

Ezequiel Agustin Piccione, MD
JaNean Engelstad, HT
Carilyn Wieland, MD
Christopher J. Klein, MD

Neurol Neuroimmunol Neuroinflamm
2014;1:e42; doi: 10.1212/NXI.0000000000000042

LANGERHANS CELL ACTIVATION IN DIABETIC SMALL FIBER POLYNEUROPATHY

OPEN

A 63-year-old man with type 2 diabetes developed painful feet with touch allodynia. Skin biopsy revealed prominent Langerhans cells (LC) staining with the standard epidermal nerve fiber antibody PGP9.5 when compared to a normal control (figure). Fiber density was severely decreased at the leg (mean 0.2 fibers/mm, 95% confidence interval [CI] 0.1–0.4) and thigh (mean 2.2 fibers/mm, 95% CI 1.8–2.8). These findings were consistent with small fiber neuropathy.

LC are reported to be increased in the skin with diabetes, small fiber polyneuropathy, and mechanical allodynia.^{1,2} They are dendritic cells with S-100 antibody positivity and are important in antigen presentation. With denervation, PGP9.5 is upregulated within LC, but their exact role in small fiber pathogenesis is not understood.

From the Mayo Clinic, Rochester, MN.

Author contributions: Study concept and design: Dr. Ezequiel Agustin Piccione, Dr. Christopher J. Klein. Acquisition of data: JaNean Engelstad. Analysis and interpretation: Dr. Ezequiel Agustin

Piccione, Dr. Carilyn Wieland, and Dr. Christopher J. Klein. Critical revision of the manuscript for important intellectual content: Dr. Ezequiel Agustin Piccione, Dr. Carilyn Wieland, and Dr. Christopher J. Klein. Study supervision: Dr. Christopher J. Klein.

Study funding: No targeted funding reported.

Disclosure: E.A. Piccone reports no disclosures. J. Engelstad receives royalties from the book Companion to Peripheral Neuropathy: Illustrated Cases and New Developments (Saunders, 2010). C. Wieland reports no disclosures. C.J. Klein is on the editorial board of the Journal of the Peripheral Nervous System and has received research support from the NINDS. Go to Neurology.org/n for full disclosures. The Article Processing Charge was paid by the authors.

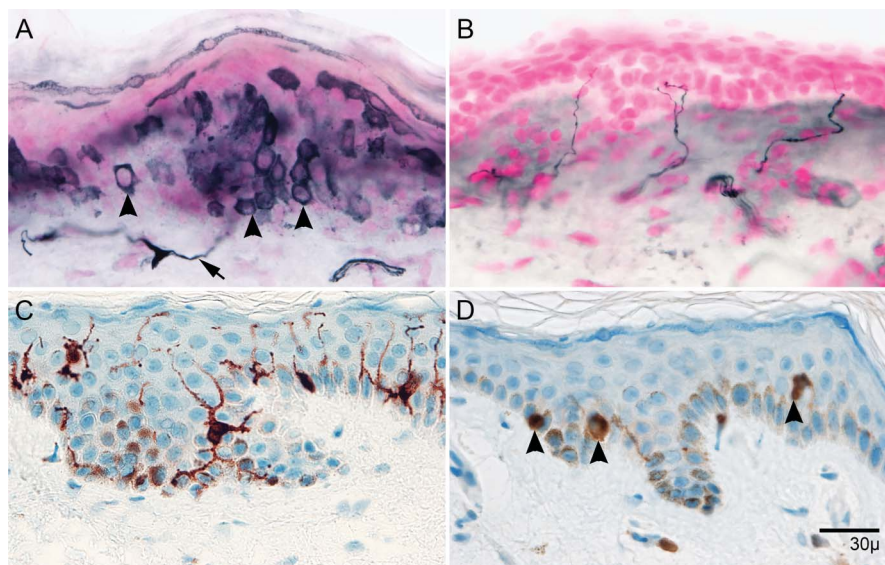
This is an open access article distributed under the terms of the Creative Commons Attribution-Noncommercial No Derivative 3.0 License, which permits downloading and sharing the work provided it is properly cited. The work cannot be changed in any way or used commercially.

Received June 4, 2014. Accepted in final form September 18, 2014.

Correspondence to Dr. Klein: klein.christopher@mayo.edu

1. Casanova-Molla J, Morales M, Planas-Rigol E, et al. Epidermal Langerhans cells in small fiber neuropathies. *Pain* 2012;153:982–989.
2. Dauch JR, Bender DE, Luna-Wong LA, et al. Neurogenic factor-induced Langerhans cell activation in diabetic mice with mechanical allodynia. *J Neuroinflamm* 2013;10:64.

Figure Comparison of LC activation in diabetic small fiber neuropathy and normal control



(A) PGP9.5 immunostaining shows decreased density of epidermal nerve fibers (ENF, arrow) and robust Langerhans cells (LC) staining (arrowheads). (B) PGP9.5 immunostaining in a 75-year-old man, normal control (distal leg 10.2 ENF/mm, 95% confidence interval [CI] 9.11, 11.4; mid-thigh 9.9 ENF/mm, 95% CI 8.87, 11.05). (C) LC are identified by their positivity to langerin (CD-207). (D) LC staining positive (arrowheads) with S-100.