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Transient Blood Transfusion Reaction Masquerading As a Post-Transplantation Lymphoproliferative Disorder Mimicking Acute Leukemia Cutis

Case Report

A 67-year-old female patient initially presented in 2007 with breast cancer, which was treated with a lumpectomy and adjuvant chemotherapy that included docetaxel, trastuzumab, and carboplatin. The patient was well until June 2009 when she developed a therapy-related myeloid neoplasm, specifically, acute myeloid leukemia. The myeloid neoplasm was initially treated with decitabine followed by a nonmyeloablative matched unrelated donor allogeneic stem-cell transplantation in June 2010. In January 2011, the patient presented to the emergency room with a sudden onset of a diffuse erythematous skin eruption (Fig 1A, thigh). Because the skin rash developed soon after the tapering of tacrolimus, graft versus host disease (GVHD) was suspected clinically. A skin biopsy was performed and did not show the prototypic histologic features of GVHD. Instead, the biopsy revealed a superficial dermal perivascular infiltrate by large atypical immature-appearing mononuclear cells

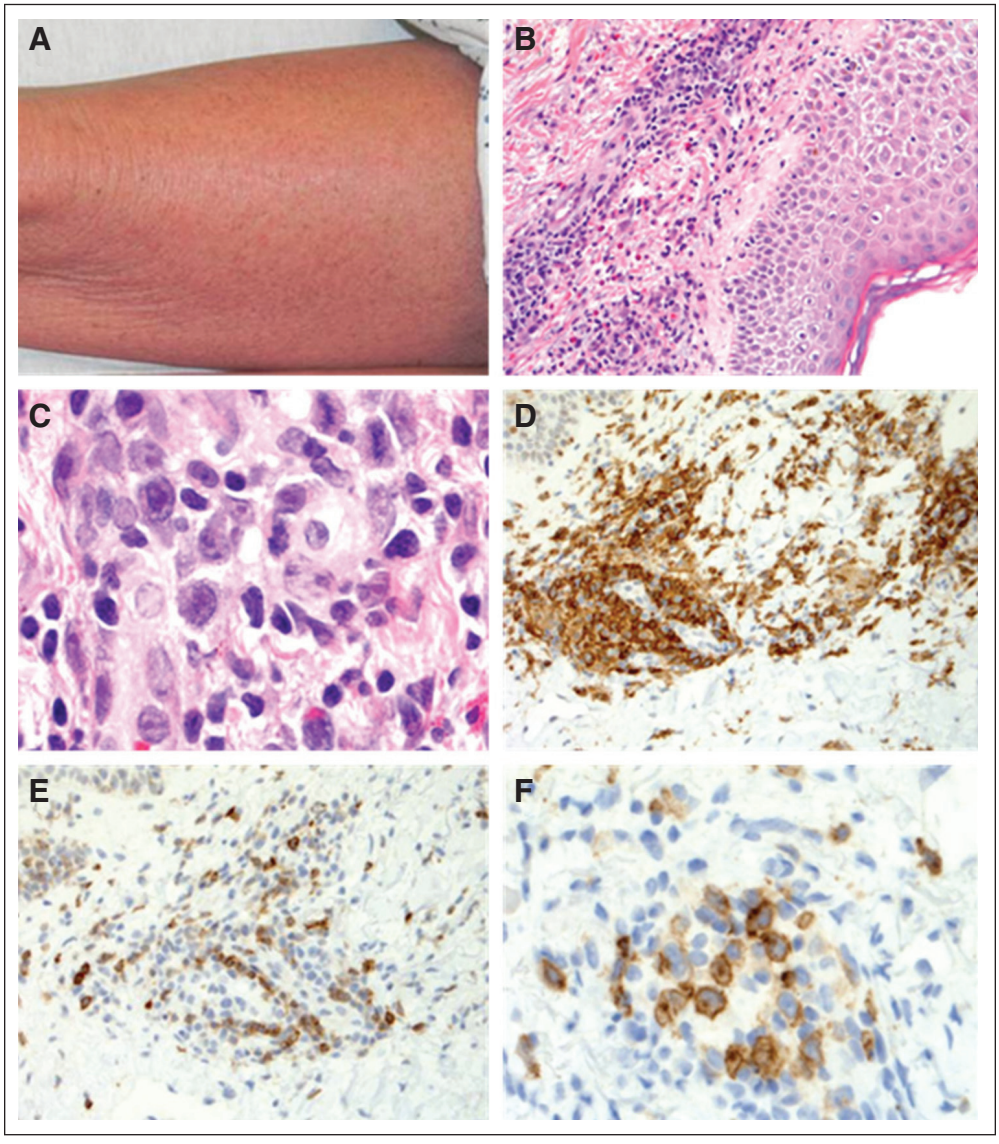

Fig 1.

