

A case report of acute cutaneous graft versus host disease

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ABSTRACT:

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We reported a case with acute graft versus host disease manifested as toxic epidermal necrolysis-like lesion after allogeneic bone marrow transplantation. The patient had progressive multiple organs involvement and eventually expired from severe pneumonia and acute renal failure.

Key words: Acute cutaneous graft versus host disease, toxic epidermal necrolysis-like lesion

บทคัดย่อ:

พรศรี พงศ์พลไพรวณ ทิมาพร ศุภภัทรานนท์. รายงานผู้ป่วย ACUTE CUTANEOUS GRAFT VERSUS HOST DISEASE วารสารโรคผิวหนัง 2546; 19: 191-197.

สาขาตจวิทยา กองอายุรกรรม โรงพยาบาลพระมงกุฎเกล้า

รายงานผู้ป่วยสัณฐานภาพที่แบบเฉียบพลัน (acute graft versus host disease) ซึ่งมีอาการแสดงทางผิวหนังคล้าย toxic epidermal necrolysis หลังจากการปลูกถ่ายไขกระดูก รวมทั้งมีอาการแสดงทางระบบอื่นร่วมด้วยและเสียชีวิตในภายหลังจากภาวะปอดอักเสบอย่างรุนแรงและไตวายเฉียบพลัน.

คำสำคัญ: ผื่นผิวหนังในภาวะสัณฐานภาพที่เฉียบพลัน, ทอกซิกอพิเดอมอลเนโครไลซิส.

Introduction

Graft-versus-host disease (GVHD) after allogeneic bone marrow transplantation (BMT) is an immunological process in which activated donor lymphocytes mount an attack on the recipient's tissues. This process involves secretion of cytokines and recruitment of additional inflammatory cells. The frequency of developing acute GVHD varies from 20-80% of the graft recipients. The skin is often the initial organ to manifest. In addition, the liver and gastrointestinal system are often involved. Acute GVHD can be graded according to its clinical severity. Outcome analyses have established the prognostic value of this staging system in that the higher the overall clinical grade, the higher the mortality rate. Toxic epidermal necrolysis (TEN) may occur after BMT with mortality rate as high as 80-100% in comparison with 30% in the classic

TEN¹. It is very difficult to distinguish the causes of TEN-like lesion after BMT.

A case report

A 30-year-old man who underwent allogeneic stem cell transplantation (with cyclosporine and methotrexate regimen for prophylaxis graft versus host disease) for his underlying acute non-lymphoblastic leukemia M4 (ANLL M4) presented with severe loose watery diarrhea and low-graded fever 31 days after the transplantation. He was admitted to the hospital 4 days later. The patient had no history of drug allergy. Physical examination revealed mildly pale conjunctivae. Other systems including skin were normal. Laboratory examinations showed anemia (Hb 28.7%) with leukocytosis (Wbc 13600), numerous white blood cells and red blood cells in urine and stool. He was initially treated with intravenous (IV) ciprofloxacin

and oral metronidazole while septic workup was being performed.

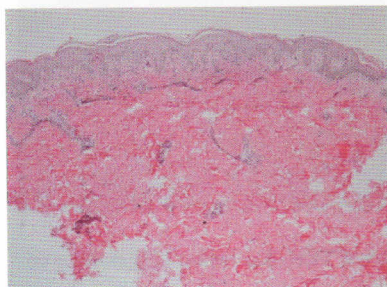


Figure 1 Sparse superficial perivascular infiltration

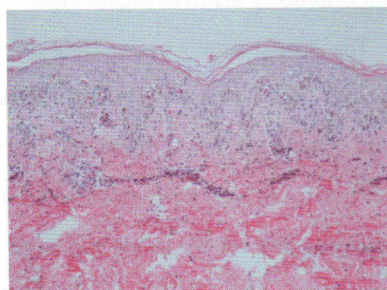


Figure 2 Basal cell vacuolization with dyskeratotic epidermal cells

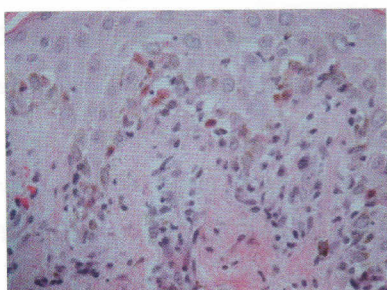


Figure 3 "Satellite cell necrosis"

