INTERNATIONAL JOURNAL OF MEDICAL AND APPLIED SCIENCES
Earthjournals Publisher
E-ISSN:2320-3137
www.earthjournals.org

CASE REPORT

ZOSTER HEPATITIS WITH MYELOSUPPRESSION IN ACUTE LEUKAEMIA ON CHEMOTHERAPY

SHREENIWAS S. RAUT, SHAILESH S. TALATI, SONIA K. PAREKH, VASHISHTH P. MANIAR, DIVESH M. GOYAL, VANDANA L. GOHEL

Department of Medical and Pediatric Oncology, Gujarat Cancer and Research Institute, Ahmedabad, India

Corresponding Author: Dr. Shreeniwas S. Raut, s.no. 92, shahu vasahat, near PMC school no. 111, laxminagar, pune :9

Abstract

We report a rare case of acute lymphoblastic leukaemia (ALL) with zoster rash developed while on chemotherapy progressing to hepatitis and prolonged myelosuppression. Such clinical presentation is not yet reported in available literature according to our knowledge. We support the atypical presentation of zoster in immunocompromised patients on chemotherapy and explore the natural history of zoster hepatitis and myelosupperssion observed in this episode. We report the morbidity of febrile neutropenia, prolonged hospitalisation of one month, delayed marrow recovery and impact on subsequent chemotherapy schedule compelling the dose reduction. We treated this patient with antivirals, and other supportive care for febrile neutropenia. This case report may guide the prognosis and expectant management in similar other cases.

Key words: Zoster, Hepatitis, Myelosuppression, Acute leukaemia, Chemotherapy

INTRODUCTION

Herpes zoster or simply ‘Zoster’ is a disease due to reactivation of varicella zoster virus (VZV). It usually occurs years after primary infection with VZV (varicella or chickenpox) or receipt of the live, attenuated varicella vaccine and is common in immunocomromised patients including those on cancer chemotherapy but nobody have reported yet its presentation as skin lesions and hepatitis further progressing to myelosuppression.

CASE REPORT

A seven year old male child presented with low grade fever, fatigue and bone pain since 1 month. He had history of full term normal hospital delivery and was immunised till date. There was no recent history of bleeding. He was conscious, oriented & his vital parameters were normal. Except severe pallor and bone tenderness his general examination was normal. His systemic examination was normal. Complete blood count (CBC) on first presentation showed haemoglobin (Hb) 9.7g/dL, total leucocyte count (TLC) 73000/µL with 50% lymphoblasts, and platelet count (PLC)-11000 /µL. He had normal liver & renal function tests. Serum lactate

dehydrogenase (LDH) was 715 IU/L. Serum uric acid level was 4.95 mg/dL. The morphologic picture on bone marrow examination was hypercellular marrow, 74 % blasts, high nucleus/cytoplasmic ratio, altered myeloid/erythroid ratio, lack of megakaryocytes, suggesting acute lymphoblastic leukaemia (ALL). Immunophenotyping (IPT) showed the blasts mainly expressing B lymphoid markers CD79a (87%), CD 19 (76%), CD22 (93%), CD 13 (15%), Tdt (96%), CD34 (78%), HLADR (58%) & CD 10 (99%). Co- expression of CD34/CD22 was 73 %, CD 34/CD 19 was 61 % CD 10/CD22 was 33 % & CD 10/19 was 76 %. He was diagnosed to have pre-pre B cell ALL. Conventional cytogenetics was normal. Philadelphia chromosome test was negative by fluorescent in situ hybridisation (FISH) method. Chest X ray was normal. Ultrasonography of abdomen also was normal except a few mesenteric lymphnodes.

He was started on first phase of induction (I1) of BFM 90 protocol of ALL therapy with daunorubicin, vincristine, steroids, L–asparaginase & intrathecal methotrexate. Postinduction bone marrow was morphologically in remission. Cerebrospinal fluid cytology was negative for malignant cells at start of induction as well as after I1. Second phase of Induction and consolidation of BFM 90 protocol was uneventful.

Reinduction (RI) was started. On RI day 15-postchemotherapy day 5 the patient presented with a severe, painful, predominantly unilateral and dermatomal rash [Figures 1, 2 and 3]. The rash was initially papular, then vesicular, and eventually crusted in 10–15 days. There were no symptoms or signs of cranial nerve involvement. There were no eyelid or nose lesions to indicate potentially sight-threatening keratitis. He had no history of exposure to patient with similar skin rash within last 2 weeks.

