cases, but noted the occurrence of endometrial carcinoma in cases with long histories. Kaufman *et al.* (1959) found a higher incidence of endometrial hyperplasia, as we have done. It may be suggested that the diagnosis in some of these cases should therefore be metropathia haemorrhagica. However, typical cases of metropathia haemorrhagica do not have periods of amenorrhoea lasting longer than three months. At this hospital cystic glandular hyperplasia is found more often than was formerly suspected, and it may occur in patients who are menstruating regularly. It is sometimes found in association with corpora lutea, and pregnancy has been seen to occur in a uterus which showed cystic glandular hyperplasia.

The earlier and larger series of cases quoted do not appear to have had routine endometrial biopsies taken, and it is possible that many more would have shown this histological picture.

The results of wedge resection in group 1 show that regular menstruation has not persisted for longer than six months, with the exception of two women who became pregnant two and three years respectively after operation. In group 2, where ovulation was occurring, of the six patients followed up, two had menstruated normally for more than a year. Regular menstrual periods had occurred in one patient for six months, but after this time she relapsed into amenorrhoea. The other three patients were still menstruating regularly at the end of four months, but a longer follow-up is not available. Stein (1958) has reported re-establishment of normal menstruation in 95% of patients, and 88% of his cases became pregnant.

Discussion

The aetiology of the Stein-Leventhal syndrome has received a great deal of attention and several theories have been advanced to explain it. However, the occurrence of the ovarian histological picture without symptoms, the absence of hyperthecosis, and the presence of corpora lutea in such a large proportion of the cases studied here make it difficult to accept any theory so far advanced. It has already been shown that it is not possible to pick out a case of this syndrome from the series presented. Since the appearance of the ovarian cells gives no true indication of the conditions which have produced this appearance we cannot go beyond reporting the features encountered in the cases seen at this hospital. The answer to the problem of aetiology is not likely to be found by ordinary histological examination.

It may be said that all our cases are in the early stages of a progressive disorder, but the age incidence is the same as that in published series. Symptomatology and histology do not necessarily go together, and it is difficult to believe that there is such a definite entity as a Stein-Leventhal syndrome.

The histological findings in the ovaries are shown to be present in the absence of symptoms, and it is strange that the only definite and constant part of the syndrome should occur also in the controls. It would be more apt to refer to the condition as multiple small follicular cysts of the ovary, rather than cling to the eponymous nomenclature suggesting symptoms and signs which may not be present.

If a patient is infertile and has palpably enlarged ovaries and no evidence of ovulation, there is adequate

justification for the performance of wedge resection, which gives her a chance of ovulating and becoming pregnant.

Summary

Histological studies were made of the follicle linings in ovarian tissue from 21 patients.

The cases were divided into three groups, and the third of these groups was used as a control.

The histological and clinical features of the cases are discussed, and the conclusion is reached that the Stein-Leventhal syndrome does not appear to be a well-defined entity.

We are grateful to all the surgeons at Chelsea Hospital for Women for permission to use the case notes of their patients.

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THALASSAEMIA IN A GURKHA FAMILY

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The thalassaemia syndrome is occasionally encountered by clinicians in Gurkha (Nepalese) subjects, but there are few reports of cases in the literature. Brain and Vella (1958) reported haemoglobin-H disease (haemoglobin-H thalassaemia) in a Gurkha woman, and a second such case has recently been found, again in a pregnant Gurkha woman, in Malaya.

The present report deals with a case of thalassaemia-like disease in a young Gurkha girl. This diagnosis is supported by a family study.

Case Report

A female Gurkha child aged 3 months was seen at the British Military Hospital, Kinrara, in July, 1954, when she was referred for investigation for a hypochromic anaemia. Examination then revealed a relatively well-nourished infant with pallor of the mucous membranes and marked hepatosplenomegaly.

Laboratory investigations showed: haemoglobin, 5.5 g./100 ml.; W.B.C., 9,300/c.mm. (neutrophils 50% lymphocytes 40%, eosinophils 5%, basophils 3%, monocytes 2%); reticulocytes, 2%. Erythrocyte osmotic fragility was decreased. Peripheral blood films showed hypochromia, anisopoikilocytosis, microcytosis, target cells, and many normoblasts. No malarial parasites were noted on repeated

investigation. Bone-marrow films showed intensive normoblastic hyperplasia, but no malarial parasites or Leishman-Donovan bodies. Total serum bilirubin, 0.4 mg./100 ml.; indirect Coombs test negative; liver-function tests normal; Wassermann and Kahn reactions negative. Urine contained only traces of urobilinogen. Examination of faeces showed no evidence of ankylostomiasis. Radiological examination of the bones revealed no abnormality. A liver biopsy performed a few weeks later showed increased amounts of iron but normal histology.

