Sir,

The risk of thrombotic complications in acute lymphoblastic leukemia (ALL) in children ranges from 1 to 37% in literature. Here, we report a case of a 9-year-old boy with ALL who developed sagittal sinus thrombosis during induction with L-asparaginase which was later introduced during reinduction with low molecular weight heparin (LMWH) as thromboprophylaxis successfully without any recurrence of thrombosis.

A 9-year-old boy presented with fever, generalized lymphadenopathy and hepatosplenomegaly. His investigations revealed hyperleucocytosis (>1 lakh/cumm), anemia, severe thrombocytopenia and lymphoblasts on peripheral smear. He was diagnosed as T-cell ALL by flow cytometry. He was started on oral steroids (prednisolone) and four drug induction with weekly doses of vincristine, daunorubicin, intrathecal methotrexate and twice weekly *Escherichia coli* L-asparaginase for a total of eight doses. He was readmitted a week later after induction with watery stools and managed symptomatically. During this episode, he developed seizures which required loading of anticonvulsants and mechanical ventilation. Clinically, he developed right hemiparesis. His CT brain showed left parietal bleed along with thrombocytopenia, deranged coagulation and low plasma fibrinogen levels. His MRI/MRV brain revealed superior sagittal sinus thrombosis. A possibility of drug induced thrombosis and coagulopathy secondary to induction with L-asparaginase and steroids precipitated by a diarrheal illness was considered. He received fresh frozen plasma concentrates and was started on LMWH which was continued for 3 months. Thrombophilia work-up was not done in view of financial constraints.

His neurological status and repeat MRI/MRV brain were normal at follow up. L-asparaginase was reintroduced during the reinduction phase of chemotherapy with LMWH as thromboprophylaxis. There were no further episodes of thrombosis and LWMH was stopped after 1 week of stoppage of L-asparaginase. There were no residual neurological deficits at follow-up. He is presently doing well on maintenance chemotherapy.

The timing of thrombosis in children with ALL is very consistent in the literature, occurring either during or immediately after chemotherapy with L-asparaginase. Thrombosis is more common during induction in view of intensive therapy and associated active disease. Factors such as the primary disease itself activating blood coagulation via procoagulant substances or by impairment of fibrinolytic or anticoagulant pathways, chemotherapy, and prothrombotic risk factors of the host have been found to play a contributory role.

L-asparaginase interferes with coagulation homeostasis depleting serum levels of several hemostatic factors, rarely leading to thrombotic or hemorrhagic cerebrovascular complications. It is suggested that prednisolone and *E. coli* asparaginase concomitantly administered in a leukemic patient suffering from a prothrombotic risk factor, is found to be responsible for the onset of venous thrombosis in the majority of cases. MRI/MRV provides us the diagnosis in such children.

Treatment of venous thrombosis includes supportive measures, anticonvulsants and anticoagulation. Elhasid *et al.* reported that LMWH is safe and effective in prevention of thromboembolism in ALL patients during L-asparaginase therapy. Grace *et al.* studied pediatric (ages 0-18 years) and adult (18-50 years) patients with acute lymphoblastic leukemia (ALL) associated with asparaginase-related venous thromboembolic events (VTE) treated at Dana-Farber Cancer Institute on clinical trials for newly diagnosed ALL between 1991 and 2008. Of 548 patients, 43 (8%) had VTE, including 27/501 (5%) pediatric and 16/47 (34%) adult patients. Sinus venous thrombosis occurred in 1.6% of patients. Thirty patients (70%) ultimately received at least 85% of the intended doses of asparaginase. This study confirms that, after VTE, asparaginase can be restarted with closely monitored anticoagulation after imaging demonstrates clot stabilization or improvement. Our child was also initiated on thromboprophylaxis with LMWH during reinduction with L-asparaginase therapy and completed the therapy without any further episodes of thrombosis. So we conclude that asparaginase should be suspended from that particular course but can be given in subsequent courses safely under prophylactic anticoagulant cover.

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**L-asparaginase-induced cortical vein thrombosis in a child with leukemia: Can we rechallenge?**

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REFERENCES

1. Athale UH, Chan AK. Thrombosis in children with acute lymphoblastic leukaemia: Epidemiology of thrombosis in children with acute lymphoblastic leukaemia. Thrombosis Res 2003;111:125-31.
2. Caruso V, Lacoviello L, Castelnuovo AD, Storti S, Mariani G, de Gaetano G, et al. Thrombotic complications in childhood acute lymphoblastic leukemia: A meta-analysis of 17 prospective studies comprising 1752 pediatric patients. Blood 2006;108:2216-22.
3. Donati MB, Falanga A. Pathogenesis of thrombosis in cancer. Hema-tol J 2003;4:63-7.
4. Elhasid R, Lanir N, Sharon R, Weyl Ben Arush M, Levin C, Postovisky S, et al. Prophylactic therapy with enoxaparin during l-asparaginase treatment in children with acute lymphoblastic leukemia. Blood Coagul Fibrinolysis 2001;12:367-70.
5. Grace RF, Dahlberg SE, Neuberg D, Sallan SE, Connors JM, Neufeld EJ, et al. The frequency and management of asparaginase-related thrombosis in paediatric and adult patients with acute lymphoblastic leukaemia treated on Dana-Farber Cancer Institute consortium protocols. Br J Haematol 2011;152:452-9.

Sir,

I read Jain V, Mohta A, Sengar M, Khurana N. Is antenatal detection of Wilms' tumor a bad prognostic marker? Indian J Med Paediatr Oncol 2011;32:214-6 with interest.

Firstly, I disagree with the authors that the tumor was in advanced stage at initial presentation. Secondly, there was no excuse for not having done a fine-needle aspiration cytology (FNAC) as figure 2 shows distinct solid areas. In fact, I would have resorted to tru-cut biopsy of the tumor; the UKW3 trial has shown no evidence to suggest that performing such a biopsy should affect tumor staging or subsequent treatment.[1] Thirdly, I believe that the management was not well planned. The child's nutrition status should have been improved preoperatively. Personally, I would have opted for upfront chemotherapy for such a large tumor. Radiotherapy should be started within 10 days of surgery, so it has to be planned before undertaking surgery, even if a preoperative histological diagnosis is not available. One cannot hide behind the logistic reasons for not administering radiotherapy in time. The infant has obviously succumbed to the toxicity of the chemotherapy used.

Contrary to authors’ assertion, excellent survival has been reported for all types of renal tumors other than rhabdoid tumor of kidney diagnosed antenatally,[2,3] especially for NWTSG/COG stage I Wilms’ tumor. I may also add some more references for the antenatally diagnosed renal tumors here.[4,5] I conclude by reiterating that appropriate management of solid tumors involves a multidisciplinary approach, judicious use of the well-established protocols and diligent compliance.

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