Disseminated intravascular clotting in kwashiorkor

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Hassanein, E. A., and Tankovsky, I. (1975). *Archives of Disease in Childhood*, 50, 308. **Disseminated intravascular clotting in kwashiorkor.** The role of disseminated intravascular clotting (DIC) in the pathogenesis of the bleeding diathesis kwashiorkor was investigated in 22 patients. According to the severity of the clinical and haematological findings, two grades of DIC were observed. A severe grade of DIC was shown in 6 cases (5 fatal) presenting with thrombocytopenia, hypofibrinogenaemia, and multiple coagulation defects, and with abnormally prolonged partial thromboplastin, prothrombin, and thrombin times. A second group of 16 patients (7 fatal) showed a less severe grade of DIC manifested by thrombocytopenia, low fibrinogen level, and a clotting factor defect shown by prolonged prothrombin and thrombin times.

Multiple coagulation defects including factors II, VII, IX, and X have been reported in kwashiorkor (Dorantes *et al.*, 1964). Deficiency of factor V, additionally, together with thrombocytopenia in one instance, was observed in cases of severe kwashiorkor complicated by infections, particularly gastroenteritis (Hassanein and Tankovsky, 1973). Disseminated intravascular clotting (DIC) has been reported in gastroenteritis (Lufti, 1971). The possibility of DIC being of importance in severe cases of kwashiorkor is the subject of this study.

Material and methods

Twenty-two patients, 10 male and 12 female, suffering from severe kwashiorkor, bleeding diathesis, and thrombocytopenia were investigated. Their ages ranged from 9 months to 3 years. They were selected out of 132 cases of kwashiorkor admitted during the period of study. Dehydration of moderate or severe degree was present in the majority of cases and appropriate fluid and electrolyte replacement given. Other measures included antibiotics based on stools and urine culture, milk feeding often by gavage, multivitamin supplements; fresh blood transfusions were given to the majority of patients when there was bleeding and severe anaemia. Haematological investigations including partial thromboplastin, prothrombin, and thrombin times, and fibrinogen level were carried out as described by Dacie and Lewis (1968). Serum fibrin degradation products (FDPs) were estimated in 10 patients using the rapid slide screening test (Diagnostic Reagents Limited, Thame, Oxon, England). The normal value for serum

FDPs was 8 µg/ml. Standard statistical methods were used and mean values were tested with Student's 't' test. The difference of the means was considered to be significant if $P < 0.05$.

Results

The cases were divided into two groups, A and B, according to their severity. Detailed clinical and laboratory data for the two groups of patients are presented in Table I. *Group A* (6 patients): all cases showed bleeding, severe degrees of diarrhoea and infections. 5 of the 6 cases died as a result of haemorrhage.

The mean values for partial thromboplastin, prothrombin, and thrombin times, fibrinogen level, and platelet count (Table II) were all abnormal. *Group B* (16 patients): the severity of bleeding, diarrhoea, and the incidence of complicating infections was less than in Group A. The mean values for prothrombin and thrombin times, fibrinogen level, and platelet count were all normal, but the mean value for partial thromboplastin time was not. Serum FDPs were estimated in the last 10 cases admitted in this group and their serum level was found to be abnormally high in 7 patients, the values ranging from 16 to 32 µg/ml. 2 of these 7 cases showed considerably prolonged thrombin time (> 50 s); in a further 2 patients it was slightly prolonged (38–39 s), while the remaining 3 were normal.

Comparison between the two groups showed significant differences in the partial thromboplastin

TABLE I
Clinical and laboratory data in two groups of kwashiorkor

	Group A (6 cases)	Group B (16 cases)
<i>Clinical</i>		
Diarrhoea	Severe in all cases	Severe in 3, moderate in 13
Bleeding diathesis	Purpuric rash in 6 cases, intestinal haemorrhage in 3 cases	Purpuric rash in all cases
Dermatosis	3 cases	5 cases
Hepatomegaly	2 cases	3 cases
Keratomalacia	2 cases	3 cases
Bronchopneumonia	1 case	2 cases
Otitis media	1 case	1 case
Skin gangrene	2 cases face and scalp	1 case, ear
Death	5/6 cases	7/16 cases
<i>Investigations</i>		
Total proteins (g/100 ml)	2.7-4.0	3.1-4.2
Serum potassium (mEq/l)	2.2-3.9	2.5-4.0
Serum sodium (mEq/l)	135-141	128-138
Blood urea (mg/100 ml)	35-70	30-65
Stools culture	Positive in 2 (pathogenic <i>Esch. coli</i>)	Positive in 3 (<i>Salmonella B</i> in 2 and pathogenic <i>Esch. coli</i> in one)
Urine culture	Negative	Positive in two (pathogenic <i>Esch. coli</i>)
Liver function tests (transaminases, flocculation tests)	Normal	Normal
Haemoglobin (g/dl)	4.5-8	5-8.2