Blood investigations revealed hyperbilirubinemia, elevated serum transaminases, pancytopenia, hypoalbuminemia, hypo globulinemia, raised activated partial thromboplastin time, raised serum lactate dehydrogenase & bone marrow hypoplasia. Laboratory investigations when plotted graphically against days [Figure 4] showed trend as follows: initial rise of serum transaminases followed by leukopenia and neutropenia, further this was followed by thrombocytopenia, hyperbilirubinemia and rise and platue of serum alkaline phosphatase. Thus this trend explains that initially the patient had zoster rash followed by liver dysfunction which was further followed by myelosuppression.

Myelosuppression and liver dysfunction were not related to chemotherapy because the same dose of chemotherapy was well tolerated before this episode. There was a significant time gap of 5 days between the last combination chemotherapy administration and the start of hepatic dysfunction again supporting that chemotherapy was not the cause for it. This patient required some transfusion support. The temporal profile of investigations against days is illustrated in the figure 4, which clearly shows that the liver dysfunction was already set 48 hours before the start of leukopenia and neutropenia, thus it was not a part of organ dysfunction secondary to septicaemia in neutropenic patient. We did not do the work up for autoimmunity due to financial constraints. Further ultrasonography (USG) of his abdomen was normal. During this episode

patient had secondary bacterial and fungal infection causing diarrhoea & fever. Stool culture detected pseudomonas aeruginosa & Candida tropicalis. Blood culture was sterile. Tests for malaria & dengue parasite were negative. Bone marrow examination was done late in this event to predict the recovery of cytopenia. It revealed hypo cellular marrow, presence of megakaryocytes, few myeloid precursors & polymorphs, mild erythroid hyperplasia with normoblastic erythropoiesis, the impression being that of regenerating marrow. We treated this patient with systemic antivirals (tablet acyclovir 400 mg, 3 times a day for 14 days), sensitive antibiotics for bacterial infections, transfusion support and local antiviral skin ointments.

This patient was hospitalised for almost one month in this episode. He had febrile neutropenia in subsequent cycle of chemotherapy also. This may be due to persistent impact of previous event on the marrow leading to poor marrow reserve. Liver dysfunction did not recur. We offered him 20% dose reduction in further chemotherapy schedule. After this, at present the patient is on chemotherapy maintenance schedule and tolerating it well for last six months.

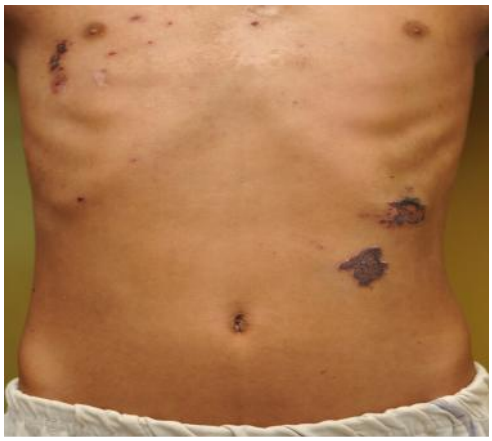

Figure 1 Thoracic dermatomal rash (anterior)

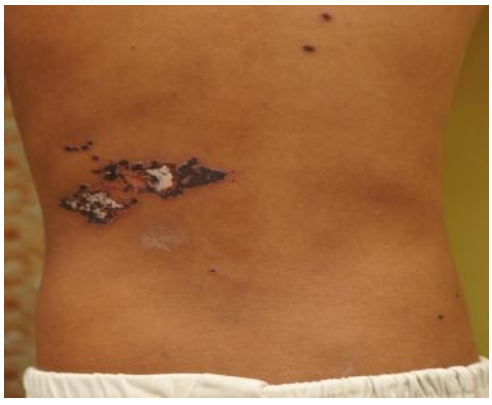

Figure 2 Thoracic dermatomal rash (posterior)

INTERNATIONAL JOURNAL OF MEDICAL AND APPLIED SCIENCES
Earthjournals Publisher
E-ISSN:2320-3137
www.earthjournals.org

