Author Contributions: Drs C. Lim and S.-L. Lim contributed equally to this study. Study concept and design: C. Lim and S.-L. Lim. Acquisition of data: C. Lim and S.-L. Lim. Analysis and interpretation of data: C. Lim and S.-L. Lim. Drafting of the manuscript: C. Lim and S.-L. Lim. Critical revision of the manuscript for important intellectual content: C. Lim and S.-L. Lim. Administrative, technical, and material support: C. Lim and S.-L. Lim.

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Additional Contributions: Kah-Beng Lim, MRCP(UK), who provided the new contrast stain used in this study, is the father of the investigators. He collected and coded the specimens and provided advice on the study design but was not involved in its evaluation. Yazhong Deng, MD, MBA, Glenecles Clinical Research Center, helped with statistical analysis.


The Isomorphic Response in Morphealike Chronic Graft-vs-Host Disease

The isomorphic response of Koebner, also known as the Koebner phenomenon, is a well-recognized dermatologic manifestation first described in psoriasis. The isomorphic response occurs when a dermatologic disease develops at a site of normally appearing skin that is injured in some manner.1

Chronic graft-vs-host disease (cGvHD) is a multisystem disorder that commonly affects the skin and may present with overt manifestations. Sclerotic GvHD features are categorized as lichen sclerosus–like, morphealike, or sclerosis involving the subcutaneous tissue and fascia.2 Morphealike lesions of cGvHD are characterized by localized dyspigmented indurated plaques of skin thickening.

Methods. A retrospective analysis was performed of 110 consecutive patients with a diagnosis of cGvHD of any type of transplant; VV, vulvovaginal; WB, waistband area.

Table. Characteristics of Patients With Morphealike cGvHD Exhibiting an Isomorphic Response

<table>
<thead>
<tr>
<th>Patient</th>
<th>Primary Diagnosis</th>
<th>Type of Allologenic Transplant</th>
<th>Type of Cutaneous cGvHD</th>
<th>Current cGvHD Treatment</th>
<th>Biopsy at Site of Isomorphic Lesion</th>
<th>Location of Isomorphic Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>M/57</td>
<td>CLL</td>
<td>NM-related PBST</td>
<td>D, S, and F</td>
<td>MMF, 1500 mg twice daily prednisone, 25 mg every other day</td>
<td>No</td>
<td>WB</td>
</tr>
<tr>
<td>M/56</td>
<td>MM</td>
<td>NM-related PBST</td>
<td>D, S, and F</td>
<td>None</td>
<td>Yes</td>
<td>WB</td>
</tr>
<tr>
<td>F/52</td>
<td>MM</td>
<td>NM-related PBST</td>
<td>E and D</td>
<td>Clobetasol ointment, 0.05%</td>
<td>No</td>
<td>BB</td>
</tr>
<tr>
<td>F/39</td>
<td>NHL</td>
<td>NM-related PBST</td>
<td>E, D, S, and F</td>
<td>ECP; hydroxychloroquine, 600 mg/d; prednisone, 35 mg every other day; tacrolimus, 1 mg every morning and 0.5 mg every evening</td>
<td>No</td>
<td>WB</td>
</tr>
<tr>
<td>F/20</td>
<td>Precursor B-cell ALL</td>
<td>Myelo-related BMT</td>
<td>D and S</td>
<td>MMF, 1500 mg every 12 h; prednisone, 100 mg/d</td>
<td>No</td>
<td>BB</td>
</tr>
<tr>
<td>M/57</td>
<td>MDS</td>
<td>Myelo-related PBST</td>
<td>E, D, S, and F</td>
<td>ECP; MMF, 1g every 12 h; prednisone, 20 mg every other day; tacrolimus, 4 mg every 12 h</td>
<td>No</td>
<td>WB</td>
</tr>
<tr>
<td>F/33</td>
<td>MM</td>
<td>Myelo-related PBST</td>
<td>E and D</td>
<td>Prednisone, 50 mg/d and 40 mg/d on alternate days</td>
<td>Yes</td>
<td>WB</td>
</tr>
<tr>
<td>M/36</td>
<td>CML</td>
<td>Myelo-related PBST</td>
<td>E, D, S, and F</td>
<td>MMF, 500 mg twice daily; tacrolimus, 2 mg twice daily</td>
<td>Yes</td>
<td>WB</td>
</tr>
<tr>
<td>M/40</td>
<td>Precursor B-cell ALL</td>
<td>Myelo-unrelated BMT</td>
<td>E, D, S, and F</td>
<td>Prednisone, 10 mg/d; tacrolimus, 0.5 mg/d</td>
<td>Yes</td>
<td>WB</td>
</tr>
<tr>
<td>F/46</td>
<td>NHL</td>
<td>Myelo-related PBST</td>
<td>E, D, S, and F</td>
<td>Prednisone, 60 mg/d and 10 mg/d on alternate days; sirolimus, 1 mg/d; tacrolimus, 4 mg/d</td>
<td>Yes</td>
<td>BB</td>
</tr>
<tr>
<td>F/49</td>
<td>NHL</td>
<td>Myelo-related PBST</td>
<td>E, D, S, and F</td>
<td>None</td>
<td>Yes</td>
<td>WB</td>
</tr>
</tbody>
</table>

Abbreviations: ALL, acute lymphoblastic leukemia; BB, brassiere-band area; BMT, bone marrow transplant; cGvHD, chronic graft-vs-host disease; CLL, chronic lymphocytic leukemia; CML, chronic myelogenous leukemia; ECP, extracorporeal photopheresis; GI, gastrointestinal tract; MDS, myelodysplastic syndrome; MM, multiple myeloma; MMF, mycophenolate mofetil; Myelo, myeloablative; NHL, non-Hodgkin lymphoma; NM, nonmyeloablative; PBST, peripheral blood stem cell transplant; VV, vulvovaginal; WB, waistband area.

aClassifications of cutaneous cGvHD: E, erythematous-type cGvHD; D, morphealike sclerosis; F, fasciitis; and S, subcutaneous sclerosis.
bT-cell depleted Myelo-unrelated BMT.
cT-cell replete Myelo-unrelated BMT (second transplantation from the same donor).
organ system evaluated in a cross-sectional cGvHD study at the National Institutes of Health (NIH).

