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メタデータ	言語: eng 出版者: 公開日: 2017-10-05 キーワード (Ja): キーワード (En): 作成者: メールアドレス: 所属:
URL	http://hdl.handle.net/2297/25262

Manuscript category: Insights

Delayed Wound Healing in Leukocyte Adhesion Deficiency Type 1

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Key words: LAD-1; delayed wound healing; CD18; granulocytes; monocytes

Source of funding: This work was supported by a Grant-in-Aid for Scientific Research from the Ministry of Education, Culture, Sports, Science and Technology of Japan; and a grant from the Ministry of Health, Labour, and Welfare of Japan, Tokyo.

Conflict of interest statement: No conflict of interest to declare.

Leukocyte adhesion deficiency type 1 (LAD-1) is an autosomal recessive immunodeficiency caused by mutations in the $\beta 2$ 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- $\beta 1$ 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 $\beta 2$ 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- $\beta 1$ 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.

References

- [1] Etzioni A. Genetic etiologies of leukocyte adhesion defects. *Current opinion in immunology*. 2009;21:481-6.
- [2] Peters T, Sindrilaru A, Hinz B, Hinrichs R, Menke A, Al-Azzeh EA, et al. Wound-healing defect of CD18^{-/-} mice due to a decrease in TGF- β 1 and myofibroblast differentiation. *The EMBO journal*. 2005;24:3400-10.
- [3] Tone Y, Wada T, Shibata F, Toma T, Hashida Y, Kasahara Y, et al. Somatic revertant mosaicism in a patient with leukocyte adhesion deficiency type 1. *Blood*. 2007;109:1182-4.

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).