One day later, he developed generalized erythematous maculopapular rash. Skin biopsy showed "satellite cell necrosis", vacuolar interface change of the basal epidermis and sparse superficial

perivascular infiltration composed predominantly of lymphocytes (Figure 1,2,3). Four days after that, he developed generalized vesiculo-bullous lesions (Figure 4,5,6) together with conjunctival and oral mucosa erosions. He also had bloody diarrhea. Septic workup revealed no causative organisms. He was diagnosed as acute cutaneous GVHD and was treated with IV dexamethasone. Antibiotic was changed to IV maxipime. His skin lesions progressively evolved into TEN-like lesions, which involved nearly total of the body surface area including conjunctivae, oral mucosae and genital area. Repeated laboratory examination showed pancytopenia and worsening of liver and renal functions. His clinical symptoms rapidly deteriorated and he eventually expired from severe hospital acquired pneumonia and acute renal failure in the next 30 days after the onset of TEN-like lesions.



Figure 4 Generalized vesiculo-bullous eruption

Discussion

Graft-versus-host disease occurs once these 3 following conditions are met i.e., (1) the organ grafted contains immunologically competent cells,

(2) the tissue antigens of the host differs from those of the donors and (3) the recipient is immunocompromised². The disease is classified into 2 stages i.e., acute stage which occurs during the first 3 months following BMT and chronic stage which develop thereafter³. The incidence of acute GVHD varies between 20-80% of graft recipients³. Several studies have identified the followings as factors associated with an increased risk of acute GVHD i.e., old age of recipients, HLA-mismatched, sex-mismatched with the donor being female (especially those once received transfusions or who are multigravida) and a suboptimal dose of immunosuppressive drugs⁴.



Figure 5 TEN-like lesion on conjunctivae, oral



Figure 6 TEN-like lesion on genital area

Acute GVHD is characterized by selective epithelial inflammation that include the skin (which is the most commonly involved organ) digestive tract and liver. The disease usually begins 10-30 days after grafting with skin pain or itching. Suddenly, generalized maculopapular exanthem develops, which often starts at acral parts as characterized by an erythematous rash on the palms and soles and a violaceous discoloration of the ears. Perifollicular papular lesions may be seen and are considered characteristic findings for the diagnosis of the acute GVHD. Extracutaneous symptoms of acute GVHD may involve the gastrointestinal tract and/or the liver. These symptoms are usually associated with concomitant cutaneous signs, although they may sometimes be isolated⁴. The clinical severity of acute GVHD can be graded as summarized in table 1 and 2⁶.

Table 1 Clinical Staging of Acute Graft-vs-Host Disease

Stage	Skin	Liver	Gut
1	Maculopapular rash <25% BSA*	Bilirubin, 35-50 $\mu\text{mol/L}$ (2.0-2.9 mg/dL)	Diarrhea 0.5-1 L/d or persistent nausea ($\pm$ vomiting)
2	Maculopapular rash 25%-50% BSA	Bilirubin, 51-100 $\mu\text{mol/L}$ (3.0-5.8 mg/dL)	Diarrhea 1-1.5 L/d
3	Maculopapular rash > 50% BSA	Bilirubin, 101-255 $\mu\text{mol/L}$ (5.9-14.9 mg/dL)	Diarrhea >1.5 L/d
4	Generalized erythema with bullous formation and/or desquamation	Bilirubin, >255 $\mu\text{mol/L}$ (>14.9 mg/dL)	Severe abdominal pain or ileus

