Title:

Cryptosporidiosis, an uncommon complication after allogeneic stem-cell transplantation.

Objectives:

Differential diagnosis of diarrhea after allogeneic stem-cell transplantation (allo-SCT) includes acute Graft-versus-Host Disease (GvHD), infections, chemo- or radiotherapy toxicities, medications, and neutropenic enterocolitis. Among infections, clostridium difficile, cytomegalovirus, adenovirus, enteric pathogens are the most frequent. Parasitic infections by Cryptosporidium species are rare but life-threatening disease in immunocompromised patients. Prompt recognition and treatment are necessary.

Methods:

It seemed relevant to report the case of a cryptosporidiosis occurred after allo-SCT.

Results:

A 64-year-old-farmer was known for a marginal zone lymphoma and received several lines of treatment (including auto-SCT) due to multiple recurrences of the disease. A first relapse with transformation in diffuse large B-cell lymphoma (DLBCL) occurred and a complete metabolic response was achieved with loncastuximab teserine and ibrutinib. Unfortunately, a second relapse of DLBCL appeared but was under control after salvage chemotherapy by R-ICE and R-Methotrexate. Then, he underwent an HLA 11/12 unrelated allo-SCT after a reduced-intensity conditioning with fludarabine and melphalan. GvHD prophylaxis comprised thymoglobulin, tacrolimus and MMF.

Around D70 after allo-SCT, he presented abundant diarrhea with negative coprocultures for clostridium difficile, enteric pathogens, virus (adenovirus, rotavirus, norovirus) and parasitis. PCR CMV in blood was also negative. In the hypothesis of a GvHD, he was hospitalized for high dose corticotherapy associated to tacrolimus and topical beclomethasone. Rectoscopy with colic biopsies confirmed GvHD with absence of CMV colitis. Following the worsening of symptoms (abdominal pain and diarrhea increase) despite on one week of systemic corticotherapy, etanercept was started but without the expected efficiency. Since CT scan still showed severe colitis and coproculture remained negative, thymoglobulin was administrated. Due to the bad evolution of patient clinical condition, a review of the biopsy was performed and evidences of cryptosporidiosis were revealed.

Therefore, methylprednisolone, etanercept and thymoglobulin were stopped and tacrolimus was progressively decreased. Paromomycin and azithromycin were started. Due to diarrhea increase, nitazoxanide was administrated for 14 days. Digestive evolution was slowly favorable.

Colic biopsies were performed on D114 for diarrhea recurrence and showed GvHD grade 2 colitis but no sign of cryptosporidiosis. Immunosuppressive therapy was intensified with methylprednisolone, topical beclomethasone and everolimus in association with tacrolimus and antiparasitic treatment, leading to clinical amelioration and hospital discharge.

The patient came back in hospitalization on D148 for colic CMV reactivation. He was treated with cymevene, then valacyclovir. Paromomycin was pursued. No change was done in the immunosuppressor treatment.

At 6 months after transplant, recurrence of cryptosporidiosis occurred. Paromomycin was stopped and relayed by azithromycin and rifaximine. Immunosuppressive therapy was reduced again. Currently, diarrhea are well controled and the patient lives at home with a good perform status.

Conclusion:

Cryptosporidium infection can complicate an allo-SCT and be mistaken for GvHD at the clinical and histologic level. An early and accurate diagnosis is all the more important as the therapeutic approach of the two conditions is opposed: reduction versus intensification of immunosuppressive therapy. Cryptosporidium species have been reported to be resistant to a large number of therapeutics. Nitazoxamide, paromomycin and azithromycin are the first therapeutic options.