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PURE RED-CELL ANAEMIA IN PATIENTS WITH THYMIC TUMOURS*

BY

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Selective bone-marrow aplasia involving erythropoiesis and leaving leucocyte and platelet production unaffected is most uncommon, being referred to by Whitby and Britton (1953) as a rare curiosity and mainly of theoretical interest. This disorder was first described by Kaznelson (1922), who called it erythrophthisis. Reports of the condition occurring both in children and in adults are now more frequently seen, and long-term studies are being made (Diamond, 1954).

The cause of this type of anaemia remains unknown. A congenital origin, ABO blood-group incompatibility between mother and affected child, allergy, riboflavine deficiency, toxins, and "hypersplenism" have all been suggested as possible explanations by various writers, and there may be a mixed aetiology underlying the unusual bone-marrow change leading to "pure red-cell anaemia," the term first used by Lescher and Hubble (1932).

A syndrome of selective erythroblastic aplasia in association with the presence of a thymic tumour has been observed in a proportion of the small number of adult cases which have been fully investigated. Davidsohn (1941) recorded the case of an adult woman with severe anaemia due to erythroid hypoplasia who was found at necropsy to have a lympho-epithelioma of the thymus. The case reported by Humphreys and Southworth (1945) and that of Chediak *et al.* (1953) both showed prompt haematological improvement after removal of thymomas. Ross *et al.* (1954), with whom we have had exchange of information for some time, record two cases showing the simultaneous occurrence of benign thymoma and refractory anaemia very comparable to those described in this paper. Removal of thymoma in both of their cases—and also splenectomy in one of them—was not followed by any haematological improvements.

This preliminary report gives abridged case histories of two adult patients with pure red-cell anaemia. One of them also had myasthenia gravis. Both had thymomas and were subjected to thymectomy, splenectomy, and A.C.T.H. therapy, with ultimate recovery. Further details, discussion, and follow-up studies will be published elsewhere.

*A description of these cases was given by Dr. Chalmers at the Fifth International Congress of Haematology, held in Paris in September, 1954.

Case 1

An electric-train driver aged 48 was transferred from the National Hospital for Nervous Diseases on June 28, 1951, for investigation of severe anaemia. Weariness, dyspnoea, and palpitation had increased progressively for a month. Dr. Denis Williams had some eighteen months previously diagnosed myasthenia gravis and the patient had been treated with oral neostigmine, belladonna, and ephedrine with excellent clinical effect. His history disclosed no apparent cause for the anaemia. He had been married for twenty-five years and had a family of three. For about six years there had been gradual loss of libido.

On examination he was a cheerful, heavily built, thick-set man—height 5 ft. 9 in. (175 cm.); weight 12½ st. (79 kg.)—showing marked pallor of the skin and mucous membranes. The heart rate was 80 and regular, there being a systolic murmur over the praecordium. His B.P. was 130/60. Clinical examination of lungs and nervous system was negative, myasthenia being controlled with neostigmine. The tongue was normal and no abdominal mass or palpable enlargement of liver or spleen was present.

Investigations and Progress

Blood examination showed severe normochromic anaemia with red cells varying little in size and shape and showing no polychromasia: Hb, 27% (4 g.); red cells, 1,340,000 per c.mm.; C.I., 1; P.C.V., 11.5%; M.C.V. 85 cubic μ; M.C.H.C., 35%; white cells, 5,200 (polymorph neutrophils 49%, lymphocytes 47%, monocytes 4%, eosinophils nil); platelets 325,000 per c.mm. No reticulocytes or nucleated red cells could be found on repeated examination. Blood group: A, Rh (D) positive, direct Coombs test negative, bilirubin less than 0.5 mg. per 100 ml.; blood urea, 21 mg. per 100 ml.; thymol turbidity, 1.2 units; alkaline phosphatase, 3.4 King–Armstrong units; serum proteins, 6.9% (albumin 3.4 g.%, globulin 3.5 g.%; A.G. ratio 1:1); normal red-cell fragility, bleeding-time, clotting-time, and clot retraction. Wassermann reaction and Kahn test were negative. An alcohol histamine test meal showed no free hydrochloric acid in the gastric juice, but retesting later showed free acid to be present. The urine was normal and contained no excess urobilinogen.