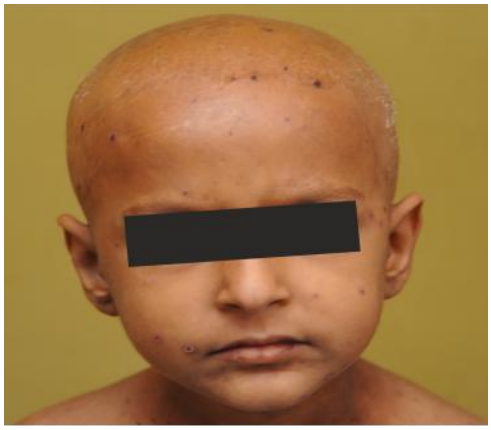

Figure 3 Atypical lesions on face and scalp

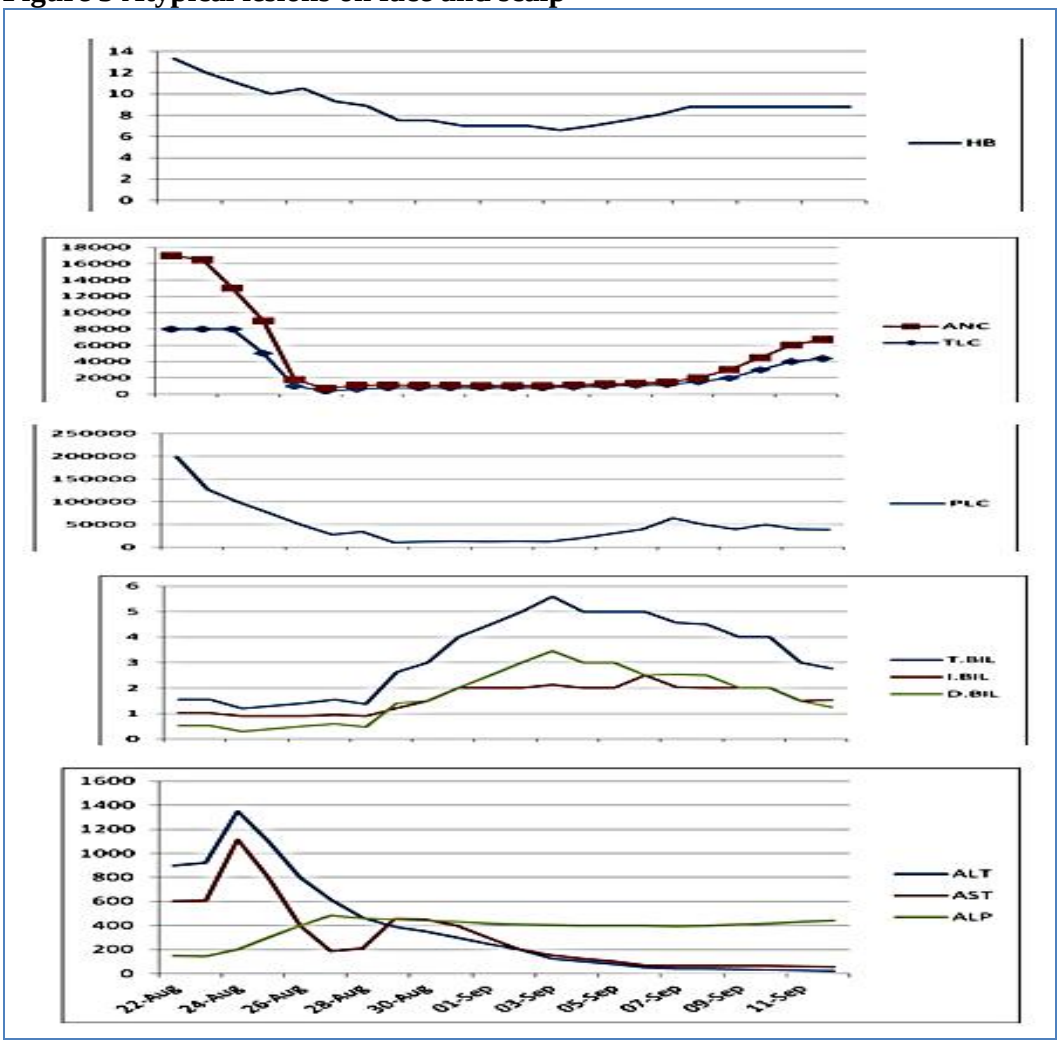

Figure 4 Graph of investigations against days. HB g/dL, TLC /cmm, ANC /cmm, PLC /cmm, T. BIL mg/dL, D. BIL mg/dL, I. BIL mg/dL, ALT IU/L, AST IU/L, ALP IU/L.

