amine (the reactive metabolite of sulfamethoxazole *in vivo*) or its precursor was the toxin that mediated the hypersensitivity reaction. They found differences in detoxification by lymphocytes of hydroxylamine between sensitive patients versus the non-sensitive patients. Simplifying this assay may allow its use as a predictive tool, making it possible to avoid adverse reactions especially in patients with a family history of sulfa hypersensitivity.

In conclusion it is vital to recognize sulfonamide drug hypersensitivity reaction, thereby avoiding the continuing use of the offending drug with its attendant morbidity and possible mortality.

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References

1. Steeper AT, Horwitz CA, Hanson M, *et al.* Heterophil negative mononucleosis like illnesses with atypical lymphocytosis in patients undergoing seroconversions to HIV. Am J Clin Path 1988, 90: 169-170.
2. Poland GA, Kathryn L. Marked atypical lymphocytosis, hepatitis and skin rash in sulfasalazine drug allergy. Am J Med 1986, 81: 707-708.
3. Mihaas AA, Goldenberg DJ, Slaughter RL. Sulfasalazine toxic reactions. Hepatitis, fever and skin rash with hypocomplementemia and immune complexes. JAMA 1978, 239: 1590-1591.
4. Wood TA, Frenkel EP. The atypical lymphocyte. Am J Med 1967, 42: 923-935.
5. Han T, Chawla PL, Sokal JE. Sulfapyridine induced serum sickness like syndrome associated with plasmacytosis, lymphocytosis and multiclonal gamma globulinopathy. N Engl J Med 1969, 280: 547-548.
6. Fifty years of sulfonamide. Lancet 1985, i; 378-379.
7. Cheson BD. Serious adverse reaction with sulfonamides. FDA Drug Bull 1984, 14: 5-6.
8. Longcope WT. Serum sickness and analogous reactions from certain drugs particularly sulfonamides. Medicine 1943, 22: 251-256.
9. Caron GA, Sarkany. Lymphoblast transformation in sulfonamide sensitivity. Br J Dermatol 1965, 77: 556-560.
10. Rieder JM, Uetrecht J, Shear NH, *et al.* Diagnosis of sulfonamide hypersensitivity reactions by *in vitro* rechallenge with hydroxylamine metabolites. Ann Int Med 1989, 111: 262-263.

Congenital Biphenotypic Leukemia

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Acute lymphoblastic leukemia (ALL) forms the majority of the cases of childhood acute leukemia, most of the remainder being acute myeloid leukemia(1,2). With the use

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of immunological markers, cases are being recognized who have blast cells of both–lymphoblastic and non-lymphoblastic types(3). We diagnosed such a case in neonatal period which is being reported.

Case Report

A 7-day-old male neonate was brought to Kalawati Saran Children's Hospital, New Delhi, with the complaints of inability to take feeds properly. There was no history of fever, seizures, apnea or bleeding. The child was second product of a non-consanguinous marriage. The age of mother and father were 30 and 38 years, respectively. On physical examination he was small for gestational age (weight 1.7 kg). He had a feeble cry and his neonatal reflexes were depressed. There was no pallor, lymphnode enlargement, skin rash or bleeding. Abdominal examination showed a soft hepatomegaly of one cm. Spleen was not palpable. Examination of cardiovascular, respiratory and central nervous system was normal. In addition, he had some features of Down Syndrome (depressed nose bridge, microcephaly, upward slant of eyes and single transverse palmar crease).

He was suspected to have neonatal septicemia with meningitis and after initial investigations was started on injection ampicillin and gentamicin. When his routine blood examination showed a total leucocyte count of more than 1.5 lacs/mm^3, a diagnosis of congenital leukemia was suspected and appropriate investigations were done.

His hemoglobin was 15 g/dl and platelet count was 83,000/mm^3. Peripheral smear examination showed 72% blast cells which were polymorphic in type. Blast cell morphology was similar on examination of bone marrow aspiration smear. Cytochemistry of the blast cells showed peroxidase and chloracetate esterase negativity. Granular positivity of lymphoid type was seen in some cells with nonspecific esterase. Results of immuno histochemical studies were as follows : myeloid markers (EBM 11 +ve 44% CD 11B +ve, 27%, HLA – DR +ve 20%, CD 33 +ve 16–18%, CD 13 –ve) and lymphoid markers (CD 19 +ve 16–18%, CD 10 +ve 20%, CD 3 – ve, CD 20 – ve; CD 22 –ve). On the basis of hematological, cytochemistry and immunological markers, a diagnosis of congenital biphenotypic leukemia was made.

