Severely Deranged Lipid Profile: Caught Unawares

Sir,

A 22-year-old lady diagnosed with B-cell acute lymphoblastic leukemia (ALL) and on treatment with parenteral L-asparaginase, daunorubicin and vincristine in addition to glucocorticoids reported severe epigastric pain with nausea on day 24 of initiation of therapy. Clinical examination was unremarkable except for epigastric tenderness. A possibility of acute pancreatitis was considered. When blood sample was drawn for evaluation, it was found to be turbid and lipemic [Figure 1]. She did not have features of arcus senilis or tendon xanthoma and previous blood samples had appeared normal. Her serum triglyceride was 10,100 mg/dL and total cholesterol was 580 mg/dL. However, serum lipase and amylase were not elevated, and a random plasma glucose done was 193 mg/dL.

There was no family history of pancreatitis, xanthomas, or treatment for high triglycerides. In view of the severe hypertriglyceridemia, she was started on an insulin infusion (0.1 unit/kg/h) with potassium correction and oral fenofibrate 160 mg/day. Glucocorticoid therapy was tapered and stopped as per protocol. Her triglyceride levels were monitored daily and displayed significant decline over the next one week. At the time of discharge, it was 239 mg/dL. She was continued on fenofibrate and one month later, her serum triglyceride was 89 mg/dL following which the medication was discontinued. At 12 months follow-up, her triglyceride and blood glucose remained normal.

L-Asparaginase is used in induction protocols for acute lymphoblastic leukaemia (ALL). Normal cells synthesize asparagine de novo via the enzyme asparagine synthase, which is absent in malignant lymphoid cells. It inhibits protein synthesis by depleting intracellular nonessential amino acid asparagine. The adverse effects includes hyperglycemia, hypertriglyceridemia, and hypercholesterolemia. Asparaginase-induced hypertriglyceridemia may be asymptomatic or it may be complicated by transaminitis, pancreatitis, life-threatening thrombosis, or hyper viscosity syndrome. The possible mechanisms of action include the inhibition of lipoprotein lipase, decreased hepatic synthesis of lipoprotein, and increased synthesis of VLDL.[1]

The effect of ALL treatment regimen on lipid metabolism was studied in two cohorts of children by Cremer *et al*.[2] Hypothyroidism was excluded in these subjects. The first cohort had received prednisone with asparaginase simultaneously and was noted to have elevated levels of total cholesterol, TG, chylomicron TG, α-cholesterol, and A1 apolipoprotein subsequent to therapy. The second cohort was initially administered prednisone followed by asparaginase. These individuals had elevations in α-cholesterol and A1 apolipoprotein initially, followed by elevations of total and chylomicron TG during asparaginase therapy.

Parsons *et al*.[3] studied the impact of steroid administration during both induction and intensification phases, and asparaginase during the intensification phase alone. TG elevations were observed during the intensification phase alone. Thus, we might attribute hypercholesterolemia and hypertriglyceridemia observed in patients with

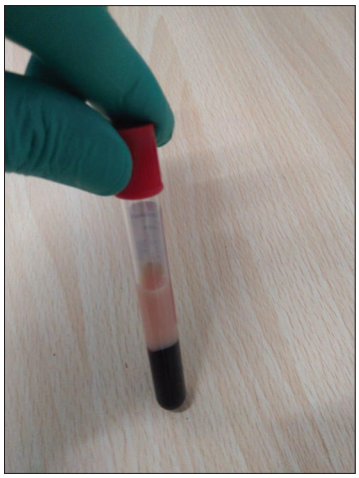

Figure 1: Turbid and lipemic serum

ALL to steroids and asparaginase, respectively. The study showed increased VLDL and Apo-B100 during asparaginase treatment in patients with TG values >400 mg/dL comparing with pre-treatment values, suggesting an increase in the production of VLDL as a mechanism of hypertriglyceridemia.

Hypertriglyceridemia secondary to asparaginase occurs in 10–50% of children being treated for ALL. Thus far, there are no predisposing risk factors, effect of a certain dose, type of leukemia, blood glucose level, gender, age, or preparation of asparaginase correlating with the magnitude of TG increase. These changes in lipid metabolism induced by L-asparaginase during chemotherapy are fully reversible. The management options target the complications and treating the hypertriglyceridemia.[4] It includes low-fat diets, fibrate therapy, heparinization, insulin infusion; and/or plasmapheresis.[5]

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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References

1. Alakel N, Heuschkel S, Balaian E, Röllig C, Bornhäuser M. Treatment of pegylated asparaginase-induced hypertriglyceridemia with continuous intravenous infusion of insulin and heparin: A case report. Chemotherapy 2019;64:210-4.
2. Cremer P, Lakomek M, Beck W, Prindull G. The effect of L-asparaginase on lipid metabolism during induction chemotherapy of childhood lymphoblastic leukaemia. Eur J Pediatr 1988;147:64-7.
3. Parsons SK, Skapek SX, Neufeld EJ, Kuhlman C, Young ML, Donnelly M, *et al*. Asparaginase-associated lipid abnormalities in children with acute lymphoblastic leukemia. Blood 1997;89:1886-95.
4. Silvano J, Marques N, Tavares I, Ferreira I. Severe L-asparaginase-induced hypertriglyceridaemia treated with plasmapheresis. Eur J Case Rep Intern Med 2021;8:002342. doi: 10.12890/2021_002342.
5. Cohen H, Bielorai B, Harats D, Toren A, Pinhas-Hamiel O. Conservative treatment of L-asparaginase-associated lipid abnormalities in children with acute lymphoblastic leukemia. Pediatr Blood Cancer 2010;54:703-6.

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