JAMA Dermatology Clinicopathological Challenge

Painful Chronic Ulcers on the Neck and Back

Emily M. Erstine, MD, MBA; Angela M. B. Collie, MD, PhD; Melissa P. Piliang, MD

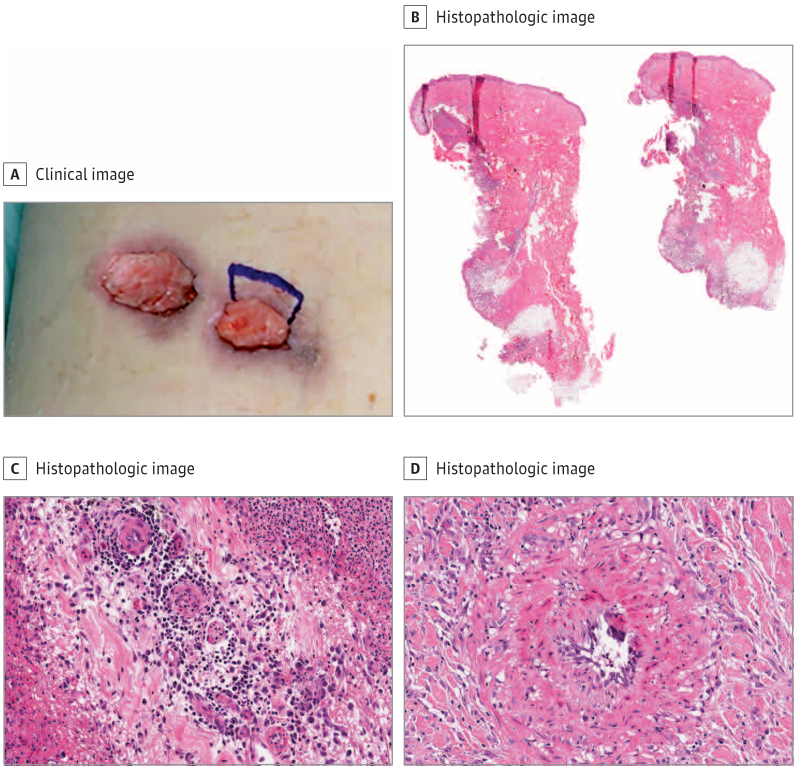

Figure. A, Two deep ulcers of the right mid-lower back with erythematous borders. B, Hematoxylin and eosin stain (original magnification × 5). C, Hematoxylin and eosin stain (original magnification × 200). D, Hematoxylin and eosin stain (original magnification × 200).

A man in his 60s who was a former smoker with a medical history of chronic obstructive pulmonary disease, type 2 diabetes, chronic kidney disease, anemia, and cervical myelopathy experienced low-grade fevers, unintentional 80-pound weight loss, productive cough, and development of cutaneous ulcers over a 6-month period after cervical spine fusion. Two ulcers developed at the surgical site, and 2 similar ulcers developed on his back shortly after cyst excision. He had been recently diagnosed with lung cancer based on computed tomographic (CT) and positron emission tomographic imaging showing an enhancing, hypermetabolic, 7-cm cavitary right upper lobe mass with mediastinal adenopathy. A chest x-ray 6 months prior revealed negative results. A few days after establishing care, he presented to the emergency department with extreme weakness and intolerable pain related to his ulcers. Physical examination revealed an ill-appearing man. In the right upper lobe, there were decreased breath sounds with clear auscultation in the remaining chest. On the right anterior neck were two, 3- to 4-cm tender ulcers extending to the deep subcutaneous fat with erythematous, friable borders (**Figure**). On his back were 2 similar 2- to 2.5-cm ulcers. Inflammatory markers were notably elevated. A complete autoimmune panel, indirect immunofluorescence assays, enzyme immunoassays for antineutrophil cytoplasmic antibodies (c-ANCA)/proteinase 3, antineutrophil cytoplasmic antibody/myeloperoxidase, a quantiferon gold test, cultures of blood, broncheoalveolar washings, and tissue analysis were performed. Only c-ANCA testing revealed positive results. A CT scan of the sinus showed multiple bony defects and acute and chronic sinusitis. A transbronchial biopsy of the lung and excisional biopsy of the skin bridge between back ulcers were performed.

