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Multiple complications of the induction phase chemotherapy for childhood acute lymphoblastic leukemia

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ABSTRACT

Chemotherapy for childhood acute lymphoblastic leukemia (ALL) despite of high efficiency often leads to many different complications, what bring consequences like therapy failure, death, breaks in chemotherapy, elongate hospitalization. We reported case old 6-year-old girl treated with ALL, who experienced many, severe complications of chemotherapy during the induction phase of treatment.

Key words: complication, chemotherapy, acute lymphoblastic leukemia, children

INTRODUCTION

Acute lymphoblastic leukemia is the most common childhood cancer accounting for about 30% of all children malignances.[1] The 5-year overall survival rates above 80% [2]. Therapy for ALL is based on multi-drug regimen and steroids. The intensive treatment is effective and leads to high curability, but on the other hand it carries risk of many complications. About 50% children treated with ALL experience side effects of chemotherapy[3]. The main complications are: mielosupression, infections, mucositis, polineuropathy, subileus, hypersensitivity reactions, electrolytes disorders, coagulation disorders. Consequences of treatment complications include therapy failure, death, breaks in chemotherapy, elongate hospitalization and increased treatment costs. To avoid or decrease side effects supportive therapy is applied, what include anti-infectious prevention, G-CSF, anticoagulant drugs, constipation prevention, blood products, diet modifications and rehabilitation.

In the study, we present the case of girl treated with ALL, who experienced many, severe complications during induction phase of chemotherapy.

CASE

The 6-years-old girl diagnosed with pre B common positive ALL was started treatment in February 2019 according to AIEP BFM 2017 (BCR/ABL1 and KMT2A/EPS15 negative, ETV6/RUNX1 positive). During the induction phase of therapy severe complications were observed. On 29th day of this phase she presented severe headache, three episodes of seizures. Chemotherapy was stopped. The computer tomography (CT) of central nervous system (CNS) did not show any changes. Laboratory abnormalities were hyponatremia (Na – 127 mmol/l) and leukoneutropenia (leukocytes – 670/ul, neutrophils – 60/ul). Anticonvulsant drugs were applied. However, her condition deteriorated. She was transported to Intensive Care Unit for 3 days and returned back to our department. The magnetic resonance imaging (MRI) of CNS was performed and small ischemic foci were found. Next three days she developed acute pancreatitis (maximal levels of lipase: 2 102 U/l, amylase: 693U/l), hepatotoxicity (maximal levels of AST: 597U/l,

ALT 820 U/l), subileus and coagulation disorders. The child's condition was poor, she complained about sever abdominal pain. CT of abdomen showed an enlarged pancreas and necrotis foci, the X-ray (RTX) of abdomen showed fluid levels with no features of perforation. These complications were reason for interruption in chemotherapy for 4 weeks. After recovery, bone morrow puncture was performed and the hematological remission was confirmed. She continued chemotherapy without severe side effects. Currently, she completed the induction phase of therapy for ALL.

DISCUSSION

Most complications occur at the induction phase. Chemotherapy of Induction phase for ALL include: vincristine, daunorubicine, L-asparaginase, corticosteroids, 6-mercaptopurine, cytarabine, cyclophosphamid. The main side effects of L-asparaginase are: hypersensitivity reactions, acute pancreatitis, hyperlipidemia, coagulation disorders. L-asparaginase toxicity occur in 20-25% of patients. Acute pancreatitis occur in 2-18% of patients [3]. Susan L. Kearney and others analyzed 403 patients with ALL treated in 1987-2003. 28 of them (7%) presented acute pancreatitis, 18% at induction phase of chemotherapy after first dose of L-asparaginase. The peak levels of pancreas enzymes was: amylase 553u/l, lipase 1143u/l. All children with acute pancreatitis complained about abdominal or back pain, 89% of them presented vomiting and/or nausea. Corticosteroids use in ALL is connected with increased risk of hiperglicemia, electrolytes disorders, adrenal insufficiency, hypertension, obesity, infections due to immunosupression. Corticosteroids are proved to intensify L-asparaginase toxicity – coagulation disorders, hyperlipidemia, pancreatitis. Moreover, corticosteroids cause gastrenterotoxicity, what in combination with vincristine enlarge risk of presence of typhlitis and perforation of gastrointestinal tract [5, 6]. Aylin Canbolat Ayhan and others presented case of 4-years-old girl treated for ALL, who developed fever as an only symptom on 27^{th} day of induction phase, the only finding in laboratory tests were agranulocytosis and increased level of CRP. On 29^{th} day of induction phase she presented severe abdominal pain, abdominal distension and tenderness in physical examination. Plain abdominal radiograph shows subdiaphragmatic free air and perforation of gastrointestinal tract was diagnosed. The patient was operated and after 15 days, after recovery the chemotherapy was continued. [6]

