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Case Report (Open Access)

CYTOMEGALOVIRUS ENTERITIS POST AUTOLOGOUS STEM CELL TRANSPLANT FOR MULTIPLE MYELOMA: A CASE REPORT

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ABSTRACT
Cytomegalovirus (CMV) complications are rare after autologous stem cell transplant (auto SCT). We report here a 50-year-old multiple myeloma patient with persistent, severe diarrhea following auro-SCT. While repeated blood PCR tests for CMV were negative, an ileal biopsy confirmed tissue-invasive CMV enteritis. After two weeks of ganciclovir, a repeat biopsy was negative, and the patient recovered completely. This case highlights the need for early colonoscopy in auto-SCT when GI symptoms don't resolve as expected.

Keywords: *Multiple Myeloma, Autologous Stem Cell Transplant, Cytomegalovirus, Enteritis, Biopsy*

INTRODUCTION
Stem cell transplant (SCT) is the treatment for various benign and malignant hematological and some non-hematological conditions. Indications for auto SCT include multiple myeloma, lymphoma and benign diseases like multiple sclerosis and scleroderma (1). SCTs have some inherent complications associated with the procedure most commonly linked to conditioning chemotherapy given for SCT. The common complications of conditioning chemotherapy induced mucositis and pancytopenia which in-turn give rise to risks of infections and bleeding. Mucositis involving gastrointestinal tract gives rise to diarrhea and pain. Among infections Gram negative bacteria, various viruses, protozoal and fungal infections are common. Risk of CMV reactivation is increased post auto SCT for multiple myeloma but rarely causes significant morbidity or mortality unlike in patients undergoing allogeneic SCT (2, 3). The case reported here was unusual as the blood PCR for CMV and gut biofire were negative. However, biopsy from terminal ileum revealed CMV ileitis and patient showed dramatic response to ganciclovir.

CASE
A 50-year-old man with IgG kappa multiple myeloma in complete remission after 4 cycles of bortezomib, cyclophosphamide and dexamethasone , was admitted for an autologous SCT. He also had chronic kidney disease (creatinine clearance 27ml/min) and coronary artery disease. His pre-transplant CMV-IgG was reactive.
He received conditioning with melphalan (140 mg/m^2) on and CD34+ stem cell dose was 3.8x10^6 cells/kg. Neutrophils engrafted on day +10. Initially, he had Grade III oral mucositis and diarrhea, which was managed as per protocol.
After day +14 the mouth sores healed but the diarrhea worsened. He was having frequent small volume watery diarrhea with occasional blood in stools. He developed severe malabsorption leading to dyselectrolemia (with hypocalcemia and hypokalemia) and metabolic alkalosis. His stool for routine and microscopic examination was negative and clostridial difficile toxin A and B were absent. Blood CMV-PCR was also negative. Since his diarrhea was persistent, colonoscopy was performed which revealed normal colon but ulcers were seen in distal ileum. Biopsy from the ileal ulcers showed CMV ileitis (inclusion bodies). The CMV-DNA PCR from the ileal biopsy was positive. He was started on modified doses of intravenous ganciclovir, which slowly improved the symptoms and frequency and volume of stools decreased after 15 days of intravenous anti-CMV therapy. Later the treatment was changed to oral valganciclovir. After 15 days a repeat colonoscopy and biopsy was performed which was negative for CMV and showed healing ulcers.

DISCUSSION

There is a high prevalence of cytomegalovirus (CMV) seropositivity in developing countries (4). Hematopoietic SCT is considered as a high risk for CMV reactivation. Among all types of SCTs autologous SCT for multiple myeloma has least risk of CMV reactivation if the patient has not received multiple lines of previous chemotherapies or it is not a tandem SCT.

With effective surveillance and pre-emptive treatment, the morbidity and mortality associated with CMV reactivation has been reduced. Diarrhea is one of the most common complications following autologous SCT for myeloma and is due to drug induced mucositis affecting small and large intestine (5), other causes include infections (6). Other significant pathogens include viral agents like CMV, Norovirus, Adenovirus, and parasites such as Blastocystis sp. Antibiotic associated diarrhea also needs consideration since these patients are on multiple antibiotics. Our patient had persistent diarrhea even after resolution of oral mucositis and after stopping all antibiotics. Since the diarrhea worsened, he underwent colonoscopy which revealed the diagnosis. In all such cases where diarrhea does not resolve, colonoscopy should be considered (7). Autologous GVHD is rare but has been reported (8). Gut biopsy can help in distinguishing such cases where there is diagnostic dilemma. After adequate and complete treatment our patient responded completely, and repeat biopsy confirmed the clearance of the disease. Risk of CMV reactivation increases with age and leads to higher transplant related mortality, however, in patients without peripheral blood based PCR positivity, the suspicion of disease should be considered by adequate biopsy of the involved organ and should be treated accordingly (9).

CONCLUSION

In autologous transplant patients, melphalan induced mucositis is the most common cause of diarrhea but it usually resolves after recovery of blood counts. A negative blood test does not rule out CMV in the gut. If a patient has persistent diarrhea, a biopsy is the only way to make a diagnosis.

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