Smears of sternal marrow showed average cellularity with a striking absence of all forms of erythroblasts. Only a very occasional equivocal red-cell precursor could be found, but a large number of small densely staining cells with little or no cytoplasm were seen. These were regarded as probably of lymphoid type. A slight increase in plasma and reticulum cells was observed. Myeloid series and megakaryocytes seemed of normal morphology and distribution.

Transfusion of concentrated red cells derived from approximately 2,000 ml. of citrated blood gave benefit. The blood count figures rose to Hb 46% (6.8 g.), red cells to 2,000,000, and P.C.V. to 18%. No reticulocytes could be found.

While tomography was not performed in this case, there was no good evidence of mediastinal tumour on the plain *x*-ray film of the chest. Treatment for myasthenia gravis with oral neostigmine, 15 mg. q.d.s., together with belladonna and ephedrine, was continued. No haematological benefit was obtained from prolonged treatment with various haematinics. A course of intramuscular A.C.T.H. (1,425 mg. over two weeks) also caused no change in the marrow or blood findings, reticulocytes being consistently absent. Repeated blood transfusions seemed the only means of keeping the patient alive.

After reading the remarkable case recorded by Humphreys and Southworth (1945), in which removal of a tumour of probable thymic origin appeared to have a direct influence on pure red-cell anaemia, we were led to consider this operation for our patient. It was also possible that this

procedure would benefit his myasthenia gravis, though no conclusive *x*-ray evidence was present to suggest thymic enlargement. After repeated preliminary transfusions, together with pre-operative increase of neostigmine dosage, Mr. A. H. M. Siddons performed exploratory thoracotomy on October 23. A lobular thymoma of 120 g. weight and 10 by 9.5 by 3 cm. in size was successfully removed. Though it was adherent to the left pleura, there was no evidence of the tumour invading other surrounding structures, and the histology was that of a thymoma of lympho-epitheliomatous type. Ten days after the operation reticulocytes were found in the patient's blood for the first time since he had come under our observation. They reached a maximum of 19.5% eighteen days after thymectomy (see Fig. 1). The patient showed obvious clinical improvement and there was spontaneous gain in haemoglobin, red-cell count, and P.C.V. Puncture of the right iliac crest two weeks after operation showed fairly frequent erythroblasts at all stages of normoblastic development. Six weeks after thymectomy, neostigmine, which had been gradually reduced in dosage after the operation, was discontinued without evidence of myasthenic relapse. In contrast, haematological improvement was not maintained, and seven weeks after thymectomy the blood count was falling, reticulocytes were again absent, and marrow examination (right iliac crest) showed a virtual absence of erythroblasts.

Folic acid, liver, multivitamin tablets, nicotinamide, and cobalt chloride (the latter causing nausea and being given for only a short time) were all ineffective. Repeated transfusions were again necessary. No return of myasthenic symptoms was observed, but haematologically the prognosis seemed grave.

