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Risk Factors of Acute Pancreatitis in Pediatric Acute Lymphoblastic Leukemia Patients: A Single-Center Experience

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Background: Acute pancreatitis during chemotherapy of acute lymphoblastic leukemia (ALL) is an often fatal complication which is mainly associated with asparaginase. Despite of the improvement of supportive care during treatment of ALL, the prediction of acute pancreatitis has not been feasible. The aim of this study was to identify the risk factors of acute pancreatitis in pediatric ALL patients.

Patients and methods: This study included total 421 patients under 18 years old of age who were newly diagnosed with ALL and treated at Asan Medical Center Children's Hospital between January 2000 and December 2018. Patients in standard-risk group received a modified COG AALL0331 based treatment, and those in high-risk group received Korean multicenter high-risk ALL treatment. For national insurance coverage, native L-asparaginase was used as a first choice in all patients except patients who accepted the expanses of Pegylated-asparaginase (PEG). Patients who developed hypersensitivities to native asparaginase or PEGs, Erwinia-asparaginase was administered. Fibrinogen, triglyceride, amylase, lipase, and coagulation battery were checked before every asparaginases in all patients. The diagnosis and grading of acute pancreatitis were based on Common Terminology Criteria for Adverse Events (CTCAE) version 5.0. The cases of acute pancreatitis after relapse or allogenic hematopoietic stem cell transplantation were excluded. All the laboratory data were collected and analyzed retrospectively.

Results: The incidence of acute pancreatitis in pediatric ALL was 3.3% (14 patients) and asparaginase associated acute pancreatitis was 2.8% (12 patients). Acute pancreatitis occurred in mainly in induction chemotherapy (n=8, 67%). Two patients were developed acute pancreatitis in consolidation

chemotherapy, 1 in interim maintenance chemotherapy. Among 8 patients who developed acute pancreatitis in their induction chemotherapy, 1 patient was not associated with asparaginase. Among 14 patients, 2 patients were expired of disease progression and none of patient died of acute pancreatitis. Grade 2, 3 of acute pancreatitis patients were 6 and 8 respectively. There was no grade 5 acute pancreatitis. Eleven out of twelve patients who developed acute pancreatitis associated with asparaginase medication re-challenged asparaginase medication after experiencing acute pancreatitis. Among re-challenged patients, only 1 had second acute pancreatitis and discontinued asparaginase medication. There was no significant difference in incidence of acute pancreatitis with initial BSA, protein C, protein S, and age at diagnosis. Multivariate analysis identified prolonged activated partial thromboplastin time (aPTT) before acute pancreatitis in 1 week was significantly involved with risk factor of acute pancreatitis (p=0.013) Eight patients (67%) received a fresh frozen blood transfusion(FFP) before acute pancreatitis in a week.

Conclusions: Prolonged aPTT and FFP transfusion are particularly at risk for acute pancreatitis in pediatric ALL patients. Cautious re-challenging asparaginase medication after experiencing grade 2 and grade 3 acute pancreatitis is needed. Early diagnosis and manage asparaginase-associated acute pancreatitis will contribute patients with sufficient effect of asparaginase medication.

Disclosures

No relevant conflicts of interest to declare.

Author notes

*Asterisk with author names denotes non-ASH members.