DISSEMINATED LUPUS ERYTHEMATOSUS PRESENTING AS IDIOPATHIC THROMBOCYTOPENIC PURPURA

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Since the discovery of the L.E. phenomenon by Hargreaves[1] in 1948 the concept of disseminated lupus erythematosus (DLE) as an immunological disease has been gaining ground.

False positive serological tests for syphilis in this disease have been recognized for many years. Lately there have been a number of reports both overseas and here in South Africa[2] of haemolytic anaemia associated with DLE. There have also been reports of a haemorrhagic tendency with thrombocytopenia and/or a circulating anticoagulant complicating or preceding the disease.

Eversole[3] reported 6 cases of DLE presenting as thrombocytopenic purpura where the correct diagnosis of DLE was only made on post-mortem examination or after splenectomy. He states that splenectomy does not exert a harmful influence on this disease. Swift[4] reported 2 cases with thrombocytopenia and/or a circulating anticoagulant where the prothrombin concentration at no stage exceeded 57%. He considered the circulating anticoagulant to be an antithromboplastin produced by an auto-immunological response to thromboplastin released by the breakdown of platelets. Frick[5] reported 3 cases in whom the presence of a circulating anti-coagulant, ++++ cephalin-cholesterol flocculation, and false positive serological tests for syphilis, were common features.

There are a number of other reports of similar cases seeming to mark this disease as one in which protein metabolism is markedly affected.

CASE REPORT

The patient, a 16-year-old European schoolgirl, was admitted to the gynaecological ward on 18 January 1957 for vaginal bleeding. Her last normal menstrual period had been towards the end of November 1956. Since 5 January she had been bleeding continuously. Apart from the vaginal bleeding, she showed marked pallor and a bruise over the sacral area. Erythrocytes 2,200,000 per c.mm. Leucocytes 13,200 per c.mm. Platelets normal in number and morphology. Corrected sedimentation rate (Wintrobe) 7 mm. Her condition was regarded as being an incomplete abortion, and 6 pints of whole blood were transfused and a dilatation and curettage performed. She was discharged from hospital on 28 January, apparently well.

On 12 February 1957 she was admitted to the surgical unit as a case of acute appendicitis. Owing to concurrent epistaxis and a few petechial haemorrhages on her ankles she was transferred to a medical ward. On enquiry it was stated that she had suffered numerous nose-bleeds during the past 3 months and that she had bruised very easily during this period, but no history of a familial bleeding tendency could be elicited. She denied having used any drugs. Examination showed tenderness and guarding over the right iliac fossa. There was slight bleeding from the nose and vagina. Old purpuric haemorrhages were visible over the ankles. The Rumpel-Leede sign was markedly positive.

The laboratory findings at this stage were as follows: Bleeding time 22 minutes. Coagulation time 21 minutes. Urine. nothing abnormal. Haemoglobin, 8·8 g.%. Erythrocytes 3,200,000 per c.mm. Leucocytes 4,800 per c.mm. Platelets less than 1,000 per c.mm. Prothrombin concentration 51%. Corrected sedimentation rate 33 mm. Blood urea 36 mg.%. Total serum protein 5·8 g.% (albumin 3·8, globulin 2·0). The Eagle test and the V.D.R.L. tests were positive. Blood samples were forwarded to the S.A.I.M.R., Johannesburg, for examination and Dr. H. B. W. Greig reported as follows: 'Prothrombin time (single stage) greater than 120 seconds (normal 13·6 seconds). This was corrected to 28 seconds by the addition of normal serum. The thromboplastin regeneration test showed a defect in both serum and plasma components. The patient's plasma did not correct plasma from a case of haemophilia and her serum did not correct a known case of Christmas disease. An inhibitor of thromboplastin generation could be detected in the patient's plasma after alumina treatment but not in the patient's serum.' Dr. Greig commented as follows: 'These findings suggest an inhibitor but to what extent the abnormality found in the plasma may be due to the age of the plasma is not known. The serum defect appears to be complex; it results in an abnormal prothrombin time, suggesting a factor VII or X deficiency, and abnormal thromboplastin generation, suggesting a Christmas factor defect. There seem to be so many defects in the patient's clotting mechanism that it is difficult to give a diagnosis. Further samples of both serum and plasma would be welcomed.'

During the next fortnight profuse vaginal bleeding took place, necessitating the administration of 24 pints of fresh blood. The blood was given by 'cut downs' because 'push ins' were not found possible. ACTH was given by intramuscular injection, and penicillin in full doses because the Eagle test remained positive. The platelet count remained negligible and there was no improvement.

In desperation protamine sulphate and vitamin K1 was given by injection, and the ACTH was replaced by oral prednisone; within 48 hours bleeding stopped and it has not been necessary to administer blood since. The Rumpel-Leede sign became negative and the platelet count rose to 90,000 per c.mm. At this stage a specimen of sternal marrow was examined; megakaryocytes were present in adequate numbers. She was discharged on a maintenance dose of prednisone on 23 March, to return for splenectomy should the remission not be sustained, the diagnosis at this stage being 'thrombocytopenic purpura'.

She was readmitted for splenectomy on 10 April 1957. The platelet count had remained around the 40,000 per c.mm. mark during her stay at home. A normal menstrual period occurred during her first 5 days in hospital. Prednisone was slowly with-

drawn and completely stopped on 19 April. She then developed a swinging temperature and burning on micturition. Penicillin was given from 3 May, but as the temperature persisted splenectomy could not be performed.

