Case Report

Cutaneous graft-versus-host disease on 7th day of blood transfusion in an adult male

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Abstract

Graft-versus-host disease (GVHD) occurs when immunologically competent cells are introduced into an immunoincompetent host. The leading cause of GVHD is hematopoietic cell transplantation (HCT). Solid organ transplants, blood transfusions, and maternal-fetal transfusions also reportedly cause GVHD. We report a case of a 58-year-old male who presented with large erythematous to violaceous papules and plaques scattered on trunk and limbs, on the 7th day of whole blood transfusion. There was no evidence of systemic involvement. Diagnosis was confirmed on histopathological findings of skin lesion. Patient was treated with local steroids with resolution of lesions.

Key words

Graft-versus-host disease

Introduction

Graft-versus-host-disease (GVHD) refers to both the immunologic insult and the consequences to the organism. The leading cause of GVHD is hematopoietic cell transplantation (HCT), both allogenic (between 2 individuals) and autologous (from the same individual). Solid organ transplants, blood transfusions, and maternal-fetal transfusions also reportedly cause GVHD. Acute GVHD occurs within the first 100 days of transplantation and consists of the triad of dermatitis, enteritis, and hepatitis. Chronic GVHD develops after 100 days and consists of an autoimmune syndrome directed toward multiple organs. The skin often is the earliest organ affected in GVHD. Acute GVHD usually starts as scattered erythematous macules and papules that involve a greater percentage of total body surface area as the severity of GVHD increases. Erythroderma and bullae may occur in the most severe form of acute GVHD. Chronic GVHD may occur either as a late phase of acute GVHD or as a distinct entity. The skin is the primary organ involved in chronic GVHD, which can manifest as a lichen planus-like eruption or as scleroderma. GVHD remains the primary cause of morbidity and mortality in hematopoietic cell recipients. The best treatment for GVHD is prevention. For skin GVHD of mild to moderate severity, observation or a trial of topical corticosteroids (e.g. triamcinolone 0.1%) may be used. Systemic treatment is warranted in patients with severe to life threatening disease.

Case report

An 80-year-old male presented with seven days history of high grade fever and erythematous rash on left side of abdomen and right thigh. There was no associated
complaint of diarrhea, vomiting, anorexia, abdominal pain or any other complaint pertaining to any other system. On examination patient was ill looking with pulse rate of 102/min, blood pressure of 110/80mm of Hg, respiratory rate of 16/min and temperature of 101ºF. Patient was neither jaundiced nor anemic on clinical examination. There was no other positive finding on general physical examination. On dermatological examination, patient had maculopapular rash on erythematous base arranged in groups, on left side of abdomen and right thigh (Figure 1). There were few bullous lesions also. They were non tender and non itchy. Initially patient had applied dressing on the rash that was removed later.

On systemic examination, there was no hepatomegaly or any other visceromegaly. On investigation, blood complete picture showed hemoglobin of 12.5 g/dl with normal cell counts. Serum sodium was 135mEq/l and potassium was 3.9mEq/l. Liver function tests were normal with total bilirubin of 0.3 mg/dl. Ultrasonography showed normal liver texture. Skin biopsy of lesion was done for histopathological confirmation of diagnosis, which showed basal cell vacuolization, acantholysis in the lower layers of epidermis with subepidermal cleft formation. According to the histological grading, patient was put in grade III. Patient was treated with tapering dose of oral steroids starting with the dose of 60mg/day. Patient responded well and became afebrile along with healing of skin lesions in the form of disappearance of erythema and crusting of lesions (Figure 2) within 2 weeks of treatment.

Discussion

GVHD that develops between 1 week and 3 months after transplantation is termed acute, while that appearing after 3 months is termed chronic.1 The severity of reaction, clinically and histologically, varies from mild to severe and provides basis for grading from 1-4. Grades 2-4 carry a mortality exceeding 75%. Our case was in grade III. Early diagnosis of GVHD can be difficult, as drug reactions,2,3 viral infections and cutaneous reactions to radiotherapy may have clinical and histological similarities. GVHD occurs when immunologically competent cells are introduced into an immunoincompetent host. The pathophysiology of GVHD involves the
recognition of epithelial target tissues as being foreign by immunocompetent cells, with subsequent induction of an inflammatory response and eventual apoptotic death of the target tissue. This apoptosis occurs regardless of whether the immunoreactive T cells are derived from a non-identical donor or from the recipient. Dermatologically, the reaction against the host's keratinocytes is believed to directly influence the phenotype, which ranges from mild erythematosus macules to full-blown epidermal necrosis.