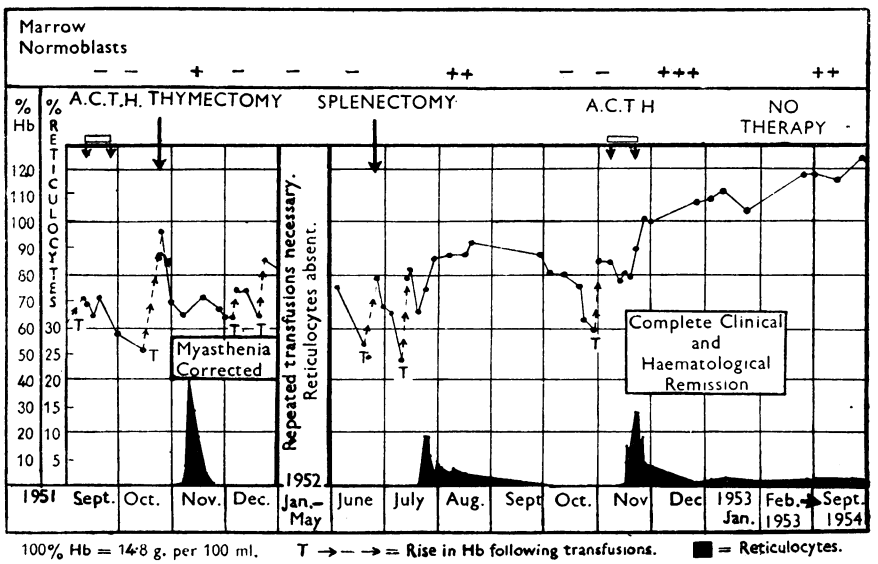

FIG. 1.—Case 1. Pure red-cell anaemia in a patient with myasthenia gravis and thymoma. Haematological and therapeutic data over a period of three years.

On the slender hypothesis that removal of lympho-epithelial thymic tissue had in some way been related to the temporary benefit, and considering that hypersplenism might be a mechanism associated with the anaemia, splenectomy was advised, the operation being performed by Mr. Ralph Marnham on June 24, 1952. Marrow examination at the time of operation showed no erythroblasts but was otherwise normal. The excised spleen weighed 400 g. and was dark and firm. Apart from the prominence of the Malpighian bodies and considerable haemosiderosis, no noteworthy histological features were reported. The patient's post-operative clinical course was stormy for about three weeks. The haemoglobin, the number of red cells, and the P.C.V. again fell after the pre-operative transfusions, and further folic acid and transfusions of concentrated cells were given, together with antibiotic therapy. No reticulocytes were observed on frequent examination until a month after the operation. They then showed an increase up to 9.5% together with a reappearance of marrow erythroblasts and an associated increase in the blood values, which reached Hb 93% (13.8 g.), red cells 4,370,000, and P.C.V. 44% on August 18 (eight weeks after splenectomy), when he was discharged from hospital looking and feeling well. No form of therapy had been given for a month.

The patient was kept under observation, and haematological relapse again occurred in four weeks. No improvement took place with intensive folic acid therapy, and as the marrow again showed absence of erythroblasts, and there were no reticulocytes in the blood, further blood transfusions had to be given. On November 5 a course of A.C.T.H. therapy was started. A daily dosage of 40 mg. increasing to 200 mg. was given intramuscularly in divided doses every six hours. On the sixth day of A.C.T.H. therapy—by which time 800 mg. had been given—reticulocytes appeared in the blood, and by the sixteenth day of treatment a reticulocyte peak of 14% was reached. There was an associated rise in haemoglobin, red cells, and P.C.V., together with remarkable clinical improvement. A.C.T.H. was discontinued after seventeen days, when a total of 2.59 g. had been given. At this stage the haemoglobin had risen to 90% (13.3 g.), red cells to 4,230,000 and P.C.V. to 43%. It was observed that, in addition to reticulocytosis during A.C.T.H. therapy, fairly frequent normoblasts and red cells containing Howell–Jolly and siderotic bodies were noted in blood films. Bone-marrow examination showed active normoblastic erythropoiesis.

The gratifying response obtained during A.C.T.H. therapy in October, 1952, has been followed by complete and maintained haematological remission for two years *without any further treatment being necessary*. Moreover, no recurrence of myasthenia gravis has occurred since removal of the thymic tumour. The patient's only complaints are chronic bronchitis and loss of libido.

Case 2

A widow aged 62 was admitted for investigation of refractory normochromic anaemia on December 11, 1952 (Fig. 2). She had suffered from weakness and breathlessness for about six months. There was nothing in her history to account for the anaemia. Treatment at another hospital with liver extracts, vitamin B_{12}, iron, and multivitamin preparations was ineffective. She had received six blood transfusions between August and December, 1952. She had had three normal pregnancies. Menstruation had ceased at the age of 55. Her previous health had always been good apart from bronchitis in 1932, when she attended the Brompton Hospital.

On examination she was found to be a pale, well-nourished, afebrile woman with no physical sign of disease apart from pallor and slight oedema of the ankles and over the sacrum. Her weight was 10 st. 4 lb. (65.3 kg.). B.P. was 160/90. Her urine was normal, containing no excess urobilinogen. A test meal showed the presence of free hydrochloric acid.

