exacerbation of the adrenal insufficiency with return of anorexia, lassitude, loss of weight, and low blood pressure. Although patients with Addison's disease, treated with cortisone, are not usually hypersensitive to insulin, in this present case, as the patient's condition improved satisfactorily, and her insulin sensitivity was uncertain, the latter drug was not used immediately.

It is interesting that her diabetes is controlled now without insulin, despite the fact that she needed

insulin on her last admission and also during her subsequent relapse.

Summary

A patient is described who initially had myxædema and later developed Addison's disease followed by diabetes mellitus.

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REFERENCES

- BEAVAN, D. W., NELSON, D. H., RENOLD, A. E., and THORN, G. W. (1959): Diabetes Mellitus and Addison's Disease: A Report of Eight Patients and a Review of 55 Cases in the Literature, *New Engl. J. Med.*, **261**, 443.
- BERNSTEIN, D. E. (1948): Diabetes Mellitus followed by Addison's Disease and Hypothyroidism, simulating Panhypopituitarism, *J. Clin. Endocr.*, **8**, 687.
- BRESLAW, L., LASHOF, J., KLEIN, C. (1953): Diabetes Mellitus, Hyperthyroidism and Addison's Disease in One Patient, *Ann. intern. Med.*, **38**, 338.
- CHRISTY, N. P., HOLUB, D. A., and TOMASI, T. B. (1962): Primary Ovarian, Thyroidal and Adrenocortical Deficiencies Simulating Pituitary Insufficiency, Associated with Diabetes Mellitus, *J. clin. Endocr.*, **22**, 155.
- CRISPELL, K. R., and PARSON, W. (1952): The Administration of Purified Growth Hormone to a Female with Hypoadrenalism, Hypothyroidism, Diabetes Mellitus and Secondary Amenorrhea, Simulating Panhypopituitarism, *Ibid.*, **12**, 881.
- GITTLER, R. D., FAJANS, S. S., and CONN, J. W. (1959): Coexistence of Addison's Disease and Diabetes Mellitus: Report of three cases with a discussion of Metabolic Inter-relationships, *Ibid.*, **19**, 797.
- HOWARD, R. P., MILLS, E. J., and MATHEWS, W. H. (1952): Pluriglandular Insufficiency Without Panhypopituitarism, *Ibid.*, **12**, 974 (Abstract).

DISGUISED PERNICIOUS ANAEMIA

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THE diagnosis of classical Addisonian pernicious anaemia is straightforward. It may prove difficult when blood values are normal, as may happen when the disease presents with nervous system manifestations. This case, which showed transitory leucoerythroblastic anaemia, demonstrates how difficult the diagnosis may be, even when the patient is anaemic.

Case History

A woman of 68 was admitted to the Victoria Infirmary on 16.2.61. She had been tired for three years, and had lost 2½ stones in weight in that time. One year previously, immediately after her husband's sudden death, she had pneumonia, and had since then complained of weakness, cough and breathlessness. She lived alone and felt depressed. For the past year she had eaten little except porridge, bread and butter and tea.

Although the patient was frail and slow of thought, she was nervous and hyperactive. There was marked sacral and leg oedema, and a sinus tachycardia of 116/min. There were signs of fluid at both lung bases, particularly the right. The liver was palpable 2 in. below the costal margin but the spleen could not be felt. No abnormality was detected in any other system. Her temperature did not exceed 99.2°F. There was no urinary abnormality.

An X-ray of the chest showed consolidation and slight collapse of the right base, with some free fluid at both

bases. Electrocardiographic complexes were of low voltage with flattening of the T waves. On admission hæmoglobin was 6.2 g/100 ml.; packed cell volume 21% MCHC 29.5%. The total nucleated cell count was 13,100 per c.mm., of which 7,900 were white cells. (Neutrophils 73%, lymphocytes 14, monocytes 5, neutrophil metamyelocytes 7, neutrophil myelocyte 1.) Most of the nucleated red cells were orthochromic normoblasts, but a few were polychromatic. The nuclei of some were normal, others lobulated and distorted. The periodic acid Schiff reaction was negative. There was moderate anisopoikilocytosis, marked polychromasia, and a number of hypochromic microcytes.

Pleural aspiration was performed and subsequent culture and animal inoculation were negative for *M. tuberculosis*. Treatment was commenced with crystalline penicillin, mersalyl and chlorothiazide, and ordinary ward diet was given.

