CHRONIC IDIOPATHIC THROMBOCYTOPENIA IN THE BANTU

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The literature on idiopathic thrombocytopenia in the Bantu consists largely of papers on 'Onyalai'. The acute nature of the condition has been repeatedly stressed, but the existence of recurrent[1-3] and chronic[4, 5] forms, have been suggested. Manson-Bahr[6] considers that the bullae of Onyalai, once resolved, never recur, and concludes that it is an acute form of thrombocytopenic purpura.

During the course of a study of idiopathic thrombocytopenia in the Bantu, 7 cases regarded as examples of the chronic form, were encountered. The material reviewed, and the methods used, have been described in a previous paper.[7] The 7 comprise 4 cases seen in at least 2 attacks and 3 cases where bleeding and thrombocytopenia have so far persisted for 2 years, 18 months and 10 months respectively. The platelets have failed to return to normal levels, and the bleeding tendency is constant. In view of the fact that few authentic cases have hitherto been described in the Bantu, the cases are briefly reported individually.

CASE REPORTS

Case 1

A.M., a Bantu female aged 27 years, was admitted to hospital in October 1953 with a 2-day history of epistaxis. There had been previous epistaxis 16 months before. Physical examination showed generalized purpura, bleeding gums, and a single haemorrhagic vesicle on the palate. The spleen was not palpable. The patient was 32 weeks pregnant. The haemoglobin was 6·8 g. per 100 ml., leucocytes 10,200 per c.mm. (eosinophils 102 per c.mm.), and platelets 45,000 per c.mm. The marrow contained normal numbers of megakaryocytes, but these showed no evidence of platelet formation.

Blood transfusion was given, and ACTH 100 mg. daily was commenced on the 4th day. Clinical remission coincided with the exhibition of ACTH, but thrombocytopenia persisted (platelets 20,000-30,000 per c.mm.), and the patient was discharged after 1 month, still thrombocytopenic (platelets, 30,000 per c.mm.).

Two months later, with platelets 30,000 per c.mm., she bore a live infant. There was no excessive postpartum haemorrhage, and the infant was not thrombocytopenic and showed no purpura. Relapse, with bleeding from the mouth and purpura, occurred in the mother 2 days after delivery, with platelets 20,000 per c.mm.; the marrow picture was as before. The direct Coomb's test was negative, and 'L.E. cells' were not detected. Haemorrhagic manifestations (purpura, epistaxis, and vaginal bleeding) and thrombocytopenia persisted over the following 3 months, in spite of therapy, including blood transfusion, ACTH 80 mg. daily, and cortisone 100 mg. daily. Splenomegaly was not noted at any stage.

With haemoglobin 6·6 g. per 100 ml. and platelets 75,000 per cu.mm., and in spite of continued haemorrhage, the patient refused splenectomy, and left hospital against medical advice. She died at home one week later—autopsy was not possible. The total observed course in this patient was 6 months.

Case 2

E.N., a Bantu female aged 36, was transferred in March 1955 from an outside hospital, where she had received 2,000 ml. of blood over a period of 2 months for persistent epistaxis. One month before the onset of epistaxis she had borne an infant without excessive haemorrhage, and there was no purpura in the infant.

Physical examination on admission showed bullae in the mouth, generalized purpura, epistaxis, and fundal haemorrhages. The spleen was not palpable. Bleeding time longer than 15 minutes, and tourniquet test negative. Haemoglobin 6·0 g. per 100 ml., leucocytes 6,200 per c.mm. (eosinophils 0%), and platelets 20,000 per c.mm. Megakaryocytes were present in the marrow in normal numbers, but showed no evidence of platelet-budding. Direct Coombs test negative. 2,000 ml. of blood was transfused, and cortisone, 300 mg. daily, was commenced on the 4th day, decreasing over the following week to 75 mg. daily. There was clinical remission, but thrombocytopenia persisted (platelets less than 20,000 per c.mm.), and the patient was discharged 1 month after admission.

In May 1956, 14 months later, she was readmitted to hospital. Four months before she had delivered another infant, with no excessive postpartum haemorrhage. There was no purpura in the infant. A few days after delivery there was epistaxis, bleeding gums, and vaginal bleeding, these symptoms persisting up to the time of admission. Examination showed generalized purpura, numerous bullae in the mouth, and haematuria; the spleen was not palpable. Blood count showed haemoglobin 4·4 g. per 100 ml., leucocytes 6,600 per c.mm. (eosinophils 0%), and platelets less than 20,000 per c.mm. Numerous megakaryocytes were present in the marrow, but they showed cytoplasmic hyalinization, 'lymphoid' forms, and failure to bud. 'L.E. cells' were not detected.

Blood transfusion (1,000 ml.) was given, and 30 mg. of prednisone daily was commenced on the 6th day. Fresh purpura, bullae and ecchymoses occurred 1 week later, and the prednisone was increased to 60 mg. daily. Two days later the patient complained of severe left-sided headache, and lapsed into coma with a left third-nerve palsy and right-sided hemiparesis (Weber syndrome), and died the next day. Permission for autopsy was refused. The observed course in this patient was 15 months.