Haematological Investigations

Hb, 48% (7.1 g.), red cells, 2,100,000 per c.mm.; P.C.V., 18%, M.C.V., 90 cubic μ; M.C.H.C., 38%; E.S.R., 50 mm. in one hour (Wintrobe); direct Coombs test negative; blood group O Rh-negative (cde/cde). No abnormal antibodies were found in serum. No reticulocytes could be found on

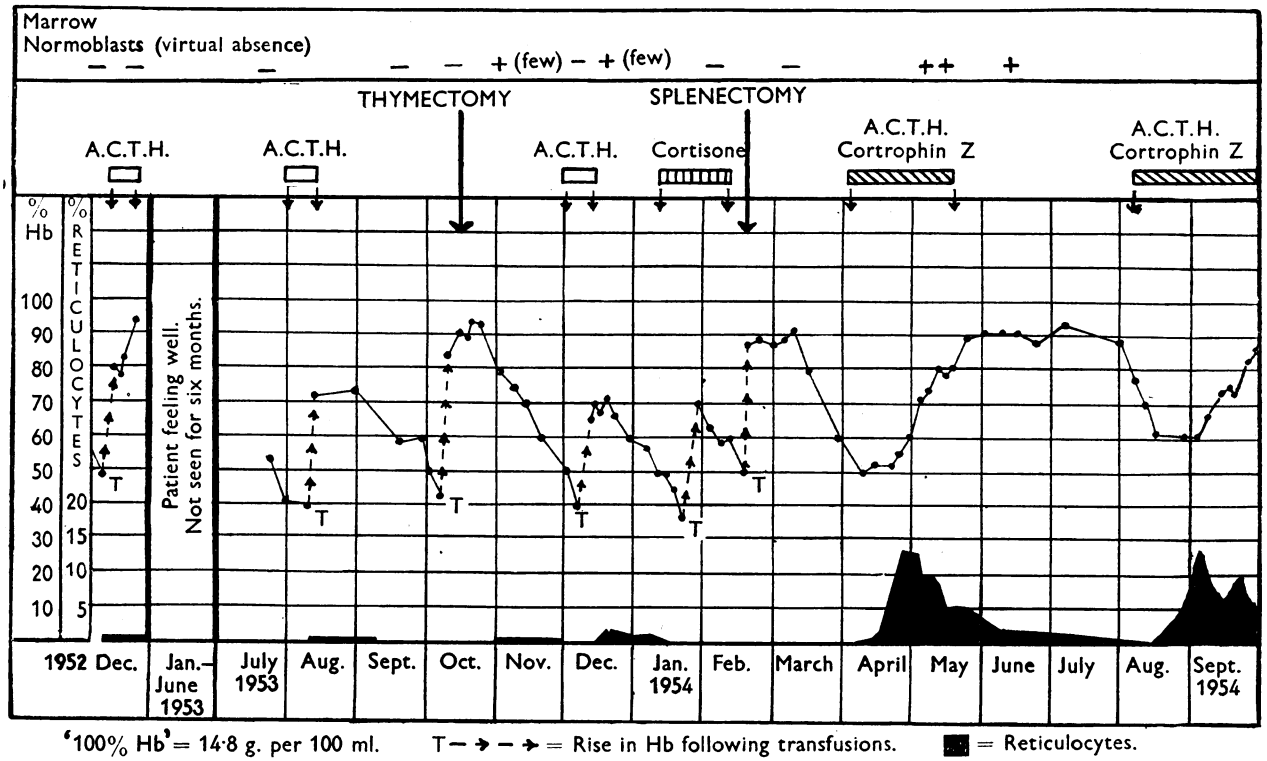

FIG. 2.—Case 2. Pure red-cell anaemia in a patient with thymoma. Haematological and therapeutic data over a period of two years.

