

Erythema Nodosum: A Presenting Sign of Acute Myelogenous Leukemia

Robert Sullivan, MD; Holly Clowers-Webb, MD; Mark D.P. Davis, MD

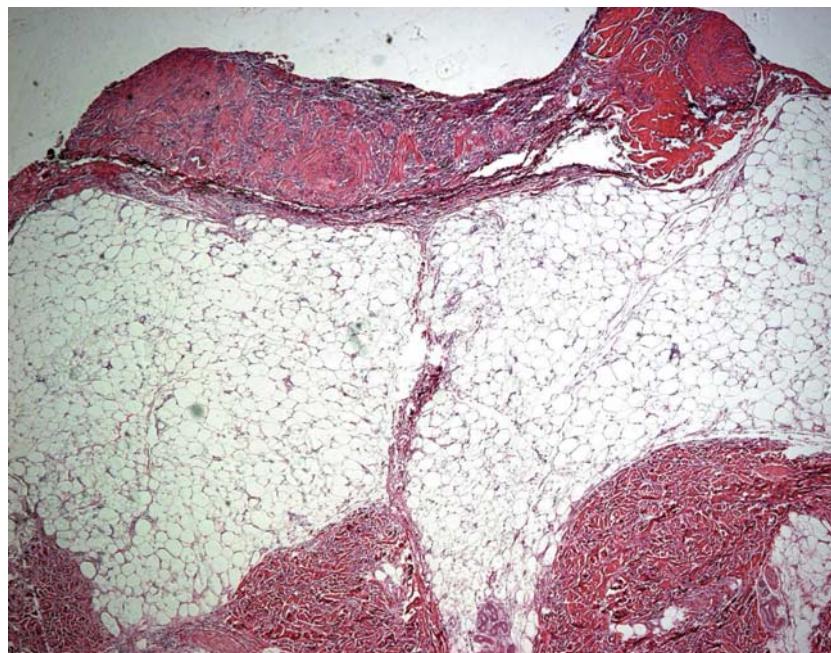
A 15-year-old girl presented to our institution with erythema nodosum. Results of a workup for underlying disease revealed acute myelogenous leukemia. Underlying malignancy should be investigated in patients presenting with erythema nodosum.

Cutis. 2005;76:114-116.

Few reports exist of acute leukemia associated with erythema nodosum, and most such cases were not proven by biopsy results. Our case suggests that an underlying malignancy should be included in the differential diagnosis for patients presenting with erythema nodosum.

Case Report

A 15-year-old girl with a history of myelodysplasia, congenital subaortic stenosis, and associated heart failure presented with a 4-month history of intermittent painful lesions on her upper and lower extremities, with associated fever and fatigue. The nodules initially responded to oral antibiotics (amoxicillin/clavulanate for 2 weeks, then ciprofloxacin for 2 weeks) prescribed by her family physician; however, the lesions recurred despite further treatment with antibiotics. At the time of presentation to our clinic, the patient was taking no medications. Results of an examination revealed tender subcutaneous nodules measuring



Septal panniculitis consistent with erythema nodosum (H&E, original magnification $\times 20$).

2 to 4 cm in diameter, with overlying erythema in the affected areas.

An incisional biopsy of one of the nodules was performed. Results of a microscopic examination of the skin biopsy specimen revealed septal panniculitis consistent with a diagnosis of erythema nodosum (Figure). Results of special stains and cultures for microorganisms (ie, bacteria, mycobacteria, fungi) were negative. Results of direct immunofluorescence showed nondiagnostic inflammatory reaction, with diffuse deposition of fibrinogen throughout the deep dermis and panniculus.

Results of a complete blood cell count and blood smear showed acute myelogenous leukemia with a predominantly monocytic pattern. Results of a bone marrow biopsy showed trisomy 8, unbalanced 1;7 translocation. Results of a lumbar puncture were within reference range.

Accepted for publication June 29, 2004.

Dr. Sullivan was from the Department of Dermatology, Ross University School of Medicine, Edison, New Jersey. Drs. Clowers-Webb and Davis are from the Department of Dermatology, Mayo Clinic, Rochester, Minnesota.

The authors report no conflict of interest.
Reprints not available from the authors.