Case 3

M.T., a Bantu female aged 37, was seen in February 1955 complaining of persistent spontaneous bruising for 2 weeks, and bleeding from the mouth for 1 day; 3 months before there had been an episode of epistaxis and bleeding from the mouth. Physical examination showed generalized purpura, ecchymoses, and bullae in the mouth. The bleeding time was longer than 15 minutes and the tourniquet test was negative. Haemoglobin 7·6 g. per 100 ml., leucocytes 9,500 per c.mm. (eosinophils 0%), and platelets less than 20,000 per c.mm. Megakaryocytes were present in the marrow in normal numbers, but showed cytoplasmic hyalinization and failure to bud. A blood transfusion of 1,000 ml. was given, and cortisone, 300 mg. daily decreasing to 25 mg. daily on the 18th day. Clinical remission accompanied this therapy.

In March and in April 1955, there were recurrent episodes of purpura with platelets 20,000 and 25,000 per c.mm. respectively. The patient was seen again in August 1955 when the platelets had increased in numbers on the smears.

A further episode of purpura occurred in November 1955, and the patient was readmitted. Bleeding time longer than 15 minutes, tourniquet test positive; platelets 35,000 per c.mm. 'L.E. cells' were not detected. Spontaneous clinical remission

followed in 1 week, but thrombocytopenia persisted. In December 1955 platelets were scanty on the smears.

Re-examination in November 1956 showed haemoglobin 10·9 g. per 100 ml., platelets 40,000 per c.mm., 'L.E. cells' negative, and the spleen not palpable. There had been no further bleeding since the previous November. Admission with a view to splenectomy was refused. The course in this patient has so far been 2 years.

Case 4

E.K., a Bantu female aged 15, was admitted in July 1955 for uncontrolled epistaxis. There had been recurrent epistaxis over the previous 7 years. Physical examination was negative. Haemoglobin 6·0 g. per 100 ml., leucocytes 13,800 per c.mm. (eosinophils 138 per c.mm.), and platelets less than 25,000 per c.mm. Megakaryocytes were present in the marrow in increased numbers, but showed cytoplasmic hyalinization, 'lymphoid' forms, and failure to bud. 'L.E. cells' were not detected. Over the following 6 weeks there were repeated epistaxes requiring transfusion of 6 pints of blood. Two weeks after admission a large bulla was noted on the tongue. Splenectomy was refused.

In June 1956, platelets were less than 25,000 per c.mm. and 'L.E. cells' negative. There had been minimal epistaxis over the previous 9 months. In November 1956, platelets were 25,000 per c.mm. and 'L.E. cells' negative. Her symptoms had remained minimal, and she again refused splenectomy. The course in this patient has so far been 8½ years, with an observed course of 18 months.

Case 5

G.S., a Bantu male aged 30, was admitted to hospital in November 1954 with recurrent epistaxes for 1 month. He had had a haemorrhagic bullous eruption of the skin over the forehead 1 year before. Examination showed purpura but no bullae in the mouth. The spleen was not palpable. Blood count showed haemoglobin 9·0 g. per 100 ml., and platelets less than 20,000 per c.mm. 'L.E. cells' were not detected. The marrow showed numerous megakaryocytes but no evidence of platelet formation; hyaline and 'lymphoid' forms were noted. In spite of adequate ACTH and cortisone therapy, epistaxis, purpura and thrombocytopenia persisted during the following 2 months. Splenectomy was refused.

In May 1956, 15 months later, the patient presented in outpatients complaining of headache, and only on direct questioning about the scars on his forehead, was the previous history elicited. He had remained relatively well in the interim, but with occasional epistaxis. Examination showed a few petechiae, but there were no lesions in the mouth. Blood count showed haemoglobin 16·0 g. per 100 ml. and platelets less than 20,000 per c.mm. Bleeding time was longer than 15 minutes. 'L.E. cells' were not detected. The patient was treated with 'adrenosem' (carbayochrome salicylate) followed by ACTH, with no effect on platelets or bleeding time, over a period of 1 month. In view of this and the previous episode, he was submitted to splenectomy in June 1956, whilst still in a thrombocytopenic phase. The operation was uneventful; 4 hours after the operation bleeding time was 4 minutes and platelets returned to normal after 48 hours. The patient is well, with platelets 300,000 per c.mm., 18 months after the operation.

Case 6

D.N., a Bantu child aged 3 years, was admitted to hospital in December 1954 with a diagnosis of malnutrition. After 1 week he developed generalized purpura; he was on no treatment other than ward diet at the time. Blood count showed haemoglobin 12·0 g. per 100 ml., leucocytes 21,000 per c.mm. (eosinophils 210 per c.mm.) and platelets less than 20,000 per c.mm. Bleeding time 13 minutes. The marrow contained normal numbers of megakaryocytes, with failure to bud and the presence of forms showing cytoplasmic hyalinization.

The child remained in hospital for 7 months, during which time there was frequent epistaxis and occasional haematemesis and malaena, necessitating blood transfusion. There was no clinical response to steroid therapy and he remained thrombocytopenic throughout. In June 1955 the marrow still showed megakaryocytic abnormalities, with failure of platelet formation. Nutrition was normal after about 2 months.

