Table 1–*Summary of Arterial Blood Gases*

Parameter	Before treatment	After treatment
pH	7.097	7.345
PO_2	204.0	172.0
PCO_2	8.2	11.2
HCO_3	2.4	6.0

days and recovered fully with no neurological sequelae. She was discharged on the fifth day, now comes for routine immunization and is doing well.

Discussion

Nalidixic Acid is a commonly used quinolone. Severe metabolic acidosis is a rare complication of overdosage. The youngest child with this complication to be reported was a seventeen-month-old baby(1). Nalidixic Acid causes metabolic acidosis by affecting the lactic acid metabolism(2). *Lactobacillus* also causes an increase in serum lactic acid levels. *Lactobacillus* induced metabolic acidosis has been reported, in a young adult(3). There was no evidence of hemolysis, though Nalidixic acid is known to produce hemolytic anemia. Pseudotumor cerebri is a well known complication of Nalidixic Acid therapy.

When a child presents with a history of Nalidixic Acid intake and rapid breathing, Nalidixic Acid induced metabolic acidosis should be thought of. The acidosis, if corrected promptly, leads to complete recovery with no sequelae. Also, a combination of Nalidixic Acid and lactobaccillus is better avoided.

REFERENCES

1. Reynolds JEF. Antibacterial Agents. *In:* Martindale The Extrapharmacopoeia, 29th edn, London, The Pharmaceutical Press, 1989, pp 266-267.
2. Mc Anally TF. Acid Base Balance. *In:* Clinical Management of Poisoning and Drug Overdose, 2nd edn. Ed Haddad Winchester. Philadelphia, W.B. Saunders Co, 1990, p 125.
3. Oh MS, Phelps KR, Traube M, *et al.* Severe metabolic acidosis and neurological manifestations in a man with short bowel syndrome. New End J Med 1979, 301: 249-252.

Marked Atypical Lymphocytosis and Skin Rash Following Sulfamethoxazole

B.R. Agarwal
A.S. Sathe
Z. Currimbhoy

Heterophil-antibody negative infectious mononucleosis like illnesses that include atypical lymphocytes on a blood smear have been widely documented in literature(1-4). Several infectious agents besides Epstein-Barr virus, *viz.,* cytomegalovirus, rubella,

From the Department of Pediatrics, Hematology and Oncology, B.J. Wadia Hospital for Children, Institute of Child Health and Research Centre, Parel, Bombay 400 012.

Reprint requests: Dr. Bharat R. Agarwal, Consultant Pediatric Hematologist and Oncologist, 63, Gandhi Nagar, Bandra (East), Bombay 400 051.

Received for publication: June 14, 1990; Accepted: March 15, 1993

hepatitis B, human immunodeficiency virus, human herpes virus(5) and toxoplasmosis as well as drugs including halothane, hydantoin, dapsone and other sulfa drugs particularly sulfasalazine(2,3) have been etiologically linked to the above illnesses. We describe a 1½ year-old child with fever, skin rash and a marked atypical lymphocytosis following administration of co-trimoxazole (a sulfa drug).

Case Report

A 1½-year-old male child, presented in March 1989 with a history of fever and cough for which he had received co-trimoxazole for 3 days. On the third day of medication, the child continued to have fever and developed a multiple greyish violaceous skin rash, predominantly on the chest and abdomen. These lesions varied from 0.2 to 3 cm in diameter, were circular, sharply defined, not elevated and nonpruritic. Their appearance suggested a "fixed drug eruption." There was history of a similar rash appearing predominantly around the lips following co-trimoxazole prescribed for a respiratory infection at the age of 6 months.

Clinical examination apart from the skin lesions were entirely negative. Hematological investigations revealed a white blood cell (WBC) count of 6,100 with polymorphonuclear leucocytes 14%, eosinophils 6%, monocytes 12%, lymphocytes 17% and atypical lymphocytes 51%. He had been on co-trimoxazole which was discontinued. Follow-up after 2 weeks revealed a total WBC count of 14,800 with polymorphonuclear leucocytes 17%, eosinophils 6%, monocytes 5%, lymphocytes 62% and atypical lymphocytes 9%. After another week only one atypical lymphocyte was present (*Table I*).

Discussion

The sulfonamides have the distinction of being the oldest microbial agent in clinical use, having been first developed more than 50 years ago(6). Despite this, adverse reactions associated with sulfonamide therapy remain poorly understood. The side effects of sulfa drugs that occur in 3-5% of patients are usually benign and selflimited, consisting of nausea, anorexia and skin rashes. Rarely, more serious adverse effects such as hypersensitivity, Steven's Johnson Syndrome, agranulocytosis, hepatitis, hemolysis, leucopenia and toxic epidermal necrolysi occur(7).

Previous reports have described an infectious mono-nucleosis-like syndrome after sulfa administration associated with atypical lymphocytosis (2-3, 8-9). Mihaas *et al.* in 1978(3) and Poland *et al.* in 1986(2) reported cases of a toxic reaction to sulfasalazine characterized by fever, skin rash, hepatitis, atypical lymphocytosis and eosinophilia. They believed this reaction was secondary to circulating immune complexes. Additionally, hypocomplementemia was seen in their patients(3). Our patients was not actually ill, yet had a remarkable number of atypical lymphocytes: a total of 68% lymphocytes including 51% atypical lymphocytes.

Rieder *et al.*(10) offer an alternative view. Their studies showed that hydroxyl-

TABLE I—*Hematological Profile at Admission and Follow up*

Parameter	On admission	At follow up 2 weeks	At follow up 3 weeks
WBC count	6,100	14,800	10,200
Neutrophils (%)	14	17	22
Eosinophils (%)	6	6	5
Monocytes (%)	12	5	4
Lymphocytes (%)	17	62	68
Atypical lymphocytes (%)	51	9	1

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.

Acknowledgement

The authors are grateful to the Dean, B.J. Wadia Hospital for Children for permission to publish this case.

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

J. Chandra
S. Narayan
D.K. Shome
P. Sahni
R.N. Mandal
K.B. Logani
D. Sharma

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

From the Department of Pediatrics, Kalawati Saran Children's Hospital, Department of Pathology, Lady Hardinge Medical College, and Department of Pathology, Maulana Azad Medical College, New Delhi.

Reprint requests: Dr. Jagdish Chandra, Associate Professor of Pediatrics, Kalawati Saran Children's Hospital and Associated Lady Hardinge Medical College, New Delhi 110 001.

Received for publication: January 4, 1993; Accepted: March 15, 1993