WHAT IS YOUR DIAGNOSIS?

- **A.** Disseminated tuberculosis
- **B.** Paraneoplastic pyoderma gangrenosum
- **C.** Disseminated nocardiosis
- **D.** Granulomatosis with polyangiitis

Diagnosis

D. Granulomatosis with polyangiitis

Microscopic Findings and Clinical Course

Histopathologic evaluation of the excisional skin biopsy demonstrated deep ulceration with associated small and medium vessel leukocytoclastic vasculitis, necrosis and abundant infiltrating neutrophils. Transbronchial biopsy results showed acute and necrotizing granulomatous inflammation. Pulse dose corticosteroids and intravenous rituximab were started, which stabilized and improved his condition. At 5-month follow-up, the lung and cutaneous lesions had substantially healed, and no new lesions had developed. No malignant abnormalities of the lungs were present.

Discussion

Granulomatosis with polyangiitis (GPA), formerly called Wegener granulomatosis, is a rare autoimmune disease often associated with c-ANCA and manifests as widespread granulomatous inflammation and necrotizing vasculitis commonly involving the upper and lower respiratory tracts and kidneys.[1] Skin involvement can occur in up to 50% of patients, with primary skin lesions presenting up to 25% of the time.[2-4] A subset of the primary skin lesions is pyoderma gangrenosumlike ulcers, an initial feature in about 5% of cases.[1-9] Other cutaneous manifestations include palpable purpura, papules, vesicles, and bullae.

Histologic tissue examination demonstrates small and medium-vessel leukocytoclastic vasculitis with a mixed acute and chronic, necrotizing inflammatory infiltrate with a variable degree of granulomatous inflammation. The histopathologic findings of GPA are not specific and may be seen in infectious or other autoimmune diseases, it is therefore important to consider the distribution of the disease process and laboratory findings. This patient was comprehensively evaluated with a complete autoimmune panel and batteries of studies searching for bacterial (especially mycobacterial), fungal, viral, and parasitic organisms, which eliminated an infectious etiology.

Pyoderma gangrenosum, as an idiopathic or paraneoplastic process, was originally in the clinical differential diagnosis. It is a diagnosis of exclusion with potential for misdiagnosis if a true etiology for cutaneous ulceration exists yet is never discovered. The pathology in our case is most consistent with GPA, a sterile vasculitis rather than a sterile neutrophilic dermatosis. The overall diagnosis in this case was multifactorial and based on clinical presentation (ie, sinus and lung involvement), laboratory test results (ie, positive c-ANCA and negative workup for infection, malignant abnormalities, etc), and skin biopsy, all of which pointed to a diagnosis of GPA.

Generalized GPA is rapidly progressive with death occurring an average of 5 months after presentation without adequate immune suppressive and/or modulating therapies.[10] Therapeutic regimens depend on disease severity, including extent of involvement and degree of end-organ damage. Systemic corticosteroids are first line therapy and are often combined with cyclophosphamide. Additional therapies include tacrolimus and rituximab. As with this patient, recovery is often slow, requiring close clinical follow-up to ensure patient improvement and long-term stability.

ARTICLE INFORMATION

Author Affiliations: Department of Pathology, Cleveland Clinic Foundation, Cleveland, Ohio (Erstine, Piliang); Dermpath Diagnostics Indiana, Indianapolis, Indiana (Collie); Department of Dermatology, Cleveland Clinic Foundation, Cleveland, Ohio (Piliang).

Corresponding Author: Melissa P. Piliang, MD, Departments of Pathology and Dermatology, Cleveland Clinic Foundation, 9500 Euclid Ave, A60, Cleveland, OH 44195 (pilianm@ccf.org).

Published Online: September 14, 2016. doi:10.1001/jamadermatol.2016.3270.

Conflict of Interest Disclosures: None reported.