In November 1956 the child was re-examined. He had experienced episodes of epistaxis since discharge from hospital. There was no purpura and no splenomegaly, but he was still thrombocytopenic (platelets less than 20,000 per c.mm.). Splenectomy was refused.

The clinical course in this case so far has been 2 years.

Case 7

K.V., a Bantu child aged 1 year, was seen in February 1956 with purpura of 3 days' duration. There was no previous bleeding and no history of drugs. No bullae were seen in the mouth, and there was no splenomegaly, but the child was febrile. Blood count showed haemoglobin 8·4 g. per 100 ml., leucocytes 7,500 per c.mm. (eosinophils 75 per cu.mm.), and platelets 25,000 per c.mm. The marrow showed megakaryocytes in normal numbers, but poor smears rendered any opinion on morphology impossible.

Blood culture taken 3 days after admission yielded *B. typhosus*, and the patient was put on to chloramphenicol; splenomegaly was noted at the time. There was clinical improvement and purpura diminished, but thrombocytopenia persisted. Three weeks after admission, with the child clinically recovered from the typhoid and no longer on chloramphenicol, there was exacerbation of purpura with platelets less than 20,000 per c.mm. Fresh episodes of purpura with thrombocytopenia persisted for another month, and the child was eventually discharged at the beginning of April 1956, still thrombocytopenic.

Three weeks later (24 April) he was readmitted with fresh purpura, and both liver and spleen were palpable. Blood count showed haemoblogin 9·8 g. per 100 ml., leucocytes 9,600 per c.mm. (eosinophils ·0%), and platelets less than 25,000 per c.mm. Six days later, with no further purpura, platelets were reappearing in the peripheral blood, and had reached 150,000 per c.mm. on discharge on 9 May.

The child was seen again on 30 October, 5½ months later, with generalized purpura. The spleen was palpable 2 finger-breadths below the costal margin. Blood count showed haemoglobin 8·4 g. per 100 ml., leucocytes 10,800 per c.mm. (eosinophils 324 per c.mm.) and platelets 40,000 per c.mm. The marrow contained numerous megakaryocytes but these failed to show any platelet budding. No further bleeding occurred in hospital and the child was discharged; splenectomy was refused.

The observed course in this child has been 10 months.

DISCUSSION

The criteria of either observing a case for over 6 months without remission or in at least 2 attacks with persistent thrombocytopenia in spite of clinical remission, as used here to establish the diagnosis of chronicity, are probably too strict; however, a history of bleeding or bruising easily or, for example, epistaxis in childhood in a case of idiopathic thrombocytopenia is not considered necessarily indicative of chronicity. For these reasons it is felt that a case must be observed for a sufficiently long period or in repeated episodes, before being labelled chronic; the cases of Lewis and Lurie[5] based on previous history or an unstated observed course, cannot be accepted as proved examples of chronic idiopathic thrombocytopenia in the Bantu.

The limited experience with chronic cases presented here does not warrant any conclusions; the cases are, however, very similar to the large group of American Whites described by Hirsh and Dameshek.[8] Of the 7 patients, 2 were children and 5 adults—1 male and 4 females. Clinical remissions in spite of persistent thrombocytopenia are common. In 3 cases, bullae in the mouth were noted accompanying relapse. The platelet count varies, being very low in relapse, and often rising, but not to normal levels, during remission. Eosinophilia is not a feature. The marrow picture is generally similar to that in the acute form, except that megakaryocytes are here more likely to be present in greater than normal numbers. Clinical remission of the first observed attack in 2 cases occurred with the administration of cortisone, but in 4 cases, 2 in the first and 2 in their second observed attacks full

dosage of cortisone was valueless in controlling bleeding. Clinical remission in one case in her first attack accompanied the administration of ACTH.

Of the 5 surviving cases splenectomy has been performed with cure in one case, and has been refused in the other 4. The two deaths were probably due to cerebral haemorrhage. It is worthwhile re-emphasising that the development of severe headache in an uncontrolled chronic idiopathic thrombocytopenia after the age of 30 is an indication for urgent splenectomy. The few cases here reported do not allow any dogmatism, but it is suggested that should a chronic case fail to respond to massive steroid therapy in a limited period, then, depending on the clinical course, splenectomy should be considered.

Thrombocytopenia associated with pregnancy is a problem of considerable practical importance. Of the acute cases 2 were 26 and 32 weeks pregnant respectively; they were discharged in remission and were not delivered in hospital. In 2 chronic cases 3 pregnancies were followed by exacerbation of the clinical picture, with resultant death of the patient in both cases. In the pregnant chronic case splenectomy should certainly be performed in the first 5 months. The 3 pregnancies resulted in live infants who showed no purpura, and delivery was not accompanied by any excessive haemorrhage.

SUMMARY

Seven cases of chronic idiopathic thrombocytopenia in the Bantu are described. The disease appears to behave no differently from that in the European with regard to clinical and haematological features. The response to steroid therapy in relapse is unpredictable. Pregnancy is often followed by severe relapse in this group.

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