Malignancies Associated With Erythema Nodosum

Leukemias

- Acute granulocytic leukemia¹
- Acute monocytic leukemia²⁻⁴
- Acute myeloblastic leukemia⁵
- Acute myelogenous leukemia^{6,7}
- Acute promyelocytic leukemia^{8,9}
- Acute stem cell leukemia⁴
- Aleukemic leukemia¹⁰
- Chronic granulocytic leukemia^{4,11}
- Chronic lymphocytic leukemia^{4,12,13}
- Chronic myelogenous leukemia¹⁴
- Chronic myelomonocytic leukemia^{15,16}
- Hairy cell leukemia¹⁷
- Monoblastic leukemia¹⁸
- Myelogenous leukemia¹⁹

Lymphomas

- B-cell lymphoma²⁰
- Hodgkin disease²¹⁻³²
- Lennert lymphoma³³
- Non-Hodgkin lymphoma^{32,34-37}
- T-cell-rich B-cell lymphoma³⁸

Solid Malignancies

- Adenocarcinoma of the colon³⁹
- Carcinoma of the uterine cervix⁴⁰
- Disseminated Kaposi sarcoma⁴¹
- Gastric centrofollicular lymphoma⁴²
- Metastatic pancreatic carcinoma⁴³
- Renal cell carcinoma⁴⁴

The patient was hospitalized and started receiving chemotherapy (cytarabine and a protocol drug regimen) for the leukemia. Her skin lesions cleared after initiation of chemotherapy. Subsequently, multiorgan failure developed, and she died 2 months after presentation.

Comment

Erythema nodosum is most often associated with a reaction to drugs or infection. Our patient had

underlying acute myelogenous leukemia, and erythema nodosum was the presenting sign. Erythema nodosum has been reported to be associated with chronic and acute leukemias, lymphomas, and solid malignancies (Table).¹⁻⁴⁴ Underlying malignancy should be considered as a possible cause of erythema nodosum.

REFERENCES

1. Sumaya CV, Babu S, Reed RJ. Erythema nodosum-like lesions of leukemia. *Arch Dermatol.* 1974;110:415-418.
2. Lynch FW. Cutaneous lesions associated with monocytic leukemia and reticulo-endotheliosis. *AMA Arch Dermatol Syphilol.* 1936;34:775-796.
3. Bluefarb SM, Wallk S, Gecht ML. Acute monocytic leukemia with erythema nodosum. *AMA Arch Dermatol.* 1957;75:596-597.
4. Pinski BJ, Stansifer PD. Erythema nodosum as the initial manifestation of leukemia. *Arch Dermatol.* 1964;89:339-341.
5. Thwe M. Acute myeloblastic leukaemia presenting with erythema nodosum. *Postgrad Med J.* 1966;42:51-53.
6. Suzuki Y, Kuroda K, Kojima T, et al. Unusual cutaneous manifestations of myelodysplastic syndrome. *Br J Dermatol.* 1995;133:483-486.
7. Papadaki HA, Kosteas T, Gemetzi C, et al. Two patients with nonimmune chronic idiopathic neutropenia of adults developing acute myeloid leukemia with aberrant phenotype and complex karyotype but no mutations in granulocyte colony-stimulating factor receptor. *Ann Hematol.* 2002;81:50-54.
8. Hakimian D, Tallman MS, Zugerman C, et al. Erythema nodosum associated with all-trans-retinoic acid in the treatment of acute promyelocytic leukemia. *Leukemia.* 1993;7:758-759.
9. Hatake K, Uwai M, Ohtsuki T, et al. Rare but important adverse effects of all-trans retinoic acid in acute promyelocytic leukemia and their management. *Int J Hematol.* 1997;66:13-19.
10. Kourilsky R, Beauvy A, Anglade P. Leucose aiguë aleucémique simulant un érythème noveux et terminée par une gangrène de la verge. *Bull et Mém Soc Med d Hôp de Paris.* 1937;53:1378-1390.
11. Wintrobe MM, Mitchell DM. Atypical manifestations of leukemia. *Q J Med.* 1940;9:67-90.
12. Gate J, Cuilleret P. A propos des manifestations cutanées des leucémies. *Bull Soc Franc de Dermat et Syph (Réunion Dermat, Strasbourg).* 1937;44:1213-1217.
13. Sanz Moreno J, Aranegui Lasuen P, Martin Rico P, et al. Erythema nodosum associated with chronic lymphatic leukemia [in Spanish][letter]. *An Med Interna.* 1990;7:599.
14. Piacentini G. Mielosi cronica leucemia ed eritema nodoso: osservazioni cliniche e terapeutiche. *Clin Ter.* 1956;10:341-349.