prolonged examination. The white cells numbered 8,500 per c.mm. (polymorphs 41%, lymphocytes 46%, monocytes 9%, eosinophils 4%); platelets 260,000 per c.mm. Smears of sternal marrow showed a severe depression of erythropoiesis, only a very occasional late normoblast being seen. Numerous small dark "lymphoid" cells, as observed in Case 1, were present. Apart from a slight increase in plasma cells and eosinophils no abnormalities in the white-cell series were observed. Megakaryocytes were numerous and of normal morphology. Bilirubin, 0.3 mg. per 100 ml. Alkaline phosphatase, 9 King–Armstrong units. Plasma protein and liver function tests were normal. Wassermann and Kahn reactions were negative. Repeated counts showed an occasional reticulocyte, but they were always under 0.1% and often were not demonstrable.

Slow transfusions with 1,600 ml. of concentrated group O Rh-negative (cde/cde) cells raised the blood values to Hb, 79% (11.7 g.); red cells 4,360,000; P.C.V., 37%. A course of A.C.T.H. was started on December 14, a total of 1.25 g. being given by intramuscular injection over nine days. The patient was most anxious to get home, and she left hospital on December 23 much improved and before the chest could be *x*-rayed. While very occasional reticulocytes could be found they remained under 1%, and a repeat sternal bone-marrow examination following the A.C.T.H. therapy showed no significant change, erythroblasts being very scanty. On discharge, Hb was 94% (13.9 g.), R.B.C. 4,610,000; P.C.V., 38%; W.B.C., 15,700.

The patient felt well for the next six months, but when seen on July 25, 1953, she complained of tiredness. Hb had fallen to 54% (8 g.), with R.B.C. 2,320,000; C.I. 1.2; P.C.V., 21%; M.C.V., 91 cubic μ; W.B.C., 7.800. Marrow puncture showed absence of erythroblasts and a moderate increase of eosinophilic granulocytes. *X*-ray examination of the chest showed a large oval mass in the mediastinum measuring about 4 by 5 in. (10 by 12.5 cm.) and lying in the anterior mediastinum in front of the heart.

This finding, when considered in relation to Case 1, made us wonder whether the patient also had a thymoma in association with her unusual anaemia. She, in contrast, never had suffered from any symptoms suggestive of myasthenia gravis. We were able to find out that she had attended the Brompton Hospital in 1932 and a mediastinal shadow had been observed at that time, long before she had any symptoms of anaemia. A further course of 1.25 g. of A.C.T.H. was given over ten days (comparable to that given seven months before). While no reticulocytes could be found during the course of A.C.T.H. therapy, during the subsequent three weeks they reached 1%, and even occasional normoblasts could also be found in the blood. Improvement was very transient, however, and repeated marrow examination again showed virtual erythroblastic aplasia. Further blood transfusions were necessary.

In view of the possible connexion between the anaemia and the mediastinal mass, which we thought might well be a thymoma, thoracotomy was performed by Mr. A. H. M. Siddons on October 15. A large lobulated tumour weighing 331 g. and 13 by 9 by 4.5 cm. in size was removed. It lay anterior to the pericardium, extending up to the origin of the great vessels, and had a small pedicle. Histological appearances were those of a thymoma with lympho-epithelial tissue divided by many fibrous septa. Convalescence was uneventful, and the patient was discharged from hospital nineteen days after removal of the tumour. Ten days after the operation reticulocytes, previously absent, appeared in small numbers, but they were always less than 1%. Marrow examination showed a few intermediate and late normoblasts, whereas none were found at the time of the operation. This change was transient, and six weeks after thymectomy the Hb was 50% (7.4 g.); R.B.C., 2,200,000; and P.C.V. 17%. No reticulocytes could be found. Erythroblasts were not observed in marrow smears. A further course of A.C.T.H. was given at this stage as well as another transfusion. Neutrophil leucocytosis occurred during A.C.T.H. therapy, as had been noted before. A.C.T.H. had to be discontinued because of pain at injection sites after 980 mg. had been given over ten days. While no reticulocytes had been found during the course of A.C.T.H. therapy they suddenly appeared two days later and rose progressively to 2.2%, associated with some clinical improvement and gain in haemoglobin, red cells, and P.C.V. Erythroblasts at this time were fairly often present in marrow smears. Once