Initial CSF examination showed protein of 186 and sugar of 95 mg/dl. There were 160 cells/mm^3 of which 20% were neutrophils. After 2 weeks of therapy, the CSF cells decreased but now blast cells could be seen on cytological examination. Blood and CSF culture were sterile. Chromosomal analysis of the patient and the mother were attempted but the results could not be obtained because of contamination of cell cultures.

After 3 weeks of antibiotic therapy antileukemic drugs were started (prednisolone, vincristine and doxorubicin) but soon after the first dose, the child developed necrotizing enterocolitis and expired.

Discussion

When a patient of acute leukemia shows blast cells of both lymphoid and myeloid lineage it is called biphenotypic or mixed lineage leukemia(4). Morphologically the blast cells in the present case were polymorphic–some cells of lymphoblastic and other myeloblastic type. Myeloid marker positivity (EBM 11, CD 11B and HLA-DR) and lymphoid marker positivity (CD 19 and CD 10) in the blast cells confirmed the biphenotypic nature of acute leukemia in

this neonate, hence the diagnosis–congenital biphenotypic leukemia. In the review of literature we could not find any report of congenital biphenotypic leukemia.

With the use of immunological markers cases of biphenotypic leukemia are being diagnosed increasingly. Mirro *et al.* reported myeloid marker positivity of 19% in cases of childhood ALL, while of the AML 25% cases had lymphoid marker positive blast cells(4). Incidence of such cases in other series varies from 4.3 to 33% (3,5-7). Whether such cases correspond to primary ALL or AML with aberrant expression of antigens, or represent proliferation of early progenitor cells is uncertain(8,9).

Presence of myeloid marker positive cells in ALL and lymphoid marker positive cells in AML has any influence on clinical presentation and prognosis is controversial. Sobol *et al.* and Urbano Ispixua *et al.* reported no significant difference in the clinical features and outcome in childhood ALL with myeloid marker positive blast cells while some adult patients had poorer response to therapy(3,5).

Therapy in such cases is usually directed towards primary morphological type. However, some cases of AML (with lymphoid marker positive blast cells) who fail to respond to AML directed therapy have responded when ALL directed therapy is added(4).

REFERENCES

1. Sallan SE, Weinstein HJ. Chldhood acute leukemia. *In:* Hematology of Infancy and Childhood, 3rd edn. Ed Nathan DG, Oski FA. Philadelphia, WB Saunders Co, 1987, pp 1028-1063.
2. Baehner RL, Miller DR. Hematologic malignancies: leukemia and lymphoma. *In:* Blood Diseases of Infancy and Childhood 5th edn. Eds Miller DR, Baehner RL. St Louis, The CV Mosby Co, 1984, pp 619-721.
3. Urbano-Ispizua A, Matutes E, Villamour E, *et al.* Clinical significance of the presence of myeloid associated antigens in acute lymphoblastic leukemia. Br J Hematol 1990, 75: 202-207.
4. Mirro J, Jipf TF, Pui CH, *et al.* Acute mixed lineage leukemia: Clinicopathologic correlations and prognostic significance. Blood 1985, 66: 1115-1123.
5. Sobol RE, Mick R, Royston I, *et al.* Clinical importance of myeloid antigen expression in adult acute lymphoblastic leukemia. N Engl. J Med 1987, 316: 1111-1117.
6. Cantu-Rajnoldi A, Putti C, Saitta M, *et al.* Co-expression of myeloid antigens in childhood acute lymphoblastic leukemia: Relationship with the stage of differentiation and clinical significance. Br J Hematol 1991, 79: 40-49.
7. Bradstock KF, Kirk J, Grimsley PG, Kabral A, Hughes WG. Unusual immunophenotypes in acute leukemias: incidence and clinical correlations. Br J Hematol 1989, 72: 512-518.
8. Greaves MF. Differentiation-linked leukemogenesis in lymphocytes. Science 1986, 234: 697-704.
9. Perentesis J, Ramsay NK, Brunning R, Kessey JH, Filipovial AH. Biphenotypic leukemia-Immunologic and morphologic evidence for a common lymphologic evidence for a common lymphoidmyeloid progenitor in humans. J Pediatr 1983, 102: 63-67.