Five days later nucleated red cells had almost disappeared. Total nucleated cells numbered 8,600 and were practically all white cells, which were fully mature. Hæmoglobin had risen to 7.6 g., and the reticulocyte count was 13.2%. Sternal marrow aspiration showed erythroid hyperplasia, and many megakaryocytes. Erythropoiesis was normoblastic and macronormoblastic, with predominant early and intermediate forms. A few very early forms had fine nuclear structure, and appeared to be transitional between normoblasts and megaloblasts. Myeloid granulopoiesis was active, and

ratios remained unchanged. A few macropolycytes were present, and there was slight increase of plasma cells. Many cells in mitosis were seen. There was practically no free stainable iron in sections.

X-rays of skull and long bones were normal. Serum calcium was normal, relative to a low normal plasma protein concentration, with normal alkaline phosphatase but significant hypophosphatemia. These findings were regarded as consistent with first-degree biochemical osteomalacia (Dr. Ian A. Anderson). Faecal urobilinogen and blood urea were normal. No microscopic faecal abnormality was found. There was no occult blood in the stools. ESR (Westergren) was 12 mm./hr. Serum vitamin B₁₂ level (*Lactobacillus leichmanii*) 200 $\mu\mu$ g./ml., though one month later it was 110 $\mu\mu$ g./ml., which is probably low.

The patient's condition improved. Haemoglobin rose gradually, though iron deficiency remained, and ferrous sulphate was given. One month after admission it had reached 10.8 g. with normal white and reticulocyte counts. She was discharged to a convalescent home. It was thought that the anaemia was due to malnutrition and infection.

She was well when seen three weeks later and her appetite had improved. Haemoglobin 12.8 g.; MCHC 29%; white cells normal; hypochromic microcytes were present in moderate number, with occasional macrocytes.

Four months after her first admission she was pale, dyspnoeic on exertion, and paraesthesiae were present in her feet. She had taken no iron for ten weeks and was eating poorly. Central nervous system was normal. Haemoglobin 9.3; r.b.c. 2.94 mill./c.mm.; MCV 100 cu. μ . There was considerable anisopoikilocytosis, with fairly numerous macrocytes.

She was readmitted as a possible case of pernicious anaemia. Haemoglobin 6.9 g.; MCV 115 cu. μ , w.b.c. 2,400/cu.mm. There was gross anisopoikilocytosis, with many oval macrocytes. Some hypersegmented neutrophils were now present. The marrow showed greatly increased erythropoiesis which was normoblastic and megaloblastic. Megaloblasts were predominantly early, with a number of intermediate forms. Howell-Jolly bodies were seen, and a number of giant metamyelocytes. Free stainable iron was greatly decreased. Serum vitamin B₁₂ was 60 $\mu\mu$ g./ml. Achlorhydria was demonstrated.

There was a good reticulocyte response to parenteral B₁₂ therapy. When last seen, seven months after her first admission, the patient was eating fairly well, haemoglobin was 13.9 g., and serum iron was normal. Serum calcium was slightly subnormal, alkaline phosphatase minimally increased, and phosphorus normal. Examination of urine suggested that calcium excretion was somewhat increased for a person of her size; this does not suggest Vitamin D deficiency. Investigations still continue.

Comment

Three factors were probably responsible for the changes in blood and marrow in this case. When first seen the patient was entering a period of spontaneous temporary remission as often occurred in pernicious anaemia prior to the introduction of effective therapy. She had a blood crisis, with a tremendous outpouring of nucleated red cells (Whitby and Britton, 1957). The stimulus of infection may have played a part and certainly affected the white cells. Although the proportion of immature white cells in the peripheral blood was quite consistent with pernicious anaemia (Wintrobe, 1957), the normal total white count and increased marrow granulopoiesis are considered to have been due to infection. It is known that in such circumstances the marrow picture can even simulate leukaemia (Strauss, Broklaw and Chapman, 1952).

The third factor disguising the diagnosis was the severe iron deficiency. Britton (1936) described this in a high proportion of cases of untreated Addisonian pernicious anaemia, and the normoblastic crisis must have made it more marked in this case. Although persistent, the iron deficiency did not obscure the diagnosis when the relapse occurred in the absence of infection.

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REFERENCES

- BRITTON, C. J. C. (1936): Anaemia—Classification and Treatment; Analysis of 183 Cases, *N.Z. med. J.*, **35**, 154.
 STRAUSS, M. B., BROKLAW, R., and CHAPMAN, C. B. (1952): Leukæmoid Bone Marrow in Pernicious Anaemia, *Amer. J. med. Sci.*, **223**, 54.
 WHITBY, L. E. H., and BRITTON, C. J. C. (1957): Disorders of the Blood, p. 239. London: J. & A. Churchill.
 WINTROBE, M. M. (1957): Clinical Haematology, p. 480. London: Henry Kimpton.