again, however, haematological improvement was of short duration, and a month later there was again complete relapse. A course of 5.65 g. of cortisone combined with ascorbic acid, folic acid, and vitamin B_{12} was ineffective. Splenectomy was performed by Mr. Ralph Marnham on February 19, 1954, following pre-operative transfusion. On the day of operation the marrow showed complete erythroblastic aplasia. A spleen weighing 195 g. and measuring 13 by 9 by 5½ cm. was removed together with a splenunculus 1.5 cm. in diameter. Histologically no noteworthy features apart from haemosiderosis were reported.

The post-operative course was uneventful and the patient was discharged two weeks after operation. No evidence of red-cell regeneration was observed, however, and, while the platelet count rose to 500,000 per c.mm. and slight leucocytosis was observed, the haemoglobin and red cells started to fall again, and the bone marrow (right iliac crest) showed selective erythroblastic aplasia six weeks after the operation. However, in view of the effect of A.C.T.H. after splenectomy in our first case, we now considered giving similar treatment to this patient. She was apprehensive of frequent injections, and through the kindness of Dr. W. J. Tindall we were provided with a supply of "cortrophin Z," long-acting A.C.T.H. This was given at first in amounts of 40 international units daily by intramuscular injection, and the dose was gradually reduced to 20 units twice weekly. A good reticulocyte response occurred, starting on the seventh day of the A.C.T.H. course (by which time 240 units of cortrophin Z had been given), a maximum of 13.4% being reached on the twenty-fourth day of therapy. Neutrophil leucocytosis, with persistent increase of eosinophils during A.C.T.H. therapy, was also observed. Haemoglobin, red-cell count, and P.C.V. showed progressive increase, and, while the patient had fairly marked oedema in spite of limitation of fluid and salt and the regular administration of potassium citrate, she said she had not felt as well for fifteen months. Normoblasts were now frequently seen in blood films; platelets numbered 372,000 per c.mm.; and macrocytosis, polychromasia, stippling, and Howell–Jolly and siderotic bodies in the red cells were noted. When the patient had received 740 units of cortrophin Z over 48 days treatment was stopped. Marrow examination showed active normoblastic erythropoiesis at all stages of red-cell development, and blood count values continued to show maintained gain, even following discontinuation of all treatment for ten weeks, when blood examination showed Hb 88% (13 g.); R.B.C., 4,120,000; reticulocytes, 0.7%; P.C.V., 40%; E.S.R., 12 mm. in one hour (Wintrobe); M.C.V., 97 cubic μ; M.C.H.C., 32%. Persistent macrocytosis, poikilocytosis, and intra-erythrocytic dots of various types remained. Leucocytes and platelets were normal.

Within the next three weeks a fairly rapid relapse occurred —Hb, 61% (9.0 g.); R.B.C., 2,210,000; P.C.V., 26.5%; with only a very occasional reticulocyte seen. Further A.C.T.H. therapy, given as cortrophin Z, was again followed by prompt haematological improvement, and at the time of writing the patient was being maintained in good health on 40 international units of cortrophin Z twice a week.

Discussion

The association of selective erythroblastic aplasia or hypoplasia with thymic tumour has been observed, in addition to the two cases here reported, in five other adult cases that we know of (Davidsohn, 1941; Humphreys and Southworth, 1945; Chediak *et al.*, 1953; Ross *et al.*, 1954). A case with generally similar haematological findings and clinical course, and *x*-ray evidence of a large anterior mediastinal tumour, has been investigated by H. F. Brewer (1954, personal communication). She will not submit to operation, and the nature of the tumour in her case must meantime remain unknown.

Keynes (1954) in a review of the physiology of the thymus gland, made no mention of the association between anaemia and thymic tumours. Apart from those quoted above, the only references to marrow aplasia and thymic enlargement or tumour we can find are those of Opsahl (1939) and Wintrobe (1951, and personal communication). The patient mentioned by Wintrobe also had myasthenia gravis. The clinical features and types of marrow aplasia described in these cases, however, differed from those observed in ours. It would thus seem possible that a rare syndrome may exist in which pure red-cell anaemia due to selective erythroblastic aplasia or hypoplasia of the bone marrow is associated with the presence of a thymic tumour. In our Case 2 there was evidence of a mediastinal mass on *x*-ray films taken some twenty years before anaemia developed. One of the patients recorded by Ross *et al.* (1954) also showed radiological evidence of such a tumour before anaemia developed.