DISCUSSION

Varicella Zoster virus (VZV) is a double-stranded, linear virus of DNA group.The primary infection of this causes varicella in susceptible hosts. Varicella hepatitis in immunocompetent hosts is generally self-limiting and asymptomatic and associated with subclinical elevation in serum transaminase levels. Severe varicella hepatitis leading to fulminant liver failure, massive hepatic necrosis, autoimmune hepatitis, chronic active hepatitis have also been reported.[1,2,3]

It is estimated that there are 96 deaths each year in which herpes zoster was the underlying cause, almost all the deaths occurred in elderly people or those with compromised or suppressed immune systems.[4]

The diagnosis of zoster requires only physical examination to identify the typical VZV rash (Lesions which are simultaneously in all stages of development— ranging from vesicles on a red base, to umbilicated pustules and crusted lesions.) Zoster has unilateral, dermatomal distribution of a painful vesicular skin rash most commonly on thorax but can be anywhere on the body. Past history of varicella (primary infection of VZV virus) may not be evident because primary infection of varicella zoster virus may go unnoticed. Laboratory tests are not routinely required, however can be useful for confirmation of the diagnosis in case of doubt. Rapid varicella zoster identification can be done by Polymerase chain reaction (PCR) testing. Viral culture is rarely necessary. [5]

Immunocompromised patients are more susceptible to develop herpes zoster as compared to immunocompetent patients. They also have more diffuse involvement, increased severity and duration of pain, and atypical manifestations. [6]

Episodes of herpes zoster are generally self-limited and resolve without intervention in immunocompetant persons and in children than in adults. Supportive therapy consists of Nonsteroidal anti-inflammatory drugs, Wet dressings with 5% aluminium acetate, Lotions (eg, calamine). Drugs for zoster–associated pain include Narcotic and nonnarcotic analgesics, Neuro active agents (eg, tricyclic antidepressants, Anticonvulsant agents. Oral Steroids are controversial. Antiviral therapy for herpes zoster decreases the days of acute discomfort, and the severity of postherpetic neuralgia. Therapy should be started within 72 hours of beginning of symptoms. Oral antiviral treatment comprises Acyclovir, Famcyclovir and Val acyclovir. Hospital admission is recommended for severe symptoms, immunosuppression, atypical presentations (eg, myelitis), involvement of more than 2 dermatomes, significant facial bacterial superinfection, disseminated herpes zoster, ophthalmic involvement, meningoencephalitis.[6]

Surgical care is not routinely indicated for the treatment of herpes zoster, but it is required if necrotizing fasciitis occurs. Surgical separation of pain fibres can be considered in cases of intractable pain. Varicella-zoster immune globulin (VZIG) is used to prevent or modify clinical illness in susceptible hosts who are exposed to varicella or zoster. In a study of children with leukaemia, those who got varicella vaccine had a 67% lower risk of herpes zoster than children who had had varicella. [7]

Our case report adds useful information that atypical presentation of zoster in a patient of acute leukaemia on chemotherapy can include rash followed by hepatitis with prolonged myelosuppression and may necessitate subsequent dose adjustments in further cycles of chemotherapy. This may also lead to secondary bacterial reinfection and prolonged hospitalisation, thus comprising significant morbidity.

REFERENCES:

1. Ross JS, Fanning WL, Beautyman W, Craighead JE. Fatal massive hepatic necrosis from varicella-zoster hepatitis. Am J Gastroenterol 1980; 74:423-7.
2. Waleed KAH. Severe autoimmune hepatitis triggered by Varicella-Zoster infection. World J Gastroenterol 2009; 15:1004-1006.
3. Rosenfield AT, Schermer DR, Gospe J M, Hartley RA. Herpes zoster and chronic active hepatitis. The American Journal of Digestive Diseases June 1971; 16:535-539.
4. Mahamud A, Marin M, Nickell SP, Shoemaker T, Zhang JX, Bialek SR. Herpes zoster-related deaths in the United States: Validity of death certificates and mortality Rates, 1979-2007. Clin Infect Dis 2012; 55:960-6.
5. HERPES ZOSTER, Infection Control Guidelines for Long-Term Care Facilities Massachusetts Department of Public Health Division of Epidemiology and Immunization. 2007; p.2.
6. Whitley RJ, Varicella-Zoster virus infections, Harrison's Principles of Internal Medicine, 18th Ed. Asia: Mc Graw Hill; 2011. p.1462-1466
7. Hardy I, Gershon AA, Steinberg SP, LaRussa P. The incidence of zoster after immunization with live attenuated varicella vaccine.A study in children with leukaemia. Varicella vaccine collaborative study group. N Engl J Med 1991; 325:1545-50.