Table 2 Overall Clinical Grading of Acute Graft-vs-Host Disease

Grade	Skin Stage	Liver Stage	Gut Stage
I (Mild)	1 to 2	0	0
II (Moderate)	3* or	1 or	1
III (Severe)	0 to 3, and	2 to 3 or	2 to 4
IV (Life threatening)	4 or	4, or	0 to 4 plus 4 of skin or liver

* Skin stage 3 alone is considered overall grade II

Table 3 Histologic Grading Scheme for the Acute Cutaneous GVHD

GRADE	Descripton
0	Normal skin or changes not referable to GVHD
1	Basal vacuolization of the dermal-epidermal junction
2	Basal vacuolization, necrotic epidermal cells, lymphocytes in the dermis and/or epidermis
3	Subepidermal cleft formation plus grade 2 changes
4	Separation of epidermis from dermis plus grade 2 changes

Source: Adapted from Lerner KG et al. Histopathology of graft-versus-host reaction (GVHR) in human recipients of marrow from HLA-matched sibling donors Transplantation 18: 367, 1974.

Histopathologic findings are characteristically referred to as satellite cell necrosis⁵. Other epithelial changes are focal or diffuse vacuolar degeneration of basal cells⁶. The lymphocytic subtypes responsible for allogeneic acute GVHD are unknown⁷. There was a report of CD8+ lymphocytes in the blister fluid of severe acute GVHD⁸. Histological findings are classified into 4 grades as shown in Table 3.

Proper preparation of patients before transplantation is essential. Cyclosporine and methotrexate should be used as prophylaxis, which can reduce the incidence of acute GVHD by 15-40%⁴. Unfortunately, the medication does not prevent chronic GVHD. Once the disease develops, the first line of treatment is high dose corticosteroids (1-3 mg/kg/day) and symptomatic treatment with adequate hydration and antihistamines. Cyclosporine, cyclophosphamide or antithymocyte globulins are given as second-line treatments. Beneficial therapeutic response with extracorporeal photochemotherapy (ECP) has been reported⁹.

Mortality rate of grade IV GVHD is as high as 80-100% compared with only 30% in the classic TEN⁴. Factors of poorer prognosis are the increase risk of infection and the severe extracutaneous involvement.

In our case, the most likely cause of TEN-like lesions was acute graft versus host disease. The differential diagnosis included cutaneous reaction to chemotherapy or radiation therapy, adverse drug

reaction and some viral infection. In the absence of extracutaneous involvement the diagnosis of chronic GVHD can be very difficult because neither skin nor histopathologic findings were pathognomonic.

In conclusion, we reported a case of acute GVHD presented with GI symptoms before skin manifestations. His skin lesion was maculopapular rash initially then progressed to extensive TEN-like lesions. The patient died of pneumonia and acute renal failure.

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negative open application test: a case

report

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ABSTRACT:

KANEECHORN NA AYUTHAYA P, TANGTATSAMPAN C. FORMALDEHYDE ALLERGY WITH INITIALLY NEGATIVE OPEN APPLICATION TEST: A CASE REPORT. *THAI J DERMATOL* 2003; 19: 198-202.

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A 33-year-old housewife was referred with a 3-year history of recurrent dermatitis on the extremities and buttocks. The patch test revealed formaldehyde hypersensitivity. A 7-day repeated open application test (ROAT) to her lotion which contained DMDM hydantoin (formaldehyde donor) was negative in the antiepileptic foam. When she applied it on eczematous skin, however, she felt an itching and stinging sensation. But when she applied a new lotion (no formaldehyde or formaldehyde donor) on eczematous skin it felt normal. Dermatologists often recommend moisturizers on eczematous skin. We usually ask patients to perform ROAT on normal skin only. We may need to recommend them do it on eczematous skin as well.

Key words: formaldehyde, DMDM hydantoin, repeated open application test, test, allergic contact dermatitis

*Adapted from Tangtatsampan C. Allergic contact dermatitis from formaldehyde with initially negative open application test.

Contact Dermatitis 2003; 48(3):171-2