Two possible hypotheses have occurred to us to explain these unusual cases. Firstly, endocrine dysfunction may be the underlying cause. The thymus is known to be enlarged in some cases of thyrotoxicosis and Addison's disease. The polycythaemia seen in some cases of Cushing's syndrome might be regarded as the opposite extreme of the aplasia here described, especially as our cases latterly responded to A.C.T.H. therapy. Secondly, lymphoid proliferation in the thymus, marrow, and possibly other sites may in some way, as yet unknown, impede erythropoiesis. Depending on the degree of such interference, removal of the tumour may correct the anaemia (Humphreys and Southworth, 1945; Chediak *et al.* (1953) or, on the other hand, have no effect (Ross *et al.*, 1954). In our Case 1 temporary haematological remission occurred after removal of the thymoma, in which complete dissection was performed; but in Case 2 insignificant changes took place. This could possibly be due to some thymic tissue remaining. Splenectomy also seemed to cause temporary improvement in Case 1, as also occurred in a patient without known thymoma described by Loeb *et al.* (1953). This operation had no effect in Case 2.

While A.C.T.H., given earlier, caused no very significant haematological changes, *prompt and well-maintained responses occurred in both our cases when A.C.T.H. was given subsequent to splenectomy.* This has also been observed by Loeb *et al.* (1953) and Tsai and Levin (1954) in patients with erythroid hypoplasia but with no recorded evidence of thymoma. At the time when their reports were written their patients had not relapsed following discontinuation of cortisone or A.C.T.H., given after splenectomy.

While spontaneous recovery from pure red-cell anaemia is not unknown (Heilmeyer and Begemann, 1951; Baar, 1952) it seemed likely that the several responses obtained in our patients were related to surgery or A.C.T.H. therapy. In our second case haematological relapse following discontinuation of A.C.T.H. therapy after splenectomy, and the subsequent remission on giving further amounts of the hormone, adds force to this view. Apart from blood transfusion, all other treatment, including riboflavine, given to Case 2 (cf. Foy and Kondi, 1953) was of no avail.

More detailed discussion of these unusual cases will be made after their further study. This paper is concerned with recording the phenomena observed during the last three years and suggesting the possibility that this unusual association might be more widely recognized and investigated.

Summary

Two adult patients suffering from pure red-cell anaemia (erythroid aplasia or hypoplasia) were found to have thymic tumours.

One of the patients also suffered from myasthenia gravis. Both underwent thymectomy and splenectomy.

Haematological changes in probable relationship to such operations and the use of A.C.T.H. therapy are recorded and briefly discussed.

Both patients are at the time of writing in clinical remission. Thymectomy corrected myasthenia gravis which had been present in Case 1.

Thanks are due to Mr. A. H. M. Siddons for thymectomy; to Mr. Ralph Marnham for splenectomy, and to Professor Theodore Crawford and numerous other colleagues of the hospital and medical school staff for valuable assistance; to Dr. W. S. Killpack, of the King Edward Hospital, Ealing, for early notes and laboratory data of Case 2; and to Dr. W. J. Tindall, of Organon Laboratories Ltd., for supplies of cortrophin Z. Not least, we would again mention the patients, who submitted themselves to innumerable medical and surgical procedures with cheerfulness and optimism.

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SOME CLINICAL EPILEPTIC ODDITIES*

BY

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In any gathering of people interested in the many intriguing problems of epilepsy, I fear that the so-called oddities among patients to whom I shall refer may be regarded as somewhat commonplace. But epileptic patterns and associations are so variegated that I am encouraged to mention some cases seen in recent years and to hope that other clinicians may describe odd features of which they have experience.

