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Hemolytic Uremic Syndrome in Children

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SUMMARY

Of the 4070 children admitted in the departement of pediatrics at Shaikh Zayed Hospital, 830 (24%) presented with diarrhoea. Eleven of these (1.3%) were diagnosed as cases of hemolytic uremic syndrome characterised by microangiopathic hemolytic anaemia, thrombcytopenia and acute renal failure. Only 3 had positive stool cultures (E. coli in 2 and shigella dysenterie in 1). Two children expired (mortality 18%). The rest recovered with conservative management and peritoneal dilaysis (82%). This syndrome has not been reported from other centers in Pakistan. It needs to be remembered as a complication of diarrohea and a cause of acute renal failure in children.

INTRODUCTION

The triad of thrombocytopenia, microangiopathic hemolytic anemia and acute nephropathy characterises the hemolytic uremic syndrome(HUS). This presents the final common pathway for a number of pathogenic processes. The name (Haemolytish-uremishe syndrome) was given by Gasser and Coworkers in 1955, with the belief that future studies would reveal a variety of causes, pthogenic mechanisms and subsets of this syndrome(1). We present our experience with the 11 patients admitted to our hospital with this diagnosis.

MATERIALS AND METHODS

All admitted patients suffering from gastrointestinal and respiratory problems were screened to rule out the diagnosis of hemolytic uremic syndrome (HUS). A diagnosis of HUS was established if evidence of acute renal failure, thrombocytopenia and fragmented RBCS were found on peripheral blood picture. Diagnostic workup included a CBC, with platelet count, estimation and evalution of peripheral smear by a hematologist and a complete urine analysis Determination of blood urea (Buw), creatinine, and serum electrolytes were also carrried out. Fibrin degradation product(FDP) estimation was requested. Stool examination was done and cultures of stools and blood were also requested. The management was mostly conservative, (correction and maintenance of fluid and electrolyte balance, blood transfusion, antibiotics as needed). Peritoneal dilaysis was done in face of continued deterioration of clinical condition, rising BUN, creatinine, persistent anuria, oliguria and acidiosis etc. These children were followed during the stay in the hospital till discharge and then in the out patient department.

RESULTS

A total of 11 children met the criteria for diagnosis of HUS (acute nephropathy, thrombocytopenia, microangiopathic hemolytic anaemia) during the period from January 1987 to June 1989. During this time 830 cases of diarrhoea were admitted, (24% of all 4070 admissions) A break down of the clinical features is given in table-I. The majority (73%) were boys, the average age at presentation was 32 months. All children presented with loose stools while 9(82%) had bloody diarrhoea. Ten (91%) were visibly pale, four (36%) had clinical evidence of purpura/ecchymoses. Three(27%) were in coma grade III and three(27%) were hypertensive on admission. Six (55%) were anuric of duration more than 5 days, three (27%) oliguric (duration more than 7 days) and only 2 (18%) had normal urine output. All patients were on antibiotics on arrival (more than half on septran) Hemoglobin levels (table 2) ranged from 4.5 G to 12.6 G (average 7.6 G) and platelet count varied from 28400 to 95000 (average 65216). All patients had evidence of crenated RBCS, burr cells, helmet cells on peripheral blood smear. Profile of renal function is given in table-3. The average BUN was 100 mg/dl (range 28-210 mg/dl) and creatinine 5 mg/dl (range 1.6-9.6 mg/dl) at admission.

Nine (82%) out of the total eleven recovered. Two (18%) died despite peritoneal dialysis (Table-4). Out of the nine survivors, seven (64%) recovered competely with normal mental, hematology and renal functions (maximum follow up 1.5years).Two(18%) showed normal mental function but evidence of residual renal damage (Table-4).

Clinical Features

Features	No of Pt's (Total = 11)	Percentage
Bloody diarrohea	9	82
Diarrohea	11	100
Neuroglogical symptoms	8	73
More than one seizure (observed)	4	36
Coma(Not responding to normal stimuli)	3	27
Abdominal Cramps	9	
Pallor	10	91
Edema	9	82
Hypertension	3	27
Ascites	3	27
Purpura/Echymosis	4	36
Anuria	6	55
Oliguria	3	27

