Case 22

A 43-year-old Thai male from Bangkok

Chief complaint :

Pigmentary change of skin for 2 years

Present history :

The patient was diagnosed with chronic myeloid leukemia and received systemic chemotherapy 4 years ago. 2 years later; he was successfully treated with sibling-derived, fully HLA-matched allogeneic stem cell transplantation. 20 days preceeding transplantation, he developed generalized erythematous maculopapular rash, compatible with acute graft-versus-host disease (GVHD), both clinically and histologically. Systemic, high-dose corticosteroid and cyclosporine A was commenced. His skin lesion latter resolved with residual diffuse hyperpigmentation. In addition, he also had chronic renal insufficiency as a consequence of acute GVHD.

Thereafter, without seeking help from dermatologist, he noticed that his skin gradually developed asymptomatic, hyper & hypopigmentation, accompanying with focal areas of white scalp and facial hair. During follow-up period in Hematology clinic, he developed concurrent cholestatic jaundice.

A year ago, he came to Dermatology clinic due to painful mouth.

He denied using any topical medications or products.

Past history :

No other underlying disease

Family history :

No family history of vitiligo

Physical examination :

Vital signs: normal

General appearance: sthenic build, not pale, no icteric sclera

Skin: diffuse, irregularly hypo- & hyperpigmented macules and patches, distributed mainly at head, neck, trunk, and few small lesions of hypo- to depigmented patches with follicular pigmentation at dorsum of acral skin. (Fig. 22.1)

Hair: white hairs randomly distributed in area of scalp, beard and mustache

- Oral mucosa: whitish, lichenoid and erythematous reticulated plaques (Fig. 22.2)

- Eyes: (Ophthalmologic examination) dry eyes
- CVS and Respiratory system: normal
- Abdomen: liver and spleen- not palpable
- Lymph node: not palpable

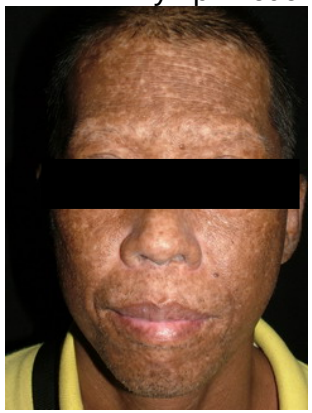

Fig. 22.1

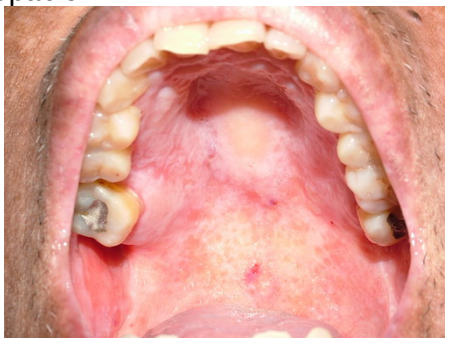

Fig. 22.2

Investigations :

CBC: Hct 32%, Hb 10.7 mg/dl, WBC 1990/mm^3, N 34%, L 50%, M 10%, E 5%, B 1%, Plt. 179,000/mm^3

LFT: ALP 282 U/L, GGT 732 U/L, AST 58 U/L, ALT 125 U/L, TB 9.2 mg/dL, DB 3.0 mg/dL, ALB 40.3 mg/dL, TP 70.3 mg/dL, Chol 219 mg/dL
BUN 25 mg/dL, Cr 1.4 mg/dL

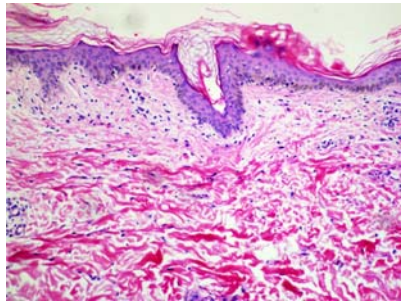
Fig 22.3

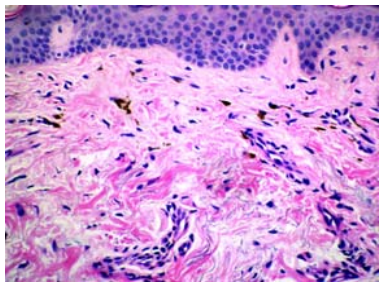
Fig 22.4

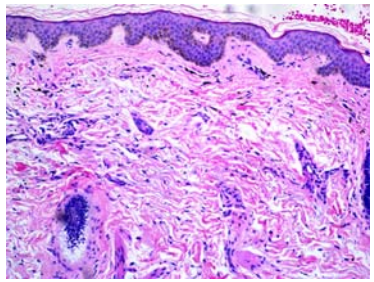
Fig 22.5

Histopathology :