On 7 May her temperature rose to 103·4° F and she developed a butterfly erythema on her face; the penicillin was discontinued. A diagnosis of DLE was made and confirmed by the finding of LE cells by means of a modification of the technique described by Snapper[7] in which a substrate of normal or lymphatic leukaemic blood is prepared by filling a plastic ring 1 cm. in diameter on a slide with freshly obtained blood. After incubation at 37° C in a water bath the clot and ring was slid off. A plastic ring was now placed over a portion of the prepared substrate and filled with the patient's fresh blood. This was then incubated for 2 hours as before. The results obtained were as follows:

Lymphatic leukaemic substrate, 212 LE cells per 500 leucocytes.

Normal blood substrate, 20 LE cells per 500 leucocytes.

Two-hour clot method, 5 LE cells per 500 leucocytes.

Prednisone was again administered orally and dramatic improvement followed. The rash disappeared and the temperature subsided within 72 hours. The other laboratory findings at this stage were as follows: Haemoglobin 10·8 g.%. Erythrocytes 3,700,000 per c.mm. Leucocytes 6,300 per c.mm. Platelets 80,000 per c.mm. Corrected sedimentation rate (Wintrobe) 14 mm. C-reactive protein absent. Cephalin cholesterol flocculation test +++. Total serum protein 6·5 g.% (globulin 3·0, albumin 3·5). Blood urea 43 mg.%. Eagle test positive. Direct Coombs test positive.

During the subsequent weeks the patient developed a 'moon-face' and generalized swelling of the body without any pitting oedema. She was discharged from hospital on 27 May still taking prednisone by mouth.

On 7 June 1957 she was readmitted to hospital in a comatose state with associated Jacksonian-type fits. Generalized oedema was present. Her temperature was 101·6° F and her blood pressure 160/90 mm. Hg. Lumbar puncture yielded clear fluid under a pressure of 270 mm. water with a protein content of 200 mg.%. The urine contained 4·6 g. of albumen per litre; pus cells, granular casts and hyaline casts were present. Haemoglobin 9·7 g.%. Leucocytes 10,600 per c.mm. (polymorphs 83% with a marked shift to the left). Platelets 56,000 per c.mm. Total serum protein 4·6 g.% (albumin 2·9, Globulin 1·7); sodium 366 mg.%, potassium 17·2 mg.%, chlorides 635 mg.% (as NaCl).

Intramuscular ACTH was substituted for prednisone but only slight improvement ensued; the patient remained semi-comatose for the week that followed. On 17 June she developed right-sided fits which could not be controlled by sedation. After 3 hours 80 c.c. of triple-concentrated plasma was administered intravenously; within 6 minutes the fits ceased and she returned to consciousness, and within an hour coherent speech was possible. She received further triple-concentrated plasma during the days that followed. Lumbar puncture was performed again the day after her recovery and showed no abnormality whatever. From her urine a B. coli, sensitive to chloromycetin, was cultured. After this antibiotic had been administered for a short period the leucocytosis and the shift to the left was no longer present. However, she remained oedematous and lethargic until the ACTH was replaced by oral prednisone; thereafter improvement was rapid and she could be discharged from hospital on 22 July on a maintenance dose of prednisone.

She remained well until February 1958, when she developed pyelocystitis and was again admitted. The B. coli infection responded again to chloromycetin. Laboratory examinations revealed a persistent massive albuminuria varying from 6 to 13 g. per litre. Her platelet count had dropped to 17,000 per c.mm. The Eagle test and the direct Coombs test were negative. Cephalin-cholesterol flocculation test +. The LE-cell test was also negative. She was discharged on a maintenance dose of prednisone on 6 March, feeling perfectly well.

DISCUSSION

The development of the L.E. cell in *in vitro* preparations is to some extent dependent on the coagulation of blood, the process of coagulation acting as a potentiating agent.[8] In a purely speculative discussion Hargreaves[9] mentions 45 cases of DLE where the platelet count was above 50,000 per c.mm. In these cases bleeding was not a feature of the disease and the LE-cell test was positive. However, in 3 cases with thrombocytopenia the LE-cell test was negative and the true nature of the disease only became evident after splenectomy had been performed and the LE test became positive. It is therefore conceivable that in the case described here the prednisone had the effect of raising the platelets to a sufficiently high level to allow the symptoms and signs of DLE to become prominent 2 weeks after withdrawal of the prednisone, thus paralleling Hargreaves' case where splenectomy had been performed.

Another point arising from the above cases is that the circulating anticoagulant and/or the thrombocytopenia may interfere with demonstration of the LE-cell phenomenon by the clot methods.

The last point of note in the case described here is that the patient presented all the protein disturbances that have been reported to date, viz. (1) positive LE-cell phenomenon, (2) false positive serological tests for syphilis, (3) positive direct Coombs test, (4) circulating anticoagulant and thrombocytopenia, and (5) positive cephalin-cholesterol flocculation test.

The convulsive incident might have been due to overdosage with prednisone. On the other hand it might have been due to the renal involvement or to the DLE *per se*. Clark and Bailey[10] report 28 cases of DLE with neurological or psychiatric disturbances, of which 14 had convulsions.

SUMMARY

A case of acute disseminated lupus erythematosus presenting as thrombocytopenic purpura is described. All the previously published protein disturbances could be demonstrated in this patient. The possible relationship between the symptomatology of the disease, the LE-cell phenomenon, and the blood platelet level, is discussed.

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