Table 2: Hematological Values In Hemolytic Uremic Syndrome

P/Name	Age	Sex	Hb% (G)	WBCS (Thousand)	Platelet count	RBCS Morphology.	FDP#
S	2 Yrs	F	7.8	35.5	50,000	MAH*	R +
SA	5 Mon	M	4.6	8	95,000	MAH	N ++
AR	9 Mon	M	7.8	15	80,000	MAH	N
A	2 Mon	M	8.4	12	82,000	MAH	R -
M	10 Mon	F	12.6	7.1	80,000	MAH	N -
N	4 Yrs	F	9.7	49.5	29,000	MAH	R
R	6 Yrs	F	6.4	25	80,000	MAH	R +
-	3 yrs	F	5.4	23	50,000	MAH	N
S	6 Yrs	M	4.5	25	70,000	MAH	R +
U	5 Yrs	M	9	12.8	28,400	MAH	N +
WA	1 Yrs	M	7.9	42	73,000	MAH	R +

#FDP. Fibrin degradation products.
*MAH. Microangiopathic hemolysis.
**N. Normal.
*R. Raised.
-. No growth.

Table 3: Biochemistry of Hus Patients

ON ADMISSION Bun mg/dl	Creat mg/dl	*PEAK VALUES* Bun mg/dl	Creat mg/dl	Na+ Eq/L	K+ Eq/L	Ca++ mg/dl
96	5.2	96	5.2	127	5.6	8.2
40	2.1	70	3.2	134	4.9	8.5
60	2.4	60	2.4	148	6.8	7
33	4.9	33	4.9	119	5.7	9
28	1.6	48	2.6	139	2.1	12.6
70	3.1	156	5.2	124	4.5	9
200	9.6	200	9.6	129	7	8
100	3.5	400	16.8	147	7.5	8.4
210	6.8	210	6.8	130	7	6.5
100	2.8	172	7.2	118	6	8.2
170	3.1	216	4.4	128	7.2	8

DISCUSION

Haemolytic uremic syndrome (HUS) presents the final common pathway for a number of pathogenic processes. In children HUS is a well defined clinicopathological entity whose exact etiology and pathogennesis is not yet known. Most responsible etiological agents are listed in table -5. The syndrome occurs mainly in infants and children and rarely in neonates with mean age of 3.6 years[2,3]. The mean age was 2.7 year in our patients This disorder is usually preceded by prodromal gastrointestinal (typical) or respiratory symptoms (atypical)[4,5]. In our study all patients presented with gastrointestinal symptoms Enterotoxigenic E. coli were isolated in two patients whereas in one patient shigella dysenteric was cultured from stools. Physical examination of these patients reveals pallor, lethargy and irritability. Patients are usually dehydrated and may be mildly jaundiced. Hypertension, abdominal distension and hepatosplenomegaly may be found in some of the patients. Fluid overload with congestive heart failure may also be present More severe neurological manifestations, including somnolence, disorientation, seizures and coma, have been observed in 30-50% of patients[2]. In our patients 8 (73%) patients had neurological manifestations.

On investigating these patients anaemia is invariably present, with hemoglobin levels between 2 and 10 gms/dl. The peripheral smear shows fragmented erythrocytes, which are characteristic of microangiopathic hemolytic anaemia. Leukocytosis is also a common

Table 4: Treatment And Outcome

No	Name	Age	Sex	Treatment	Reason	Prognosis.
1.	S	2Y	F	P. Dialysis	Worsening of clinical condition	Improved
2	SA	5M	M	Conservative	Stable	Improved
3	AR	9M	M	P.Dialyes	Worsening of clinical condition	Improved
4	A	2M	M	conservative	Stable	Improved
5	M	10M	F	conservative	Stable	Improved
6	N	4Y	M	Conservative	Stable	Improved
7	R	6Y	M	P.Dialysis	Worsening of clinical + Biochemical condition	Expired
8	ZI	3y	M	P.Dialysis	Worsenieng of condition.	Improved
9	S	6Y	M	P.Dialysis	Worseneing clinicaly & Biochemicaly	Expired
10	U	5Y	M	Conservative	Stable	Residual Renal damage.
11	WA	1Y	M	Conservative	Stable	Residual Renal demage.

finding[2]. It was observed in all of our patients. Hypoalbuminemia which may reflect intestinal losses of albumin and hypocalcemia with hyperphosphatemia which are consequences of renal failure are found in some of these patients. Platelet count is usually reduced but may be normal or elevated at the time of diagnosis and does not correlate with the severity or duration of the disease[1,3,4,5]. It was found in all of our patients. The thromboctyopenia is secondary to platelet consumption, since most patients have shortened platelet survival. External counting following administration of radio labelled platelets has demonstrated accumulation of radioactivity over spleen, liver and kidney suggesting that platelets are damaged in these organs.[1,2,3,5,7].

