Delayed Wound Healing in Leukocyte Adhesion Deficiency Type 1

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Leukocyte adhesion deficiency type 1 (LAD-1) is an autosomal recessive immunodeficiency caused by mutations in the β2 integrin, CD18, and characterized by recurrent bacterial infections, impaired pus formation, and delayed wound healing.[1] Recent studies of CD18 knockout mice have demonstrated that defective migration of neutrophils into wound sites causes a severe reduction of transforming growth factor-β1 secretion by monocytes, resulting in impaired myofibroblast differentiation and delayed wound healing.[2] However, little is known about cellular events of wound healing in human LAD-1. Here, we described 3-month-old boy affected with LAD-1 who showed the complete lack of CD18 and its associated molecules CD11b and CD11c on his granulocytes and monocytes. His immunological and sequencing data have been reported elsewhere.[3] He showed delayed wound healing after surgical excision of an infected urachal cyst from the age of 2 months (Figure A). Similar to the findings of CD18 knockout mice, his wound specimens obtained from the surgical debridement revealed the absence of neutrophils and the presence of monocyte/macrophage infiltrates (Figure B, C). The infiltrating cells also included low numbers of plasma cells as well as lymphocytes, most of which were $CD20^+$ B cells by immunohistochemical staining (Figure D). Although our patient showed somatic revertant mosaicism within the $CD8^+$ T-cell subset,[3] $CD18^+$ cells were not detectable in the wound. These findings suggest that β2 integrin-independent mechanisms may play a role in transmigration of monocytes and B cells through vascular endothelium. In addition, like CD18 knockout mice, the local injection of recombinant transforming growth factor-β1 could be a potential therapy for delayed wound healing. Improved understanding of physiology of cutaneous wound healing in LAD-1 may lead to better therapeutic approach

for LAD-1 patients with delayed wound healing.

List of abbreviations: Leukocyte adhesion deficiency type 1, LAD-1.

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Figure Legend

Figure. Delayed wound healing that was located just below the umbilicus (A). Wound specimens were stained with May-Giemsa (B) or anti-CD68 antibody (C). The percentage of cells in wound specimens is shown (D).