Erythema Nodosum

15. Bolla G, Lambert M, Bosagli A, et al. Erythema nodosum revealing chronic myelomonocytic leukemia: two cases [in French][letter]. *Rev Med Interne*. 1998;19:838-839.
16. Maxit MJ, Paz RA. Diffuse plane xanthoma with arthritis, serositis, erythema nodosum, vasculitis and myelomonocytic leukemia. description of a case with autopsy [in Spanish]. *Medicina (B Aires)*. 2001;61(2):187-190.
17. Schved JF, Benoist D'Azu G, Brunel M, et al. Hairy cell leukemia associated with tuberculosis, disclosed by erythema nodosum [in French]. *Sem Hop*. 1983;59:2716-2717.
18. Forman L. Erythema multiforme and nodosum-like eruption as the presenting sign of monoblastic leukaemia. *Proc R Soc Med*. 1964;57:1097-1098.
19. Costello MJ, Canizares O, Montague M, et al. Cutaneous manifestations of myelogenous leukemia. *AMA Arch Dermatol*. 1955;71:605-614.
20. Matsuoka LY. Neoplastic erythema nodosum. *J Am Acad Dermatol*. 1995;32(2 pt 2):361-363.
21. Fuller CJ. Hodgkin's disease with erythema nodosum. *Br J Dermatol*. 1934;11:1172-1173.
22. Fraser J. A case diagnosis (erythema nodosum?). *AMA Arch Derm Syphilol*. 1936;34:1080.
23. Macpherson P. A survey of erythema nodosum in a rural community between 1954 and 1968. *Tubercle*. 1970;51:324-327.
24. Chalmers RJ, Proctor SJ, Marks JM. Erythema nodosum and Hodgkin's disease. *Br J Dermatol*. 1982;106:593-596.
25. Simon S, Azevedo SJ, Byrnes JJ. Erythema nodosum heralding recurrent Hodgkin's disease. *Cancer*. 1985;56:1470-1472.
26. Taillan B, Ferrari E, Fuzibet JG, et al. Erythema nodosum and Hodgkin's disease. *Clin Rheumatol*. 1990;9:397-398.
27. Laraki R, Zorgui A, Bletry O, et al. Hodgkin's disease disclosed by erythema nodosum [in French]. *Ann Med Interne (Paris)*. 1992;143:488-489.
28. Lopez Dupla M, Delegido Sanchez-Migallon A, Guionnet Anguera N, et al. Recurrent erythema nodosum as a presenting form of Hodgkin's disease [in Spanish][letter]. *Sangre (Barc)*. 1997;42:253-254.
29. Blanco P, Neau D, Pellegrin JL, et al. Erythema nodosum and cutaneous vasculitis revealing Hodgkin's disease: apropos of 2 case reports [in French]. *Rev Med Interne*. 1999;20:160-163.
30. Kakourou T, Drosatou P, Psychou F, et al. Erythema nodosum in children: a prospective study. *J Am Acad Dermatol*. 2001;44:17-21.
31. Bonci A, Di Lernia V, Merli F, et al. Erythema nodosum and Hodgkin's disease. *Clin Exp Dermatol*. 2001;26:408-411.
32. Pileckyte M, Griniute R. Erythema nodosum association with malignant lymphoma [in Lithuanian]. *Medicina (Kaunas)*. 2003;39:438-442.
33. Junca Piera J, Flores Lopez A, Ojanguren I, et al. Lennert lymphoma and erythema nodosum [in Spanish][letter]. *Med Clin (Barc)*. 1987;88:82.
34. Reverter JC, Coca A, Font J, et al. Erythema nodosum and pulmonary solitary nodule as the first manifestations of a non-Hodgkin's lymphoma. *Br J Dis Chest*. 1987;81:397-399.
35. Thomson GT, Keystone EC, Sturgeon JF, et al. Erythema nodosum and non-Hodgkin's lymphoma. *J Rheumatol*. 1990;17:383-385.
36. Taillan B, Fuzibet JG, Ferrari E, et al. Malignant non-Hodgkin's lymphoma disclosed by erythema nodosum: 2 cases [in French]. *Ann Med Interne (Paris)*. 1991;142:546-547.
37. Szeimies RM, Kaudewitz P, Braun-Falco O. Erythema nodosum and non-Hodgkin lymphoma [in German]. *Hautarzt*. 1992;43:583-586.
38. Navarro JT, Ribera JM, Vaquero M, et al. Erythema nodosum as a presenting feature of T-cell-rich B-cell lymphoma. *Ann Hematol*. 1995;70:107-108.
39. Lillo A, Gil MJ, Jimenez R, et al. Erythema nodosum and adenocarcinoma of the colon [in Spanish][letter]. *Med Clin (Barc)*. 1997;108:318.
40. Altomare GF, Capella GL. Paraneoplastic erythema nodosum in a patient with carcinoma of the uterine cervix [letter]. *Br J Dermatol*. 1995;132:667-668.
41. Hohl D, Gueissaz F, Gerain J, et al. Erythema nodosum and AIDS [in German]. *Hautarzt*. 1992;43:86-88.
42. Parodi A, Cestari R, Rebora A. Erythema nodosum as the presenting symptom of gastric centrofollicular lymphoma. *Int J Dermatol*. 1989;28:336-337.
43. Durden FM, Variyam E, Chren MM. Fat necrosis with features of erythema nodosum in a patient with metastatic pancreatic carcinoma. *Int J Dermatol*. 1996;35:39-41.
44. Weinstein A, Bujak D, Mittelman A, et al. Erythema nodosum in a patient with renal cell carcinoma treated with interleukin 2 and lymphokine-activated killer cells [letter]. *JAMA*. 1987;258:3120-3121.