Contents lists available at ScienceDirect

Acta Haematologica Polonica

journal homepage: www.elsevier.com/locate/achaem

Case report/Kazuistyka

Visceral varicella-zoster virus (VZV) infection as an underestimated differential diagnosis of acute abdomen in a patient after allogeneic hematopoietic stem cell transplantation

Półpasiec trzewny u pacjenta po allogenicznym przeszczepie komórek hematopoetycznych szpiku – nieuwzględniana przyczyna w diagnostyce różnicowej ostrego brzucha

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ARTICLE INFO

Article history:
Received: 24.08.2016
Accepted: 20.02.2017
Available online: xxx

Keywords:
- Hematopoietic stem cell transplantation
- Visceral varicella-zoster virus
- Cholecystits
- Acute abdomen
- Graft-versus-host disease
- Acyclovir prophylaxis

ABSTRACT

We report a case of 18-year-old male patient who 5.5 months after allogeneic hematopoietic stem cell transplant (HSCT) developed severe abdominal pain not responding to high dose of opioids. The pain was accompanied by gradually increasing activity of liver enzymes and bilirubin concentration. The patient had a history of acute GVHD and was on steroid taper. Importantly, he was also temporarily off standard acyclovir prophylaxis. Provisional diagnosis of acute cholecystitis was made, however, cholecystectomy did not improve patient's condition. Clinical picture of severe abdominal pain without clear surgical cause, resistant to high doses of opiates with increasing activity of liver enzymes was highly suspicious of visceral varicella zoster virus (VZV) reactivation. Immediate introduction of intravenous acyclovir led to full recovery and complete resolution of abdominal pain. We conclude that reactivation of latent VZV with absent or delayed occurrence of characteristic skin vesicles may still pose a diagnostic challenge resulting in delay of the proper diagnosis and start of life saving antiviral treatment. Severe intractable pain in HSCT recipients with increasing activity of liver enzymes should evoke high

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http://dx.doi.org/10.1016/j.achaem.2017.02.001

Słowa kluczowe:
- przeszczep komórek hematopoetycznych szpiku
- półpasiec trzewny
- zapalenie pęcherzyka żółciowego
- ostry brzuch
- choroba przeszczep-przeciwko-gospodarzowi
- profilaktyka acyklowirem

index of suspicion of the possible disseminated VZV and impose start of empirical treatment with high dose acyclovir.

Introduction

Primary varicella-zoster virus (VZV) infection causes varicella (chickenpox). VZV remains latent in dorsal root ganglia after recovery from acute illness. Zoster also known as shingles results from the reactivation of dormant VZV, which in immunocompetent individuals commonly begins with classical skin manifestation localized within a dermatomal region with potential subsequent cutaneous spread. VZV reactivation might be promoted by aging, stress and prolonged, deep immunosuppression that occurs in hematopoietic stem cell transplant (HSCT) recipients [1]. Among these patients several specific factors facilitate VZV reactivation such as total body irradiation (TBI) in the pretransplant conditioning [2–5] or presence of active graft versus host disease (GVHD) especially requiring treatment with high doses of corticosteroids [3, 6–13].

The most severe and life threatening complication of VZV reactivation in HSCT recipients with high morbidity and mortality rates, is an internal organs involvement which may precede or occur without any cutaneous eruptions [2, 14, 15]. Lack of typical skin rash with blisters may delay the proper diagnosis and thus might be life threatening. Here we report a case of 18-year-old male patient, who 5.5 months after allogeneic HSCT for B-cell acute lymphoblastic leukemia developed visceral VZV reactivation without any preceding skin lesions.

Case report

An 18-year-old male after unrelated allogeneic HSCT (day +172) with late onset GVHD involving skin and liver was admitted in March 2008 to the Department of Pediatrics, Hematology and Oncology at University Medical Center in Gdansk (not a transplant center) with a sudden 1-day history of severe progressive abdominal pain. The day before admission patient underwent regular control check-up and was discharged without any remarkable symptoms or complaints. Upon admission, patient was afebrile anicteric, had normal vital signs and complained of severe crampy pain in the epigastric/right hypochondriac region with a positive Murphy sign. The pain was localized, without any radiation, periodically excruciating and no stimuli exacerbated nor alleviated the pain. On palpation there was no rigidity or rebound tenderness, vivid peristalsis was audible, stools were normal, no hepatosplenomegaly was noted. Additionally characteristic GVHD skin and mucosa lesions (stage 1) were present, however, without any skin eruptions. Laboratory tests revealed mild lymphocytopenia (0.81 G/l), with normal neutrophil (4.29 G/l) and monocytes (0.21 G/l) counts, thrombocytopenia (40 G/l) and mild anemia (hemoglobin of 114 g/l) with increased activity (200 IU/l) of gamma-glutamyl transpeptidase (GGTP; normal ranges (NR): 8–61 IU/l) and alanine aminotransferase (83 IU/l) (ALT, NR: 0–55 IU/l). Aspartate aminotransferase (AST), alkaline phosphatase (ALP), lactate dehydrogenase (LDH) activity were normal. Serum and urine amylase levels, serum bilirubin, creatinine, electrolytes, glucose and clotting screen remained within normal ranges. Mild elevation of C-reactive protein (CRP) 7.9 mg/l was noted. Early cytomegalovirus (CMV) antigen was absent; serology viral investigations for hepatitis B and C were negative. The results of directly performed abdominal ultrasound and plain film were unremarkable as well as computed tomography of the abdomen. Gastroscopy revealed mild mucosal inflammation without ulceration.

The patient was transplanted from matched unrelated donor for relapsed acute B-cell lymphoblastic leukemia. The patient VZV serostatus was positive – varicella at the age of 4. Conditioning regimen included total body irradiation combined with etoposide, anti-thymocyte globulin with standard methotrexate and cyclosporine GVHD prophylaxis. Post transplant course was complicated by mild cutaneous GVHD (stage 1, day +43) and late hepatic (stage 2, day +133) GVHD that required oral methylprednisolone (1 mg/kg/d). The patient responded to high dose of steroids – gradual decrease of bilirubin concentration and activity of hepatic enzymes was observed that allowed start of standard steroids taper. Standard prophylactic post-transplant oral acyclovir was suspended temporarily at that time (approximately 6 weeks before acute onset of abdominal symptoms) due to suspected renal and hepatic toxicities of concomitant medications.

The clinical picture was unclear therefore conservative palliative therapy with broad-spectrum antibiotics, intravenous fluids and intensive pain relief medications (opioids) was initiated. The patient did not improve. Repeated ultrasound of the abdomen on the fourth day of hospitalization showed broaden common bile duct of 7–10 mm diameter and hyperechogenic gallstone of 6–7 mm diameter at the border of the gallbladder neck and cystic duct with enhancement of intrahepatic bile ducts. Ultrasound findings were indicative for calculus cholecystitis. Therefore endoscopic retrograde cholangiopancreatography was performed and revealed mild distension of the cystic duct without visible gallstones. Subsequent abdominal ultrasound of the abdomen was performed that showed broaden common bile duct of 9 mm, gallbladder with irregular thickening of the wall up

Please cite this article in press as: Radoń-Proskura J, et al. Visceral varicella-zoster virus (VZV) infection as an underestimated differential diagnosis of acute abdomen in a patient after allogeneic hematopoietic stem cell transplantation. Acta Haematol Pol. (2017), http://dx.doi.org/10.1016/j.achaem.2017.02.001