**Results.** Eighty-one patients had evidence of cutaneous cGvHD, and 58 of these patients (72%) exhibited evidence of cutaneous sclerosis as defined by the NIH cGvHD consensus criteria.

Eleven of 58 patients with cGvHD-associated sclerosis exhibited localized morphealike lesions involving the lower abdomen (the waistband area), often in a striking linear distribution (19%) (Table and Figure, A). Lesional skin biopsies were performed in 6 patients, and all findings were consistent with sclerotic cGvHD. Six of 11 patients with waistband involvement were women, and 3 of these 6 exhibited similar morphealike lesions in the inframammary/lateral torso region (the brassiere-band area) (Figure, B).

**Comment.** Chronic graft-vs-host disease is an incompletely understood multisystem disorder with features of both alloimmunity and autoimmunity. We propose that the combination of irritation, friction, and pressure applied chronically to the waistband and brassiere-band areas of the torso is responsible for localization of cGvHD at these sites, consistent with an isomorphic response.

The mechanism by which relatively minor external trauma triggers the complex immunologic cascade that results in skin fibrosis is unclear. Interestingly, morphea and lichen sclerosus, 2 disorders that resemble cGvHD, are also associated with an isomorphic response, suggesting a common pathogenesis. Morphea-like cGvHD is characterized histologically by prominent dermal sclerosis, but apoptotic keratinocytes in the overlying epidermis suggestive of typical cGvHD may also be present. Local infiltration of T cells is thought to initiate epithelial damage and propagate tissue injury through recruitment of natural killer cells, macrophages, and mast cells. Transforming growth factor β and platelet-derived growth factor (PDGF) have been implicated in the development of skin fibrosis in cGvHD. Recently, activating antibodies targeting the PDGF receptor were reported in a group of patients with extensive cGvHD, suggesting that targeted inhibition of PDGF receptor signaling with therapies such as imatinib may inhibit the fibrotic process associated with sclerotic cGvHD.

Careful evaluation of the “high-risk” sites in the waistband area (and brassiere-band in women) may allow for early diagnosis of sclerotic cGvHD and appropriate intervention. Because it is not possible to predict which patients will develop sclerotic cGvHD, all patients at risk for cGvHD may wish to avoid excessively tight or binding garments that may irritate or apply significant pressure to the skin.

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**Study supervision:** Turner and Cowen.

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Comparison of Infantile Hemangiomas in Preterm and Term Infants: A Prospective Study

Infantile hemangiomas (IH) occur more frequently in premature infants.1,2 To our knowledge, studies comparing the clinical features of IH in term and preterm infants have not been reported. Results of the demographic and clinical characteristics of our prospective cohort study of children with IH have previously been reported.3,4 The current study compares the characteristics of IH in preterm and term infants within this cohort.

Methods. Data on gestational age (GA) was available for 1047 patients who were enrolled at the sites in the United States and formed the basis of the study. Preterm infants were defined as those with a GA of less than 37 weeks, and term infants were those with a GA of 37 weeks and greater.

Results. Demographic and clinical characteristics are summarized in the Table. Two hundred and fourteen subjects were preterm (20%), and 73 of these had a gestational age of 32 weeks or less (7%). Factors associated with preterm birth included a higher reported incidence of preeclampsia, placental anomalies, and use of infertility treatments than in term counterparts (P < .001). The female to male ratio was less pronounced in premature infants (1.85) than in term infants (2.62) (P = .04). No differences were noted in the age when IH was first noted or age at the time of presentation to a specialist. The mean (SD) number of hemangiomas was inversely related to GA: 1.37 (0.78) in term infants; 1.60 (1.15) in preterm infants with a GA of 33 to 36 weeks; and 1.83 (1.17) in preterm infants with a GA of 32 weeks or less (P < .001).

Forty percent of preterm infants had 2 to 5 lesions vs 24.5% of term infants (P < .001), and 7.5% of preterm infants had more than 5 lesions compared with 3% for term infants (P < .001) (Figure). Analysis of birth weight association alone showed that lower birth weight also correlated with increased numbers of IH (P < .001). Localized hemangiomas were more common than either segmental or indeterminate subtypes in both preterm and term groups; however, there was no significant difference in the incidence of segmental hemangiomas in preterm infants (14.6%) and term infants (18.1%) (P = .24). Anatomic location differed, with facial involvement being more common in term infants (P = .005). There was no difference in the incidence of complications (eg, visual compromise, ulceration, or cardiac or airway compromise), and need for treatment did not differ, nor did the treatment techniques used in those infants requiring treatment.

Comment. While previous studies have confirmed the higher incidence of IH in premature infants, to our knowledge, this is the first study to address whether characteristics of IH differ between term and preterm infants. The most notable differences found were the increased number of hemangiomas in preterm infants and the decreased female to male ratio (Figure and Table). The recent suggestion for a role of endothelial progenitor cells in IH development could help explain both the increase in frequency and numbers of hemangiomas in preterm infants because these progenitor cells might be more likely...