in the parietal lobe lead to complex disturbances of the body image, which finally cause anosognosia of either a body part or in some cases of the total body. Premorbid hypochondriacal personality, recent experience of death at close quarters and a more concrete comprehension of events due to the neurological or psychiatric cause are supposed to be the factors which lead to development of this syndrome. Although the present case did not have hypochondriacal personality but he had met the loss of his father six months back, which in the presence of parietal lobe tumor might have presented as Cotard's syndrome.

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REFERENCES

1. Arieti IS, Meth JM. Rare, unclassified, collective and exotic psychotic syndromes. *In:* American Handbook of Psychiatry. Ed Arieti IS. New York, Basic Books, 1959, pp 15-20.
2. Enoch MD, Trethowan WH. Uncommon Psychiatric Syndromes. Bristol, Wright, 1979, pp 21-23.
3. Lehman HE. Unusual psychiatric disorders, atypical psychoses and brief reactive psychoses. *In:* Comprehensive Textbook of Psychiatry, Eds Kaplan HI, Sadock BJ. Baltimore, Williams and Wilkins, 1985, pp 1425-1426.
4. Freeman AM, Kaplan HI. Comprehensive Textbook of Psychiatry. Baltimore, Williams and Wilkins, 1967, pp 987-988.
5. Shukla S, Mishra DN. Cotard's syndrome in schizophrenia. Indian J Psychiatry 1984, 26: 405-406.
6. Ainsworth P. Cotard's syndrome in a mentally handicapped man. Br J Psychiatry 1987, 150: 112-119.
7. Lukianowicz N. Autoscopic phenomena. Arch Neurol Psychiat. Chicago 1958, 80: 198-201.
8. Lishman WA. Organic Psychiatry. Edinburgh, Blackwell Scientific Publications, 1978, p 279.

Infection Associated Hemophagocytic Syndrome

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Infection associated hemophagocytic syndrome (IAHPS) is a systemic proliferation of mature histiocytes showing hemophagocytosis and cytopenias. These patients have fever, constitutional symptoms and hepatosplenomegaly. This disease is infection (virus/bacteria) associated(1). The pathophysiology is thought to be mediated through a defect in immunomodulation resulting in an unrestricted release of inflammatory cytokines. Diagnostic guidelines, both clinical and laboratory have been

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outlined(1,2). We have come across 4 such cases in the last 6 years and thier findings are presented.

Case Reports

Four patients with fever of greater than one week duration and splenomegaly (*Table I*) were subjected to hemogram, blood culture, urine culture, widal test, throat swab culture, *X*-ray chest, USG abdomen, liver function tests, ASO levels and bone marrow aspiration. However, these cases were put on antibiotics by 3rd day keeping in view the urine, blood culture and other findings as given in *Table I.*

Bone marrow aspiration was carried out on 3rd day in Case 2 and 4 as no bacterial growth was positive. In Case 1 and 3, marrow aspiration was resorted to on 5th and 6th day as there was no response to antibiotic therapy. Marrow aspirate of all the 4 cases demonstrated large histiocytes with phagocytosis of lymphocytes, RBCs, platelets and other nucleated cells (*Figs. 1 & 2*) and a diagnosis of infection associated hemophagocytic syndrome (IAHPS) was made. Steroids were added in Cases 1, 3 and 4 and subsequently these cases improved while Case 2 did not receive steroids and expired 10 days later.

Discussion

All the four patients manifested the clinical and marrow findings of hemophagocytic syndrome. This syndrome may develop in cases of: (*a*) immunosuppression (virus associated hemophagocytic syndrome (VAHS)(3); (*b*) fat overload syndrome; (*c*) diseases like tuberculosis, brucellosis, leishmaniasis, syphilis, rubella, other bacteria and AIDS, and (*d*) in the course of malignancies(2). In children, upper respiratory tract infection may lead to VAHS and these patients may secondarily develop bacterial infection(3). Cases 1 and 3 were positive for bacterial infection. However, a concomitant viral infection may have been present in these cases as viral culture and antibody

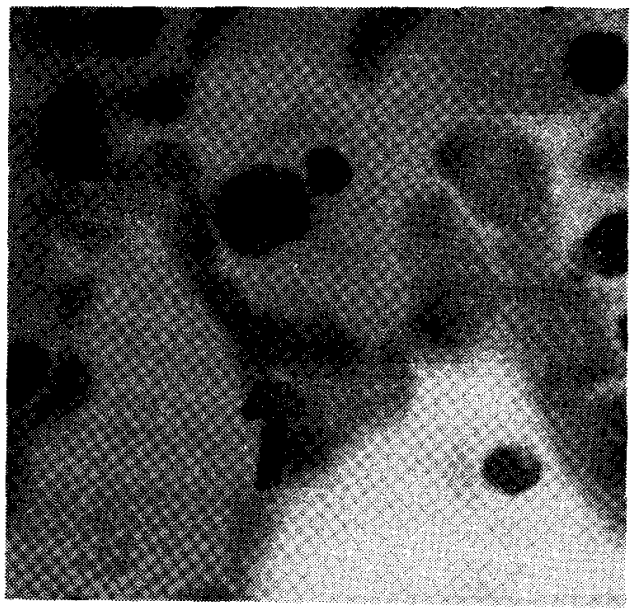

Fig. 1. Bone marrow aspirate showing a histiocyte with phagocytosis of a lymphocyte (Giemsa ×1000).