Treatment consisted of large doses of iron, ascorbic acid, aneurine, pyridoxine, folic acid, vitamin B₁₂, thyroid, and cobalt. This had no effect in alleviating the anaemia. In January, 1956, a splenectomy was performed in the hope of lengthening the interval between blood transfusions. The histology of the excised spleen was normal, but increased amounts of iron pigment were noted. There was no noticeable improvement in her condition, and a subsequent course of cortisone therapy was also ineffective. So far she has been maintained on repeated transfusions of 500 ml. of packed cells each six-week period. In April, 1957, electrophoresis of her haemoglobin, performed on filter paper (pH 8.6 and 6.5) on a blood sample obtained prior to transfusion revealed only normal adult haemoglobin. The one-minute alkali denaturation test (Singer, Chernoff, and Singer, 1951) revealed 10% foetal haemoglobin. A diagnosis of thalassaemia was made, but it was not possible to carry out a family study until August, 1959.

A physical examination of the patient carried out in April, 1959, revealed a pale child of normal stature with normal mental development. The only abnormality was a firm enlargement of the liver, the edge of which was palpable 2 in. (5 cm.) below the level of the umbilicus. X-ray films of the skull and long bones showed no abnormalities. The results of haematological investigation at this time are shown in the Table.

The patient is the fifth in a family of six children. The father is healthy and symptom-free, but the mother has a hypochromic anaemia which was detected during her last pregnancy and which has proved resistant to iron and ascorbic-acid therapy. The youngest in the family is a healthy infant, and the other four children are symptom-free. They are all normal in stature and appearance but rather pale, and none of them show enlargement of spleen or liver.

Results of haematological investigation in the family (excluding the youngest infant, 1 week old at the time of

these investigations) are shown in the Table. Peripheral blood smears from each of the parents and the four siblings studied all showed hypochromia, marked anisopoikilocytosis, microcytosis, and occasional target cells. The haemoglobin-A₂ results given in the table represent the averages of duplicate estimations, using a starch-block electrophoresis technique essentially similar to that of Kunkell *et al.* (1957). The range for 79 healthy subjects by this method was 0.00–2.51%, average 1.78% (Vella, 1960). No abnormal haemoglobin components were detected, and no intra-erythrocytic inclusion bodies were elicited on supra-vital staining of erythrocytes with brilliant cresyl blue (Gouttas *et al.*, 1955), in any members of the family.

Osmotic fragility curves from the patient and her family. 1= Mother. 2 and 3=Patient's siblings. 4=Patient.

Discussion

The early age at onset, the severe anaemia resistant to standard therapy, the peripheral blood picture, the marked hepato-splenomegaly, the evidence of visceral siderosis, and the subsequent course of the disease in this patient indicate thalassaemia or a thalassaemia-like disorder. The continued absence of radiological changes in the skull and long bones, and the normal physical development so far, may be due to regular blood transfusions from an early age. This may be responsible in some degree for her present liver enlargement. Relatively low levels of foetal haemoglobin are not unknown in thalassaemia major (Itano, 1955).

The finding of an iron-resistant hypochromic microcytic anaemia in the mother in the presence of 4.0% of haemoglobin A₂ suggests that she is heterozygous for the thalassaemia abnormality. Similarly, the mild anaemia and the presence of 5.56% haemoglobin A₂ in the father, even in the presence of a normal erythrocyte osmotic fragility curve, suggest that he also is a thalassaemia carrier. The anaemia in the siblings may well have a nutritional element, though the findings in both parents and the increased haemoglobin A₂ concentrations (3.21–5.56%) point to a thalassaemic background for their anaemia.

We are grateful to Major S. E. M. Jarvis, R.A.M.C., for his interest in this patient and in this report, and to Lieut-Colonel J. P. Baird, R.A.M.C., for his advice.