with vesicular chromatin and brisk mitotic activity (Figs 1B and 1C; hematoxylin and eosin; original magnification: B, ×100 [low power]; C, ×500 [high power]). The epidermis was uninvolved. At the same time, peripheral blood showed a mild expansion of blasts (approximately 5%), and flow cytometry revealed that they were $CD34^+$, $CD117^+$, and MPO^+ myeloblasts, concerning for recurrent acute myeloid leukemia. On the basis of these findings, the histologic features in the skin were initially interpreted to reflect leukemia cutis/extramedullary acute leukemia. However, limited immunohistochemical studies showed that the large atypical cells were negative for CD34, CD117, and MPO, which essentially excluded this consideration. Subsequent immunohistochemical analysis revealed that the large atypical cells were T cells on the basis of their expression of CD2, CD3 (Fig 1D; immunohistochemistry; original magnification ×200) and CD5, and virtually all cells were positive for CD4. However, most cells were negative for CD7 (Fig 1E; immunohistochemistry; original magnification ×200) and positive for CD30 (Fig 1F; immunohistochemistry; original magnification ×400). Ki-67 was positive in 60% of the atypical cells. Epstein Barr virus–encoded RNA 1 was negative by in situ hybridization. At this stage, the immunohistochemical profile together with the cytologic features raised the possibility of an alternative neoplastic disorder, namely that of an unusual monomorphic T-cell post-transplantation lymphoproliferative disorder, and perhaps an anaplastic large cell lymphoma. However, in the interim while working up the skin biopsy, the skin rash resolved within 48 hours of initiation of empirical corticosteroids and tacrolimus for clinical presumption of GVHD. Polymerase chain reaction analysis of the T-cell receptor γ chain gene performed on the skin biopsy revealed the presence of polyclonal rearrangements only. Additional history revealed that the patient had received a transfusion of RBCs and platelets at an outside institution for her worsening anemia and thrombocytopenia only a few hours before the development of the eruption. There had not been any recent changes in her medications. When the final pathologic diagnosis was established, her immunosuppression was rapidly tapered with no recurrence of the rash after 3 months of follow-up.

Thus, with all of the pertinent information available, this highly atypical cutaneous lymphoid infiltrate was likely a manifestation of an atypical blood transfusion reaction. However, this process was quite deceptive pathologically, with consideration being given to two quite distinct hematologic neoplasms before it became clear that it was indeed benign and reactive. The initial concern that this was leukemia cutis, which seemed perfectly reasonable on the basis of the histology and clinical context, was rapidly excluded with a limited immunohistochemical panel. The subsequent demonstration that the atypical infiltrate was of T-cell lineage, with apparent immunophenotypic aberrancy (CD7 loss), led to an alternative, but also highly plausible, consideration that this was a T-cell neoplasm and, contextually, a possible post-transplant lymphoproliferative disorder, albeit unusual in terms of the relatively short interval since transplantation.

Discussion

Atypical cutaneous lymphoid infiltrates with reactive CD30-positive T cells are one form of so-called (in the dermatopathology literature) pseudolymphoma, in which histologic (and sometimes clinical) features resemble lymphoma but are actually reactive. Reactive CD30-positive T cells have been described in several scenarios, including drug reactions, insect bites, and viral infections such as parapoxvirus (milker's nodules), herpes viruses, and poxvirus (molluscum contagiosum). Other reported causes included cutaneous leishmaniasis, scabies, syphilis, mycotic infections, tattoos, and trauma.[1-10] To our knowledge, this is the first report of such a reaction associated with a blood transfusion.

In the case reported, the CD30-positive atypical reactive T cells revealed an aberrant loss of CD7 expression, which has often been applied as a criterion to distinguish lymphoma and benign reactive process.[11] However, CD7, which is a galectin-1 receptor, is also physiologically downregulated via the nuclear factor-κB and p38 mitogen-activated protein kinase pathways on T-cell activation,[12,13] which highlights that CD7 downregulation is not only a feature of neoplasia. Indeed, decreased CD7 expression has been well described in some benign cutaneous infiltrates.[14,15]

This case was instructive at several levels and illustrated the central role of a clinicopathologic correlation in the evaluation of abnormal skin biopsies. Diagnostic considerations evolved (or, rather, were considerably varied) from GVHD to leukemia cutis to post-transplantation lymphoproliferative disorder to a spontaneously resolving blood transfusion reaction, albeit one that was rather atypical and quite alarming histologically. Clinicians and pathologists must be cognizant of such reactive rashes that can mimic malevolence and even masquerade as myeloid malignancies.

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AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

The author(s) indicated no potential conflicts of interest.

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