Acute GVHD may initially appear as a pruritic or painful rash (median onset, day 19 post-transplantation; range, 5-47 day). A hyperacute form of GVHD has been described as including fever, generalized erythroderma, and desquamation developing 7-14 days after transplantation. After the skin, the next most frequently involved target of GVHD is the liver, where the disease causes asymptomatic elevation of bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase levels similar to those observed with cholestatic jaundice. Pruritus ensues, with hyperbilirubinemia. Hepatic coma is rare. Acute GVHD may involve the distal small bowel and colon, resulting in diarrhea, intestinal bleeding, cramping abdominal pain, and ileus.

Patients with acute GVHD are at risk for sepsis, electrolyte disturbances secondary to diarrhea, elevated liver enzyme levels, bilirubinemia, and hepatorenal syndrome. Acute and chronic GVHD appear to inhibit recurrence of malignancies, suggesting a graft-versus-leukemia effect in patients who receive HCT as treatment for a hematopoietic malignancy.

Acute GVHD is a primary or contributory cause of death in 15-40% of patients who develop GVHD. Mortality resulting from acute GVHD is directly related to severity; the more severe and extensive the involvement, the greater the risk of mortality. Overwhelming sepsis is the primary cause of death in patients with acute GVHD. In our case, the patient had limited area of skin involved in disease process, also patient presented earlier, without any complications secondary to systemic involvement, in the form of sepsis, liver function impairment and electrolyte imbalances secondary to diarrhea due to gut involvement. On examination, the skin lesions are red to violet and typically first appear on the palms of the hands, soles of the feet, cheeks, neck, ears, and upper trunk. They can progress to involve the whole body. In severe cases, bullae may be observed, and vesicles may form. In the liver, hyperbilirubinemia can manifest as jaundice, cause pruritus, and leads to excoriations. Portal hypertension, cirrhosis, and death from hepatic failure are rare. Ocular findings include hemorrhagic conjunctivitis, pseudomembrane formation, and lagophthalmos. Bronchiolitis obliterans in lungs causes prolonged expiratory breathing phase (wheezes). In gastrointestinal involvement diffuse abdominal tenderness with hyperactive bowel sounds may accompany secretory diarrhea. In severe ileus, the abdomen is silent and appears distended.

Laboratory workup of patient with acute GVHD includes blood complete picture,
liver function tests; in which elevation of the alkaline phosphatase is one of the early signs of liver involvement by GVHD. Hypoalbuminemia is typically due to GVHD-associated intestinal protein leak and a negative nitrogen balance. Hepatic and Doppler sonography can be used to distinguish GVHD from other causes of jaundice or cholestatic liver function abnormalities, such as cholecystitis and veno-occlusive disease of the liver. Serum electrolytes and chemistries (e.g. potassium, magnesium, and bicarbonate levels) may be altered. Findings on skin punch biopsy help establish the diagnosis of GVHD when the patient's clinical features are consistent with the syndrome. For acute GVHD, the cutaneous histological changes have been graded for severity. Grade I: Basal cell vacuolation with or without mononuclear cell infiltration; Grade II: Solitary epidermal cell necrosis, surrounded by mononuclear cells; Grade III: Regional epidermal cell necrosis with bullae; Grade IV: Toxic epidermal necrolysis.

The best treatment for GVHD is prevention. Prophylaxis for GVHD usually consists of methotrexate with or without prednisone, antithymocyte globulin, cyclosporine, cyclophosphamide, or tacrolimus. Marrow T-cell depletion can substantially reduce the incidence and severity of acute GVHD, but these results are offset by an increase in graft failure and recurrent leukemia. Once the diagnosis of GVHD is established, treatment with high dose steroids or cyclosporine is of value symptomatically, and antilymphocyte globulin may be of additional benefit, particularly if combined with tacrolimus. Most recently, infliximab, the monoclonal anti-TNF therapy, has been used successfully. In our case we treated the patient with tapering dose of oral prednisolone, in the dose of 60mg per day at start, to which patient responded well and recovered completely. Acute GVHD is the primary or major contributory cause of death in 15-40% of patients who develop GVHD. The primary cause of death in GVHD is overwhelming sepsis.

Conclusion

The conclusion drawn from above case and discussion is that GVHD is a life threatening condition. Early diagnosis and early treatment of patient can be life saving. As far as the diagnosis of patient is concerned, index of suspicion should be high to diagnose rare diseases and of course importance of good history taking cannot be ignored.

References


Authors Declaration

Authors are requested to send a letter of undertaking signed by all authors along with the submitted manuscript that:

The material or similar material has not been and will not be submitted to or published in any other publication before its appearance in the *Journal of Pakistan Association of Dermatologists.*