Self-assessment Credit: This article is eligible for journal-based self-assessment (1 credit) for Maintenance of Certification (MOC) from the American Board of Dermatology (ABD). After completion of an activity, please log on to the ABD website at www.abderm.org to register your credits. This may be done after each exercise or after accumulating many credits.

REFERENCES

1. Handfield-Jones SE, Parker SC, Fenton DA, Newton JA, Greaves MW. Wegener's granulomatosis presenting as pyoderma gangrenosum. *Clin Exp Dermatol*. 1992;17(3):197-200.

2. Reed WB, Jensen AK, Konwaler BE, Hunter D. The cutaneous manifestations in Wegener's granulomatosis. *Acta Derm Venereol*. 1963;43:250-264.

3. Edwards MB, Buckerfield JP. Wegener's granulomatosis: a case with primary mucocutaneous lesions. *Oral Surg Oral Med Oral Pathol*. 1978;46(1):53-63.

4. Tashtoush B, Memarpour R, Johnston Y, Ramirez J. Large pyoderma gangrenosum-like ulcers: a rare presentation of granulomatosis with polyangiitis. *Case Rep Rheumatol*. 2014;2014:850364.

5. Thomas RH, Payne CM, Black MM. Wegener's granulomatosis presenting as pyoderma gangrenosum. *Clin Exp Dermatol*. 1982;7(5):523-527.

6. Chyu JY, Hagstrom WJ, Soltani K, Faibisoff B, Whitney DH. Wegener's granulomatosis in childhood: cutaneous manifestations as the presenting signs. *J Am Acad Dermatol*. 1984;10(2 Pt 2):341-346.

7. Micali G, Cook B, Ronan S, Yadgir J, Solomon LM. Cephalic pyoderma gangrenosum (PG)-like lesions as a presenting sign of Wegener's granulomatosis. *Int J Dermatol*. 1994;33(7):477-480.

8. Szőcs HI, Torma K, Petrovicz E, et al. Wegener's granulomatosis presenting as pyoderma gangrenosum. *Int J Dermatol*. 2003;42(11):898-902.

9. Boudny C, Nievergelt H, Braathen LR, Simon D. Wegener's granulomatosis presenting as pyoderma gangrenosum. *J Dtsch Dermatol Ges*. 2008;6(6):477-479.

10. Walton EW. Giant-cell granuloma of the respiratory tract (Wegener's granulomatosis). *Br Med J*. 1958;2(5091):265-270.

【【2017 年福利：免费传递中英文文献全文啦！】】

国内（知网 万方 维普电子期刊数据库、学位文献数据库全文）、国外（Pubmed、ScienceDirect、Ovid 文献数据库全文等 ）Fulltext 传递现在完全免费了！科研、参考、晋升苦于找不到论文全文的同志们有福了，快来吧，找新浪微博@医学插画师–动画师–杜鹏 或者微信 medicaldupeng 就可以，您只需要完成如下任务之一就可以获得一篇全文，多篇就完成多次任务即可，难度大或者权限高的文献如果我搞不到可以换另一篇 until 搞到为止。免得您花费钱财和时间去别的网站求文献，我这里完全免费了！

任务（任一个）：
1. 在你的微博上转发一次，或者复制此博文到你朋友圈一次；
2. 向你的医学、生物、药物、科研、临床、编辑等相关领域的同学或工作同事、上级领导等推荐介绍下新浪微博@医学插画师–动画师–杜鹏 或者微信 medicaldupeng 从事的医学插画、动画、2D3D、虚拟、出版设计等，知道我的网站 www.medicaldupeng.com，让 TA 关注我的微博号或者微信号并让 TA 截图发私信给我确认；
3. 类似第 2 条，但要让 TA 发一封邮件给我 18147895@qq.com 写下对医学插画动画的希望和建议，并在邮件末尾留下 TA 姓名、单位、地址或者电话号码。。。

新年快乐，互相帮助，互相成长！

QQ 18147895
微信 medicaldupeng

医学插画师阿杜
广东 深圳

扫一扫上面的二维码图案，加我微信

活动详情见 http://t.cn/RMcQGm2