TABLE II

Range, mean, and standard deviation of partial thromboplastin, prothrombin, and thrombin times, fibrinogen, and platelet count in both groups of kwashiorkor, and in controls

Group	No. of cases	Partial thromboplastin time (s)	Prothrombin time (%)	Thrombin time (s)	Fibrinogen (mg/100 ml)	Platelet count ($\times 10^3$)
A	6	59-278	1-57	29-56	120-180	35-90
B	16	119.6 $\pm$ 37.3	20.7 $\pm$ 10.25	37.0 $\pm$ 9	140 $\pm$ 28.3	62.8 $\pm$ 25
		32-60.3	22-100	26.2-67	120-370	25-95
		44.4 $\pm$ 8.8	59.3 $\pm$ 25.2	37.8 $\pm$ 11	179 $\pm$ 81.8	65.5 $\pm$ 28
Controls*	7	35-110	85-110	28.2-32.6	240-320	190-255
		39.7 $\pm$ 3.5	99.3 $\pm$ 8.5	30.0 $\pm$ 1.2	284.3 $\pm$ 29.6	224 $\pm$ 22
Significance A & B		P < 0.01	P < 0.01	P < 0.01	P < 0.01	P < 0.01
B & C		NS	P < 0.01	P < 0.01	P < 0.01	P < 0.01
A & B		P < 0.01	P < 0.01	NS	NS	NS

NS, not significant.

*Control group, 7 children, without kwashiorkor or coagulation defects, aged 1-2 years.

and prothrombin times, and nonsignificant differences in the thrombin time, fibrinogen level, and platelet count.

Discussion

The most frequent cause of death in urban protein-calorie malnutrition, according to Hansen *et al.* (1968), is gastroenteritis and its consequences of dehydration and acidosis; other causes of death in hospitalized patients being infections, hypoglycaemia, hypokalaemia, and electrolyte abnormalities. This report describes another serious complication in cases of severe kwashiorkor complicated by infections, particularly those causing diarrhoea

with dehydration. The incidence of bleeding diathesis with thrombocytopenia in our study was 15%. The diagnosis of DIC in group A (severe cases) was based on the presence of thrombocytopenia, hypofibrinogenaemia, and multiple coagulation defects, i.e., prolonged partial thromboplastin, prothrombin, and thrombin times. The patients of group B (unsevere cases) were considered to show a less severe state of the DIC syndrome, with reduced platelet count, together with fibrinogen and coagulation factor defects mainly due to prothrombin deficiency. Supportive evidence was the increased level of serum FDPs in 7 out of 10 patients in this group. Clinically, the most

constant feature in all our patients was the presence of moderate or severe diarrhoea on admission, with a past history of repeated attacks of gastroenteritis. Diarrhoea is frequently met with kwashiorkor due to intestinal infection, abnormal enzymatic function, and defective absorption of the bowel (Wharton, Howells, and Phillips, 1968). Haematologically, the most constant findings in the DIC syndrome in cases of kwashiorkor were thrombocytopenia and a low fibrinogen level, while the clotting factor defects and increased serum FDPs were constant. The increase in serum FDPs found in 7 out of 10 investigated cases was not closely correlated with the antithrombin effect. This agrees with the recent findings reported by Preston *et al.* (1973).

In the management of DIC syndrome in patients suffering from kwashiorkor, early and rapid correction of dehydration with replacement of electrolyte loss is indicated. The value of additional heparin therapy has yet to be assessed.

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REFERENCES

- Dacie, J. V., and Lewis, S. M. (1968). *Practical Haematology*, 4th edition, p. 74. Churchill, London.
- Dorantes, S., Barrón, I., Arias, N., Vázquez, J., and Soto, R. (1964). Pathogenesis of purpura in the child with severe malnutrition. *Journal of Pediatrics*, **65**, 438.
- Hansen, J. D. L., Wittmann, W., Moodie, A. D., and Fellingham, S. A. (1968). Evaluating the synergism of infection and nutrition in the field. *Malnutrition, Learning and Behaviour*, p. 438. Ed. by N. S. Scrimshaw and J. E. Gordon. Massachusetts Institute of Technology Press, Cambridge, Mass.
- Hassanein, E. A., and Tankovsky, I. (1973). Disturbances of coagulation mechanisms in protein-calorie malnutrition. *Tropical and Geographical Medicine*, **25**, 158.
- Lutfi, N. S. (1971). Disseminated intravascular thrombosis in, acute gastroenteritis. XIII International Congress of Pediatrics, vol. XI, 6-8, Vienna Academy of Medicine, Vienna.
- Preston, F. E., Malia, R. G., Sworn, M. J., and Blackburn, E. K. (1973). Intravascular coagulation and *E. coli* septicaemia. *Journal of Clinical Pathology*, **26**, 120.
- Wharton, B., Howells, G., and Phillips, I. (1968). Diarrhoea in kwashiorkor. *British Medical Journal*, **4**, 608.

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