Vincristine toxicity include polineuropathy, SIADH, subileus, OUN toxicity. Neurons injury is

the most common side effects of therapy with vincristine. Polineuropathy induced by vincristine occur in 40-90 % [7]. Cienkusz and others analysed 44 children with ALL treated in 2013-2014. Polineuropathy symptoms were present in 86,36%, symphatetic system disorder in 43,18%. Life-threatening intestinal paralysis occured in 33-46% children with symphatetic system disorder [7]. Marcelina Kaleta and others reported two cases of children treated for ALL, who experienced perforation of gastrointestinal tract during the induction phase (3,5-year-old boy and 15-year-old girl). Both children were immediately operated, what was reason for interruption in chemotherapy for 22 days in the first case and for 36 days in the second case [8].

The our patient presented multiple complications, which interfered the treatment. The girl experienced neurotoxicity, acute pancreatitis, hepatotoxicity, electrolytes and coagulation disordes and mielosupression. These complications were a reason for prolonged hospitalisation and one month break in chemotherapy. Close monitoring and supportive therapy applying was necessary to manage with side effects of treatment.

CONCLUSION

Chemotherapy despite of high efficiency could lead to severe, multiple complications, which cause interruption in treatment, prolonged hospitalisation and affect the outcome. The importance of frequent monitoring and supportive care should be emphasized, what allows to prevent or minimize side effects.

References:

[1] SEER Cancer Statistics Review, National Cancer Institute. Bethesda, MD.

[2] Gaynon PS, Angiolillo AL, Carroll WL, et al. Long-term results of the children's cancer group studies for childhood acute lymphoblastic leukemia 1983-2002: a Children's Oncology Group Report. Leukemia 2010;24(2):285-297.

[3] Schmielegow K, Muller K, Mogensen SS, et al. Non-infectious chemotherapy-affected acute toxicities during childhood acute lymphoblastic leukemia therapy. F1000Res 2017;6:444.

[4] Kearney SL, Dahlberg SE, Levy DE, Voss SD, Sallan SE, Silverman LB. Clinical course and outcome in children with acute lymphoblastic leukemia and asparaginase-associated pancreatitis. Pediatr Blood Cancer 2009;53:162-167.

[5] de Lima MB, Gama LA, Hauschildt AT, Dall'Agnol DJR, Corá LA, Americo MF. Gastrointestinal motility, mucosal mast cell, and intestinal histology in rats: effect of prednisone. Biomed Res Int 2017;2017:4637621.

[6] Canbolat Ayhan A, Timur C, Bocu E, Gulcin N. Spontaneous intestinal perforation: an atypical presentation of neutropenic enterocolitis – a case report. Case Rep Hematol 2014; 2014: 925078.

[7] Cienkusz M, Drabko K, Zawitkowska J, Odój T. Vincristine-induced polyneuropathy in children with acute lymphoblastic leukemia – retrospective single-center study. Pediatr Pol 2015;90(5):391-39.

[8] Kaleta M, Zawitkowska J, Kowalczyk JR, Olcha T. Perforacja jelit jako powikłanie chemioterapii ostrej białaczki limfoblastycznej u dzieci – opis dwóch przypadków. Acta Haematol Pol 2019;50(1):36-39.

[9] Millan NC, Pastrana A, Guitter MR, Zubizarreta PA, Monges MS, Felice MS. Acute and sub-acute neurological toxicity in children treated for acute lymphoblastic leukemia, Leuk Res 2018;65:86-93.

[10] Cienkusz M, Szymańska-Miller D, Zawitkowska J, Drabko K. Perforacja przewodu pokarmowego jako konsekwencja współwystępującej polineuropatii indukowanej winkrystyną u dziewczynki z ostrą białaczką limfoblastyczną - opis przypadku Ann Acad Med Siles 2016;70, supl.1:71.

[11] Belgaumi AF, Al-Bakrah M, Al-Mahr M, et al. Dexamethasone-associated toxicity during induction chemotherapy for childhood acute lymphoblastic leukemia is augmented by concurrent use of daunomycin. Cancer 2003;97(11): 2898-2903.