Results of Haematological Study of the Patient and Her Family

	Patient	Father	Mother	Brother	Sister	Brother	Sister
Age (in years)	5	30	28	6½	4	3	1½
Hb (g./100 ml.)	3.7	11.4	9.2	9.2	7.4	8.0	6.9
Red cells (millions c.mm.)	1.61	4.0	3.78	3.1	3.2	3.0	2.5
Haematocrit (%)	17	41	32	34	29	28	Not done
M.C.V. (μ ³)	105	102	84	109	90	107	Not done
M.C.H. (μg.)	22	26	24	29	23	28	27
M.C.H.C. (%)	24	28	28	27	25	26	Not done
Reticulocytes (%)	3.0	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5
Target cells	++	—	—	—	—	—	—
Hypochromia	+	±	+	+	+	+	+
Anisopoikilocytosis	++	+	++	++	++	++	++
Microcytosis	+	+	+	+	+	+	+
Normoblasts	++	—	—	—	—	—	—
Haemolysis:							
Commences at % NaCl	0.48	0.52	0.49	0.56	0.56	0.56	0.52
Complete at % NaCl	<0.28	0.36	<0.24	<0.30	<0.24	<0.24	<0.24
Alkali-resistant Hb (%)	8.0	2.0	2.6	2.0	1.5	3.7	1.0
Hb A ₂ (% of total)	1.00	5.56	4.0	4.28	3.45	5.50	3.21
Hb on electrophoresis	A	A	A	A	A	A	A

+ Indicates present; ++ indicates marked; ± indicates slight; — indicates absent.

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Medical Memoranda

Herpes Zoster Occurring in a Patient with Chicken-pox

Clinical and epidemiological observations suggest that chicken-pox and zoster are caused by the one virus, and recent laboratory studies on the growth in tissue culture of virus from the two clinical entities support this view (Weller *et al.*, 1958; Weller and Witton, 1958). Though 2-5% of zoster patients develop a generalized rash, sometimes profuse enough to be typical of chicken-pox, it is much less common for chicken-pox patients to develop a secondary eruption with a typical zoster distribution. Stokes (1959) indicates that this is not an uncommon observation, but very few instances are recorded in the literature. Allen (1944) reported a case of chicken-pox in a boy aged 5 years who developed a zoster eruption on the right side of his body three weeks after the onset of chicken-pox. Cheatham *et al.* (1956) described the case of a 4-year-old boy suffering from a neuroblastoma with multiple metastases who developed chicken-pox and died 17 days after its onset. At necropsy a zoster eruption was found on the right side of the abdomen and back, corresponding to sensory innervation from T10. Another example of a zoster eruption developing in a patient suffering from chicken-pox is mentioned below.

CASE REPORT

An outbreak of chicken-pox occurred in a boys' boarding-school. The onset of illness in the first case was on January 21. This was followed by eight other cases between February 5 and 7, and a further eight between February 21 and 25.

On March 12 the last case occurred in a boy of 8 years who had not had chicken-pox previously. His eruption

Vesicles in right cervical sensory area, associated with extreme hyperaesthesia of surrounding skin.

was sparse, as in all the other cases in this outbreak. On March 18, when fresh lesions had not been noted for several days, 10 vesicles appeared in the right cervical sensory area (C3). They were associated with extreme hyperaesthesia of the surrounding skin, as indicated in the accompanying Figure, and the patient, though otherwise feeling quite well, was very reluctant to undergo examination. The lesions became purulent by March 21, and had healed completely on April 11, by which date the skin sensitivity had disappeared. As the school was in quarantine, the patient could not have been in contact with a case of zoster since the beginning of term.

COMMENT

In zoster patients there is usually a history of previous chicken-pox. In those over 40 years, in whom the malady is most often seen, the history of an earlier chicken-pox infection may not be remembered; but in children or adolescents suffering from zoster a history of previous chicken-pox is usually obtained (Schools Epidemics Committee, 1938). An earlier and greater rise of antibody had been found in the sera of zoster than in chicken-pox patients (Taylor-Robinson and Downie, 1959; Taylor-Robinson and Rundle, 1959); this is consistent with the view that zoster represents a second clinical infection with the virus. Little is known, however, about the pathogenesis of zoster. In the majority of zoster cases there is no known contact with chicken-pox or other zoster patients, and the seasonal prevalence of chicken-pox is not accompanied by an increased incidence of zoster (Seiler, 1949). These observations suggest that zoster is caused by the activation of latent chicken-pox virus. This view might help to explain the occurrence of zoster associated with disease or injury of the spine, x-ray therapy, or lumbar puncture. There is no evidence to indicate the tissue in which chicken-pox virus might lie latent nor, in most cases, the stimulus which leads to reactivation.

The occasional occurrence of cases such as that reported above indicates that chicken-pox virus may infect root ganglia at the time of the original chicken-pox infection, and suggests the possibility that in zoster cases the virus might remain latent in nerve tissue between the primary attack of chicken-pox and subsequent zoster. The occurrence of pain and hyperaesthesia involving the area of skin or mucous membranes, where the rash is to appear several days later, indicates that spread of virus occurs peripherally from the ganglia to the skin, probably by nerve pathways. This sequence of events is supported by histological evidence.

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