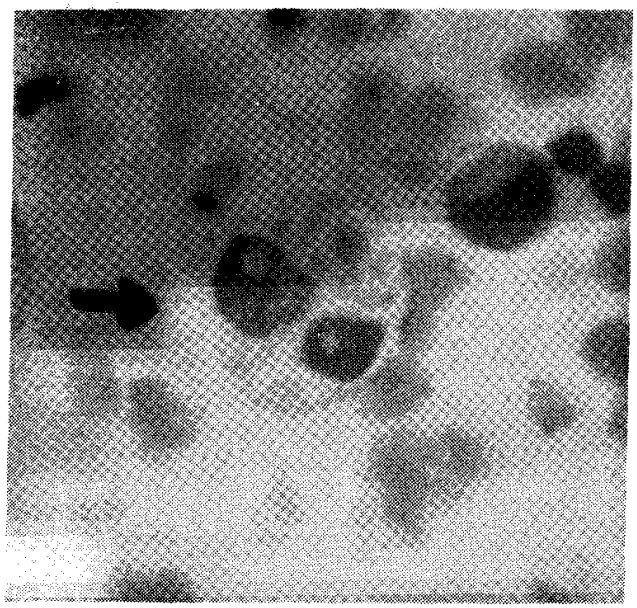

Fig. 2. Bone marrow aspirate –A histiocyte showing phagocytosis of platelets and a lymphocyte (Giemsa ×1000).

TABLE I–*Clinical and Laboratory Findings in 4 Cases of IAHPS*

S. No.	Features	Case 1	Case 2	Case 3	Case 4
1.	Age, Sex	11 yrs, male	1 yr, male	10 yrs, male	9 yrs, male
2.	Fever duration (days)	10	25	8	15
3.	Hepatosplenomegaly	Spleen 5 cm, liver 2cm Bleeding gums +	Spleen 8 cm, liver 2 cm	Spleen tip	Spleen 3 cm, liver 1 cm
4.	Peripheral blood findings				
	Hb (g/dl)	8.2	6.5	7.4	7.9
	TLC (per mm^3)	2,600	3600	2,800	3,000
	DLC	$P_{40}L_{47}M_{12}E_1$	$P_{20}L_{63}M_{15}E_2$	$P_{34}L_{59}M_4E_3$	$P_{32}L_{57}M_6E_5$
	Absolute neutrophilic count (per mm^3)	1,040	720	952	960
	Platelets (per mm^3)	90,000	60,000	1,65,000 at admission 70,000/mm^3 later on	2,10,000
5.	Bone Marrow-cellularity	Normocellular	Normocellular	Normocellular	Normocellular
	M : E	2.5 : 1	1 : 2	6 : 1	1.5 : 1
	Positive findings	-	Lymphocytes 45% Megakaryocytic Hypoplasia	Erythroid Hypoplasia	- -
	Histiocytes with phagocytosis of RBCs, platelets, lymphos & other nucleated cells	Hemophagocytosis (*Fig. 1*)	Hemophagocytosis +	Hemophagocytosis +	Hemophagocytosis + (*Fig. 2*)
6.	Other findings	Urine culture *E. coli* +	Post mortem liver & spleen biopsy showed hemophagocytosis	*Salmonella typhi* in blood culture + widal +	Pneumonitis T_4 : T_8 : 1 : 3
7.	Treatment	Ampicillin, gentamicin, steroids added after diagnosis of IAHPS	Ciprofloxacin given, steroids not given even after diagnosis of IAHPS	Ciprofloxacin given, steroids added after diagnosis of IAHPS	Ampicillin started, steroids added after diagnosis of IAHPS
8.	Outcome	Recovery	Death	Recovery	Recovery

studies could not be carried out. Cases 2 and 4 were probably caused by virus as no bacterial culture was positive. Such cases may show an acquired immune defect in the reversal of T4 : T8 ratio as seen in Case 4.

Recently, histiocytosis in children have been classified into 3 classes–I, II and III(1). Class II includes infection associated hemophagocytic syndrome (IAHPS) and familial hemophagocytic lymphohistiocytosis (FHL) resulting from accumulation of active histiocytes and lymphocytes. Morphology of histiocytes in both diseases is similar(1). However, familial cases have an autosomal recessive pattern of inheritance, a positive family history and defects in cell mediated and humoral immunity(1); while infection associated cases are due to viral/bacterial infection.

