Immune Thrombocytopenic Purpura with Acute Lymphoblastic Leukemia- An Unusual Association

Hematologic malignancies such as Hodgkins lymphoma, Non-Hodgkin lymphoma and chronic lymphocytic leukemia have been associated with immune thrombocytopenic purpura (ITP) but it is rare to see ITP in patient with acute lymphoblastic leukemia (ALL) [1,2]. ALL is a immunosuppressive disease and chemotherapy results in further immunosuppressive state. Therefore, association of autoimmune diseases with ALL is rare. Nine cases of ITP in children with ALL have been reported so far, three of them were acute ITP, and rest were chronic ITP [3]. Only one such case has been reported from India [4].

A 15-year-old girl was admitted to us with fever, increasing pallor and bleeding spots over the body in July 2010. Physical examination revealed liver 5 cm and spleen 3 cm below costal margin. Complete blood count (CBC) showed hemoglobin (Hb) 6.5 g/dL, white blood cell 24000/mm^3 and platelet 38,000/mm^3. Peripheral blood smear showed 54% blasts. The bone marrow was consistent with pre-B ALL. Cerebrospinal fluid was negative for malignant cells. Patient was started on chemotherapy using BFM-95 regimen. Bone marrow aspiration and biopsy showed remission on the 33rd day of treatment. After phases of Protocol-I, Protocol-M, and Protocol-II, patient was started on maintenance therapy including 6-mercaptopurine and methotrexate. After 20 months into therapy, the patient was noted to have a platelet count of 59000 /mm^3. Therapy was stopped for 15 days and repeat CBC showed platelet count of 38000/ mm^3, a suspicion of relapse was kept and bone marrow aspiration and biopsy was performed. An adequate number of megakaryocytes with findings of ALL in remission were detected, there was nothing suggestive of myelodysplastic syndrome. The patient was started on prednisone at 2 mg/kg orally daily**.** After 3 weeks of prednisolone, she had improvement of her platelet count to 78000/mm^3. Her last platelet count in July 2012 was 88000/mm^3. Secondary causes of ITP were ruled out: antinuclear antibodies was negative, double stranded DNA was 14 IU/mL, IgG, IgA, IgM and IgE were 540,35,118 and 18mg/dL, Hepatitis B, Hepatitis C and HIV studies were negative, and anti-phospholipid antibodies (APLA) and direct coomb's test were also negative.

To conclude, the presence of thrombocytopenia in patient of ALL does not always means relapse of ALL or as a result of chemotherapy but the possibility of ITP should also be considered.

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Hepatitis B Vaccination

Rajasthan Government has recommended in 2011 that hepatitis B vaccination be given to all institutional delivered babies within 24 hrs of birth as 0 dose so as to prevent vertical transmission. The remaining recommended doses are to be given at 6-10-14 weeks. IAP Immunization Schedule 2009-10 recommended five schedules *viz*. birth, 1 and 6 months; birth, 6 and 14 weeks; 6, 10 and 14 weeks; birth, 6 weeks, 6 months; and birth, 6 weeks,10 weeks, 14 weeks. The recent Consensus Recommendations of IAPCOI [1] has recommended the 0-6wks-6months schedule, the first dose to be administered at birth, second dose at 6 weeks and third dose at 6 months. The reason being it is more closer to immunologically ideal and most widely used 0-1-6 months schedule, and also conforms to latest ACIP recommendations wherein the final dose in the Hepatitis-B vaccine series should be administered no earlier than 24 weeks and at least 16 weeks after the first dose [2] .

Therefore, the question arises as to the rationality of

the recommendation followed in the above 4-doses schedule, wherein the first dose is given within 24 hours of birth for institutional deliveries only. With these, we will be missing out on those delivered outside the hospital and also those coming for vaccination beyond 24 hours of birth even in case of hospital deliveries also which happen many a time. If on the other hand if it is beneficial, should we recommend it?

As to the other schedules where 6-10 weeks schedule are also included, should we altogether forgo it ,despite the programmatic implications and logistic issues as it is not ideal immunologically and does not conform to the classical schedule of 0-1-6 months.

Coming back to the schedule followed here, where the birth-6-10-14 weeks are recommended, and based on what we have noted above, it is far from being ideal. First, the 'Zero' dose benefits only a section of a population and deprives those newborns delivered outside and also those of institutional deliveries presenting after 24 hours of life. Secondly, the schedule with its recommended dose at 10 and 14 weeks dose not conform to the ideal immunological response and schedule as recommended under ACIP guidelines [2]. So what should be the further course to be taken here in the context mentioned above.

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REPLY

The IAPCOI's guidelines are primarily for pediatricians in their office practice. The stress is more on providing the best practice guidelines for an individual child overlooking the programmatic and logistics considerations. Hence, these guidelines are offering the best ways of utilizing the most optimum response of an individual vaccine for an individual person. IAPCOI is also issuing guidelines for mass or public use of a vaccine in form of recommendations to Government of India including its position on incorporation of new vaccines in the national immunization schedule [1]. Let us not confuse the two recommendations.

As far as Hepatitis-B recommendations are concerned, we have offered the best 'feasible' individual schedule that can be incorporated in to current IAP's immunization timetable. Nowhere have we stated that hepatitis-B vaccine should not be administered after 24 hours of birth but the recommendations have stated clearly that it should be offered to all newborns before hospital discharge (see comments of Table 1and footnote on Hepatitis-B of Figure 1). Similarly, though the committee stresses the need and significance of birth dose, it has not out-rightly rejected the other schedules including the government's adopted 6-10-14 weeks, considering the programmatic implications and logistic issues. When a vaccine is used in a program, there are many other considerations apart from vaccine efficacy and effectiveness like vaccine cost, burden of that particular vaccine preventable disease, logistics, vaccine safety, public acceptance, etc. These issues may be inconsequential when a vaccine is used in office practice for protection of an individual subject. In the former, one may be forced to compromise on certain attributes of a vaccine, but there may be no such compulsions in the latter.

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