Epilepsy or Migraine

The peculiar relationship of epilepsy to migraine needs no emphasis. I would, however, like to mention first some examples of how these two conditions may at times almost fuse or overlap. Occasionally a patient subject to both forms of attack may develop warning sensations which are common to each. Thus, a woman of 36 had been subject to major epileptic attacks since childhood and typical migraine in recent years. For about an hour before the epileptic attacks she would experience familiar feelings of the *déjà vu* variety, and these would be accompanied by a series of coughing attacks and often by a feeling of panic until the onset of the convulsion. Major fits were almost always preceded by a prolonged warning of this sort, but on occasion her attacks of migraine were associated with exactly similar phenomena. Blurred vision and teichopsia then occurred in addition, but consciousness was not lost.

*A paper read at a meeting of the International League against Epilepsy (British Branch) at the National Hospital, Queen Square, on March 12, 1954.

On other occasions, without any warning, a patient may become unconscious during a severe attack of migraine and the loss of consciousness then generally resembles a brief akinetic epileptic attack. For instance, a girl aged 19 has characteristic attacks of migraine, as does her father. She says that, on occasion, when her headache is severe, her hands begin to tingle and feel enlarged, her limbs feel stiff, and she falls down in a brief attack of unconsciousness. She has never had any sort of faint or fall on any other occasion.

Another patient who suffers from migraine and who has a family history of epilepsy, describes similar attacks of unconsciousness at the height of a severe sick headache. She says that she falls down suddenly and may be picked up unconscious in the street, having hurt herself. She recovers consciousness after a few minutes to find that the headache has gone but she feels confused and drowsy.

Sometimes migraine is associated with attacks that seem more cataplectic than epileptic. Thus a man of 68, who has had migraine since childhood, began at the age of about 35 to fall down in some of his bouts of migraine. On such occasions he has a severe right-sided headache and suddenly falls forwards on to his knees. He says that he is not giddy and remains aware of his surroundings, but feels that he has to stay immobile for 15 to 30 seconds. He then stands up without difficulty, feels sick, and vomits shortly afterwards. He has never fallen on to his knees in this way except in association with a sick headache.

Inhibitory epilepsy, taking the form of transient hemiplegia, has its counterpart in hemiplegic migraine. The epileptic variety is usually an isolated event, whereas the migrainous type is usually associated with visual disturbances and followed by sick headache. Sometimes, however, it may be difficult to distinguish the one from the other. Thus, a man of 46, who has for some years been subject to classical migraine, recently had a sudden attack of loss of power of the right arm and leg without any associated sensory symptoms or subsequent headache or nausea. There was no impairment of consciousness, and the power returned suddenly, after about five minutes. He had an exactly similar attack later the same day. When seen next day there were no abnormal neurological signs and his blood pressure was normal. There is little in the attack itself to signify whether in this case it was a migrainous variant or an isolated inhibitory epileptic seizure.

Initial loss of sight (hemianopic or total) may form an inhibitory aura in both epilepsy and migraine, but, like the transient hemiplegia just mentioned, temporary blindness may occur as an isolated phenomenon. I have recently seen a female patient aged 27 who is subject to both epilepsy and migraine. These attacks are not preceded by visual loss, but on four occasions lately she has experienced isolated episodes of sudden and complete loss of vision. These are unassociated with headache or loss of consciousness and they have varied in duration from ten minutes to five hours.

Apart from migraine, there are some other conditions which, although usually independent, may be associated with epilepsy. An odd case of the almost coincident onset of sleep paralysis and epilepsy was as follows. A woman aged 30 woke up in the early morning, lying flat on her back and quite unable to move or speak for several minutes. She was frightened, but was fully aware of her surroundings; there had been no tongue-biting or incontinence, and her husband, who was with her, had not been disturbed. She had never experienced anything like this before, and her account is most suggestive of sleep paralysis. Next day she felt quite well, but late in the morning, while looking at a book, she suddenly felt far away, gave a cry, and had a major epileptic attack in which she bit her tongue and was incontinent. She had never had any sort of fit or faint before, and there were no obvious physical or emotional factors which might have influenced the onset in rapid succession of these two different forms of attack.