1. (S07-5543) (Fig. 22.3 H&E)
   - Sparse superficial perivascular infiltrate of lymphocytes and some melanophages in the upper dermis
   - Vacuolar alteration with occasional necrosis of basal layer
2. (s08-11354 A) (Fig. 22.4 H&E from hypopigmented lesion)
   - Superficial infiltrate of mostly melanophages in the papillary dermis
   - nearly to complete absence of melanin pigment in basal layer of epidermis
3. (S08-11354 B) (Fig. 22.4 H&E from hyperpigmented lesion)
   - Superficial infiltrate of mostly melanophages in the papillary dermis
   - focal increase of melanin pigment in basal layer of epidermis

Diagnosis :

Leucomelanoderma & leucotrichia following acute cutaneous graft-versus-host disease
Chronic graft-versus-host disease (oral, lichenoid, liver, eye)

Presenter : Panunee Ruangchainikom
Consultants : Kumutnart Chanprapaph
Suthep Jirasuthus
Treatment : Prednisolone and cyclosporine

Discussion :

Graft-versus-host disease (GVHD) is one of the major complications after hematopoietic stem cell transplantation, and the skin is considered the most common and earliest organ involvement[1]. Previously, GVHD is classified as acute and chronic entities with separate molecular and pathophysiological mechanisms, but both can be overlapped. Though the pathogenesis is still unclear, there are many evidences suggesting that acute GVHD occurs as a subsequent of allostimulation of donor lymphocytes by transplantation antigens, targeting host cells, via Th1 cytotoxic T cell-mediated mechanism[2]. While chronic GVHD is thought to be primarily Th2-type, immune mediated disease[1].

Acute GVHD, cutaneous involvement is most commonly characterized by erythematous maculopapular eruption, usually resolves with desquamation and postinflammatory hyperpigmentation[3]. Whereas chronic GVHD classically divided to lichenoid and

sclerodermoid form, can have overlapping symptoms[1]. Mucous membrane involvement, e.g. lichenoid change of oral mucosa, dryness of conjunctivae, occurs more commonly in chronic form of disease[2].

Leucoderma, usually patchy in distribution, following stem cell transplantation may not be rare and can be caused by different pathogenic processes[4], including transfer of vitiligo from donor, drug-induced, and as a distinctive GVHD-associated feature[5]. Few case reports of leucoderma and leucotrichia following GVHD revealed decreased or absence of DOPA stain, indicating loss of melanocyte, and in addition, patients' serum demonstrated elevated cytotoxic activity against melanocyte cell lines[6].

Our patient encountered acute GVHD, as maculopapular eruption, and chronic lichenoid change of oral mucosa. He subsequently developed unusual pigmentary change, irregular hypo- and hyperpigmentation, so-called leucomelanoderma and leucotrichia. This distinctive pigmentary change has rarely been reported in previous literatures. Histopathology from hyperpigmented area revealed increase in basal melanin pigment compared to normal skin, while hypopigmented lesion showed markedly decrease in basal pigment.

From one report of leucomelanoderma secondary to acute GVHD, clinically similar to our patient, revealed strong immunoreactivity of antibody against TNF-alpha in hyperpigmented lesion compared to normal skin and weakly positive staining in hypopigmented lesion[7]. On the other hand, TNF-alpha is known as paracrine inhibitor of melanocyte proliferation and melanogenesis in vitro and is highly expressed in vitiliginous lesion[8]. The investigator proposed the possibility of bifunctional effects of on melanocyte, one is to stimulate melanogenesis, and the other is to cause melanocyte apoptosis[6]. However, the pathogenesis of pigmentary change in GVHD is still inconclusive, further case studies and investigations should be undertaken.

Reference

1. Hausermann P, Walter RB, Halter J, et al. Cutaneous Graft-versus-host Disease: A Guide for the Dermatologist. Dermatology 2008; 216: 287-304
2. Ferrara JLM, Levine JE, Reddy P, Holler E. Graft-versus-host disease. Lancet 2009; 373: 1550–61.
3. Sharp MT, Horn TD. Graft-Versus-Host Disease. Fitzpatrick's Dermatology In General Medicine, vol.1, 6th edition, New York, McGraw-Hill 2008: 258-267.
4. William JS, Mufti GJ, Du Vivier AWP, et al. Leucoderma and leucotrichia in association with chronic cutaneous graft-versus-host disease. Br J Dermatol 2008; 158: 172-4.
5. Jacobsohn DA, Ruble K, Moresi JM, Vogelsang GB. Rapid-onset leucoderma associated with graft-versus-host disease. Bone Marrow Transplant 2002; 30: 705–6.
6. Nagler A, Goldenhersh MA, Levi-Schaffer F, et al. Total leucoderma: a rare manifestation of cutaneous chronic graft-versus-host disease. Br J Dermatol 1996: 134: 780-3.
7. Kang HY, Kang WH. Leukomelanoderma following acute cutaneous graft-versus-host disease. Eur J Dermatol 2004; 14: 146–9.
8. Kondo S. The role of keratinocyte-derived cytokines in the epidermis and their possible responses to UVA irradiation. J Invest Dermatol 1999; 4: 177-83.