Class I histiocytosis includes Langerhans, cell histiocytosis (LCH) and class III consists of malignant histiocytic disorders(1). In LCH the infiltrate is pure histiocytic/mixed histiocytic eosinophilic affecting mainly bones (80%) and skin (60%). However, lymphnodes, bone marrow and spleen are mainly involved in disseminated LCH(4) while in IAHPS the lymphohistiocytic infiltration is seen in bone marrow, spleen and lymph nodes(2). Histiocytes in LCH demonstrate deeply indented nuclei without appreciable phagocytosis, positivity for S-100 and Birbeck granules; while in IAHPS histiocytes are cytologically normal with striking phagocytosis of cellular blood elements like platelets, white cells and red cells(4), as seen in these cases.

Malignant histiocytosis (Class III), an uncommon malignancy in children is a systemic neoplasm involving entire RES(1); but can be differentiated from class I and II histiocytosis by morphology of cells which manifest reticular nuclear chromatin, high N/C ratio prominent nucleoli, cytologic atypia with evidence of phagocytosis in few cells(4). Bone marrow involvement occurs in 25% of cases and hepatosplenomegaly is not a prominent feature(5) in contrast to IAHPS.

IAHPS is a reactive process associated with viral bacterial infection(6,7). Cytopenias are in part due to bone marrow failure because of direct effect on hematopoiesis which is corroborated by progressive fall in granulopoiesis and erythropoiesis by sequential bone marrow examinations(3). Intravascular coagulation and hypofibrinogenemia play a part in the pathogenesis of thrombocytopenia in addition to platelet phagocytosis(3).

Management of these cases involves treatment of underlying infection, supportive care and steroids(4). It has been observed that use of antibiotics alone does not bring out recovery in bacterial type IAHPS, but addition of steroids leads to a dramatic improvement(8), as also observed by us in Cases 1 and 3. One of our cases (Case 2) suspected of viral type IAHPS was not given steroids; this patient steadily deteriorated and expired while the other one (Case 4) exhibited a good response to steroids and recovered. Cases of viral fever complicated by VAHS usually do not improve until steroids are given as noted by various workers(3,7). It appears that steroid therapy is beneficial in such cases and it should be instituted as soon as IAHPS is diagnosed.

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REFERENCES

1. Writing group of the Histiocytic Society. Histiocytic syndromes in children. Lancet 19876, 1: 208-209.

2. Henter JI, Elinder G, Ost A and the FHL study group of the Histiocyte Society. Diagnostic guidelines for hemophagoncytic lymphohistiocytosis. Seminars in Oncol 1991, 18: 29-33.

3. Risdall RJ, McKenna RW, Nesbdi MF, *et al.* Virus associated hemophagocytic syndromes. Cancer 1979, 44: 993-1002.

4. Ladisch S, Jaffe ES, The histiocytosis. *In:* Principles and Practice of Pediatric Oncology. Eds Pizzo PA, Poplack DG. Philadelphia, JB Lipincott, 1988, pp 491-504.

5. Zucker JM, Caillaux JM, Vand D, Gerard-Marchant R. Malignant histiocytosis in childhood: Clinical study and therapeutic results in 22 cases. Cancer 1980, 45: 2821-2829.

6. Jaffe ES, Malignant histiocytosis and true histiocytic lymphomas. *In:* Surgical Pathology of Lymph Nodes and Related Organs. Ed Jaffe ES. Philadelphia, W.B. Saunders Co, 1985, pp 381-411.

7. Esumi N, Ikushima S, Todo S, *et al.* Hyper ferritinemia in malignant histiocytosis, virus associated hemophagocytic syndrome and familial erythrophagocytic lymphohistiocytosis. Acta Pediatr Scand 1989, 78: 268-270.

8. Risdall RJ, Brunning RD, Hernandez JI, Gorden DH. Bacteria associated hemophagocytic syndrome. Cancer 1984, 54: 2968-2972.

Severe Metabolic Acidosis in Nalidixic Acid Overdosage

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Nalidixic Acid is a commonly used antibiotic for urinary tract infections and also acute bacterial diarrhea. Overdose leading to severe metabolic acidosis has not been reported from India. We report one such case.

Case Report

A four-month-old infant presented with a history of altered sensorium of 3 hours duration. Four days earlier, she had loose stools for which she was started on Nalidixic Acid 110 mg/kg/day for four days and lactobacillus tablets for one day. The day prior to admission, the mother noticed building of the anterior fontanelle. The next day, child became lethargic and rapidly progressed to coma. She also had one episode of generalized tonic clonic seizures. She was treated at a Nursing Home with intrauterine diazepam and calcium gluconate and then referred to our institution.

On examination, the anterior fontanelle was bulging, there was minimal response to painful stimulus. Respiration was rapid and systemic examination was non-contributory. The investigations (*Table I*) revealed a high anion gap metabolic acidosis (38.5). Correction of acidosis was done with intravenous sodium bicarbonate following which the child dramatically regained sensorium.

The child was hypotonic for the next two

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