A Crosby capsule (Crosby and Kugler, 1957) was used for gastric biopsy in the first case only. A careful dietary history was taken to exclude nutritional vitamin B₁₂ deficiency. A stool was examined for parasites and a barium meal, with a follow through, was performed to exclude gastrointestinal disorders. In Schilling's test (1953) a dose of 1.1 µg of vitamin B₁₂ labelled with 0.77 µg of ⁵⁸CO was given orally and after two hours 1,000 µg of unlabelled vitamin B₁₂ was given parenterally. The urine was collected for the next 24 hours. (This estimation was made through the courtesy of the Radiotherapy Department, Al-Sabah Hospital.) Unfortunately the test could not be repeated with intrinsic factor.

The response to treatment was followed by serial reticulocyte counts and haemoglobin estimations.

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Clinical Cases

CASE 1

S.Kh., an overweight Jordanian woman, aged 65 years, complained of weakness and soreness of the tongue but had no history of vomiting, diarrhoea, cough, or urinary trouble. She was mildly feverish (37.8°C), and had a pale lemon-coloured complexion and grey hair. The liver and spleen were not palpable and there was no abnormality of the nervous system.

Haemoglobin was 4.5 g/100 ml, WCB 4,600/cmm, MCHC 30%, and reticulocytes 0.5%.

A blood film showed marked macrocytosis, moderate ovalocytosis, and anisocytosis. Serum vitamin B_{12} was 40 μg per ml, serum folate 6 ng/ml. Bone marrow showed moderately severe megaloblastic change with giant metamyelocytes and plenty of storage iron. A Schilling test showed only 0.9% of the dose excreted in the urine. An augmented histamine test confirmed the complete absence of free acid.

Gastric biopsy performed with a Crosby-Kugler capsule showed typical gastric mucosal atrophy.

A barium meal was negative; stools showed neither ova nor occult blood, and the urine was normal.

The diagnosis of pernicious anaemia was confirmed by the response of vitamin B_{12} . The reticulocytes reached 23% on the fifth day and the haemoglobin rose steadily at the rate of 1 g per week. The patient was discharged on 250 μg vitamin B_{12} monthly and 20 months later did not show any sign of relapse.

CASE 2

M.H., a Jordanian male, aged 35 years, had for one year a history of epigastric discomfort worsened by food and relieved by vomiting. He also had generalized aching pains, malaise, loss of weight, and progressive weakness. He had a pale, lemon-coloured complexion and white hair. The tongue was smooth. A pulmonary ejection systolic murmur was audible. Spleen and lymph nodes were not palpable. The central nervous system was normal.

Haemoglobin was 7.6 g/100 ml, MCHC 33%, and reticulocytes 4%.

A blood film showed marked macrocytosis and ovalocytosis with moderate anisocytosis. The bone marrow was frankly megaloblastic. He had histamine-fast achlorhydria. The serum vitamin B_{12} was not estimated. No gastrointestinal abnormalities were detected by x-ray studies. A Schilling test showed that only 0.96% of the dose was excreted in the 24-hour urine. Serum folate was 8.7 ng/ml. Parietal cell antibodies were detected in the serum, but not intrinsic factor antibodies, antinuclear factor, or thyroid antibodies.

On the sixth day after parenteral vitamin B_{12}

the reticulocytes reached 16%. The haemoglobin rose to 12 g per 100 ml in 14 days. The patient was discharged on 250 μg vitamin B_{12} per month and has maintained a normal haemoglobin level.

CASE 3

H.M.H., an Egyptian male, aged 40 years, complained of epigastric pain, generalized weakness, palpitation and difficulty in breathing, a sore tongue but no neurological symptoms. He also gave a history of dyspepsia accompanied by vomiting and heartburn for seven to 10 years. The patient was under weight and looked very anaemic. Blood pressure, pulse, and temperature were normal. The liver was slightly enlarged but no ascites or jaundice was seen.

Haemoglobin was 4.9 g/100 ml, MCHC 32.7%, and reticulocytes 2%.

A blood film showed marked macrocytosis and ovalocytosis, and many hypersegmented polymorphonuclear leucocytes. The bone marrow was frankly megaloblastic. The serum vitamin B_{12} and folate were not estimated. A Schilling test, without intrinsic factor, showed that 0.97% of the test dose was excreted in the urine in 24 hours. Stool examination was negative for parasites and occult blood. He had histamine-fast achlorhydria. Radiological examination of the gastrointestinal tract did not show any abnormalities. The response to vitamin B_{12} therapy was rapid. A reticulocyte peak of 43% was reached on the sixth day and the haemoglobin rose to 10 g/100 ml in two weeks. On 250 μg vitamin B_{12} monthly, he is maintaining his haemoglobin level at around 16 g/100 ml.

Discussion

Reports of pernicious anaemia amongst true Arabs are very rare, but this may not be a correct evaluation of the frequency. Until recently it was thought that pernicious anaemia was also rare in Asian peoples and McNeil-Hill and Uday Raj (1965) did not demonstrate a single case in a large series of Fijians and Indians. Reports of six cases amongst Indians and Chinese in Singapore (Jayaratnam, 1967) contradict this, while Das Gupta and Chatterjee (1951) also reported a few well documented cases amongst Indians, and others have been recorded by Konar (1951) and by Misra and Singh (1961). It is our opinion that with the availability of the modern tools, including microbiological assays and radioactive vitamin B_{12} studies, more cases will be reported from the Arab world. The three cases described in this paper occurred amongst 55 cases of macrocytic anaemia investigated. These included those complicating pregnancy. However, some could not be investigated fully and there was almost certainly one further case. This

patient showed evidence of subacute combined degeneration of the spinal cord. Although there was a mild macrocytic blood picture the marrow was normoblastic. Serum vitamin B₁₂ studies were not made but the patient improved dramatically on vitamin B₁₂ therapy.

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