Renal involvement is always present but of variable severity. Elevated levels of blood urea nitrogen and serum creatinine are present reflecting a decrease in glomerular filtration rate. There is controversy with regard to the severity of renal involvement and its prognostic implication. The patients who ultimately recover have oliguria/anuria of less than two weeks duration but prolonged anuria does not necessarily mean irreversible renal and brain damage[5,8]. Renal impairment was observed in all of our patients. About 85% of children with classic HUS experience a complete recovery with supportive care and peritoneal dialysis, so specific therapy may be required only in certain subsets. Recurrence has been reported in 30% and in these about one third suffer progressive renal failure[5,9,10,]. In our patients recovery was 82% but relapse is noted only in one patient. The followup however has been of a short duration.

Table 5: Etiology

Infections:

A: Bacteria
- Verotoxin - producing Escherichia coli (VPEC)
- Shigella
- Salmonella
- Campylobacter enteritis
- Pseudomonas

B: Viruses
- Coxsackie
- ECHO
- Adenovirus
- Influenza

C: Contraceptives

E: Malignant Hypertension

F: Cytotoxic Drugs

G: Familial

Other electrolyte abnormalities in these patients are hypocaleemia, hyponatremia, hyperuricemia and metabolic acidosis.Oliguria has been reported from 21-100% of patients and anuria in 30-50% [1,5]. Anuria and oliguria were observed in 6(55%) and 3(27%) of our patients respectively whereas two(18%) patients had normal urine output.

. Thus far there is no specifc treatment for HUS. but several forms of therapy have been attempted in the past, including steroids, heparin, streptokinase and

more recently antiplatelet drugs, exchange transfusions, prostacyclin[PGI_2] infusion, vitamin E and plasmapheresis have been tried[5,8]. The benefits of newer therapies are questionable and clear superiority has yet to be marked. However the mortality decreased only after the institution of better management of acute renal failure and use of dialysis. Dialysis should be continued until there is adequate return of renal functions[3,5,6,10]. HUS has been reported from many parts of the world mainly USA, Britain, France, Argentina, Southern Africa, Netherlands and Southern India. This however is apparently the first report from Pakistan. It constituted 1.3% of the cases presented with diarrhea in our institution, a center, whose total number of admissions for diarrhea constitutes only 24% of total admissions. Whether this is only a limited out-break or that cases are missed because of lack of awareness needs to be elucidated. A registry of cases presenting with the triad of acute renal failure, microangiopathic hemolytic anemia and thromocytopenia needs to be established.

REFERENCES

1. Alfonsocampos, Sibley R, Kin Y, Miller K, Michael AF. Hemolytic uraemic syndrome. Kidney 1981; 14:23-9.
2. Kaplan BS, Vedaranayanan VV. Pathogenesis of the haemolytic uraemic syndrome. Indian J Pediatr 1988; 55:512-25.
3. Siegler RL. Management of hemolytic uraemic syndrome. J Pediatr 1988; 112:1014-20.
4. Jaek SC, Fong, Jean-Pierrede, chadrerian, Kaplan BS. Hemolytic uraemic syndrome current concept and management. Pediatr Clin North Am 1982;4:835-56.
5. Nelson WE. Nelson textbook of pediatrics. 13 ed. Philadelphia: WB Sanders 1987:1124.
6. Neild G. The hemolytic uraemic syndrome: a review. QJ Med 1987;241:367-76.
7. Havens PL, O'Rourke PP, Hahn J, Higgins J, Walker AM. Laboratory and clinical variables to predict outcome in hemolytic uremic syndrome. Am J Dis Child 1988;142:961-4.
8. Bufler T, Islam, Azad MAK, Tones PK. Risk factors for development of hemolytic uraemic syndrome during shigellosis. J Pediatr 1987:110:894-7.
9. Trompeter RS, Sihwartz R, Chanlter, et al. Hemolytic uraemic syndrome: an analysis of prognostic features. Arch Dis child 1983;58:101-5.
10. Silva FG. Onerview of pediatrics nephropathology: abstract. Kidney Int 1988; 33:1024.