Abstract:
L-Asparginase has become an integral part in treatment protocols of Acute Lymphoblastic leukemia. It has shown to improve outcome in these patients. The major detrimental side effect of using L Asparginase is thromboembolism. Among these Cortical vein thrombosis is a worrying complication. We are presenting here case series of 3 patients who has developed cortical vein thrombosis during different phases of treatment for Acute Lymphoblastic leukemia. All patients were successfully treated with low molecular heparin other supportive care and had a speedy recovery. Early recognition of this condition is very important as it is readily treatable and if not will be life threatening.

Keyword: L-Asparginase, Acute lymphoblastic leukemia, Cortical venous Thrombosis

Case 1: 14 year old boy presented with fever & lymphadenopathy of 1 month. He was diagnosed as Acute Lymphoblastic leukemia-Precursor B (high Risk due to Age). He was initiated on BFM 95 protocol. Base line coagulation parameters including PT, PTT and FDP were normal. He received 3 doses Vincristine, Daunorubicin and 3 doses of Lasparginase. 3 days post 3rd L Asparginase patient started complaining of headache & vomiting. MRI of Brain was obtained for same (Fig 1a). It was suggestive of sub acute hemorrhagic infarct in Right parieto occipital region. MR Venogram was done (Fig 1b), which showed Right transverse sinus thrombosis. Patient was started on Low molecular weight heparin (Fraxiparine) and other supportive care. His General condition improved and now on 4 months of follow up he is doing well with no residual neurological deficit.

Case 2: 18 yr old girl, presented with generalized lymphadenopathy and was diagnosed as Lymphoblastic lymphoma. Her bone marrow examination was normal. She was started on BFM 95 protocol. Base line coagulation parameters are normal. She has received 4 doses of vincristine,
Daunorubicin and L asparginase. 2 days post 4th Lasparginase patient developed severe headache. Proceeded with MRI of brain (Fig 2a). It showed lt.parietal lobe hemorrhagic infarct.MR venogram done (Fig2b) showed superior sagittal and left transverse venous sinus thrombosis.Patient was started on low molecular weight heparin & supportive care. General condition improved and now on 6 months follow up has no residual neurological deficit. Case 3 24 yr female evaluated for fever was diagnosed as Pre-T cell Acute lymphoblastic leukemia(High Risk). She was upfront CNS3 status. She was started on BFM 95 protocol.she completed 1 month of induction and intrathecal chemo therapy .Her marrow& CSF status was in remission. She then completed 2nd month of induction followed by consolidation which was uneventful.She was started on Re induction -1. Received 2 doses vincrisine,Daunoubicin and 2 doses of L asparginase. On Day4 of 2nd Lasparginase was admitted in ward with abnormal behavior and later developed an acute onset generalized tonic clonic seizures. Plain CT Scan of head was done on emergency basis which was normal. Poceeded with MRI(Fig3a),it showed B/l small hemorrhagic infarcts & Venogram (Fig3b) which showed superior sagittal &transverse sinus thrombosis.Patient was started on low molecular weight heparin& other supportive care.Her condition improved and recovered from illness without any CNS sequelae.

Discussion:
Patient with ALL are always at increased risk of thromboembolic events. The proposed mechanism include activation of coagulation system, increased tissue factor, or presence of procoagulant. Iatrogenic causes include L Asparginase & steroids. LASP has become an integral of ALL treatment protocol due to its selective action on lymphoblasts and less side effects especially myelosuppression. The main concerns are thrombo embolic episodes which are due to the imbalance between the coagulant and anticoagulant system. Up to 2% patients receiving LASP can develop sinus venous thrombosis (1). Omer et al. demonstrated low levels of antithrombin III, plasminogen and transient reduction in protein S levels in a patient with recurrent thrombosis, who received LASP(2). There are studies with prophylactic enoxaparin in LASP treated patients, but at present there is no recommendation for this(3). The treatment of cortical venous thrombosis, apart from stabilization and prevent or treat cerebral herniation, include administration of Anti coagulant (heparin) to arrest the thrombus progression. Though controversial due to the presence of coexisting hemorrhage, it has become a standard practice in the management of CVT (4). Outcome is good if detected and treated earlier. All the 3 of our patients had good response to treatment and had healthy recovery. The message is that the index of suspicion of this condition should be high. All patients may not present with classical headache& seizures. CT scan may be normal; So MRI &Venogram is warranted for confirmation. Urgent imaging & early initiation of treatment can be life saving in these patients.

Bibliography:
