21. **Horikawa I,** Barrett JC. Transcriptional regulation of the telomerase hTERT gene as a target for cellular and viral oncogenic mechanisms. *Carcinogenesis* 2003;**24**:1167–76.
22. **Poole JC,** Andrews LG, Tollefsbol TO. Activity, function, and gene regulation of the catalytic subunit of telomerase (hTERT). *Gene* 2001;**269**:1–12.
23. **Tahara H,** Nakanishi T, Kitamoto M, *et al*. Telomerase activity in human liver tissues: comparison between chronic liver disease and hepatocellular carcinomas. *Cancer Res* 1995;**55**:2734–6.
24. **Edmondson HA,** Steiner PE. Primary carcinoma of the liver: a study of 100 cases among 48,900 necropsies. *Cancer* 1954;**7**:462–503.
25. **Mary AS,** Meiling C, Georage A. Production of hepatitis B virus particles in HepG2 cells transfected with cloned hepatitis B virus DNA. *Proc Natl Acad Sci USA* 1987;**84**:1005–9.
26. **Ma CH,** Sun WS, Tian PK, *et al*. A novel HBV antisense RNA gene delivery system targeting hepatocellular carcinoma. *World J Gastroenterol* 2003;**9**:463–67.
27. **Higuchi R,** Innis MA, Gelfand DH, *et al*. PCR protocols. *Academic Press, San Diego, CA* 1990;**266**:177–83.
28. **Schliiter C,** Duchrow M, Wohelenburg C, *et al*. The cell proliferation-associated antigen of antibody Ki-67: a very large, ubiquitous unclear protein with numerous repeated elements, representing a new kind of cell cycle-maintaining proteins. *J Cell Biol* 1993;**123**:513–22.
29. **Morinaga S,** Ishiwa N, Noguchi Y, *et al*. Growth index, assessed with Ki-67 and ssDNA labeling; a significant prognosticator for patients undergoing curative resection for hepatocellular carcinoma. *J Surg Oncol* 2005;**92**:331–6.
30. **Horikawa I,** Cable PL, Afshari C, *et al*. Cloning and characterization of the promoter region of human telomerase reversetranscriptase gene. *Cancer Res* 1999;**59**:826–30.
31. **Kyo S,** Takakura M, Takahiro T, *et al*. Sp1 cooperates with c-Myc to activate transcription of the human telomerase reverse transcriptase gene (hTERT). *Nucleic Acids Res* 2000;**28**:669–77.
32. **Huang TJ,** Lu CC, Tsai JC, *et al*. Novel autoregulatory function of hepatitis B virus M protein on surface gene expression. *J Biol Chem* 2005;**280**:27742–54.
33. **Sommer A,** Bousset K, Kremmer E, *et al*. Identification and characterization of specific DNA-binding complexes containing members of the Myc/Max/Mad network of transcriptional regulators. *J Biol Chem* 1998;**273**:6632–42.
34. **Stephen TO,** Saturo K, Laimonis AL. Telomerase activation by human papillomavirus type 16 E6 protein: induction of human telomerase reverse transcriptase expression through Myc and GC-rich Sp1 binding sites. *J Virol* 2001;**75**:5559–66.
35. **Chadeneau C,** Hay K, Hirte HW, *et al*. Telomerase activity associated with acquisition of malignancy in human colorectal cancer. *Cancer Res* 1995;**55**:2533–36.
36. **Zhan WH,** Ma JP, Peng JS, *et al*. Telomerase activity in gastric cancer and its clinical implications. *World J Gastroenterol* 1999;**5**:316–9.
37. **Wu KJ,** Grandori C, Amacker M, *et al*. Direct activation of TERT transcription by c-MYC. *Nat Genet* 1999;**21**:220–4.
38. **Saxena A,** Durgapal H, Chaudhuri V, *et al*. Hepatitis B virus surface (S) transactivator with DNA-binding properties. *J Med Virol* 2000;**61**:1–10.
39. **Dou YL,** Han JH, Li YZ, *et al*. Analysis of the correlation between PreS1-Ag, PreS2-Ag, HBeAg and HBV DNA in the serum of chronic hepatitis B patients. *Zhonghua Yi Xue Za Zhi* 2007;**87**:1984–6.
40. **Taliani G,** Rapicetta M, Francisci D, *et al*. Correlation of preS antigens and clinical status during chronic hepatitis B virus infection. *Med Microbiol Immunol* 1991;**180**:239–48.
41. **Ketan S,** Stephen K. Winged helix proteins. *Curr Opin Struct Biol* 2000;**10**:110–6.

Editor's quiz: GI snapshot

Robin Spiller, *Editor*

A Crohn's disease patient with pustules and fever

CLINICAL PRESENTATION

A woman in her thirties was recently diagnosed with Crohn's disease involving the oesophagus and colon. In addition, she had aphtous mouth ulcers and peri-anal fistulas. She was successfully treated with steroids, 6-mercaptopurine (6-MP) and infliximab. Two months later she presented with a flare-up of disease and recurrence of the mouth ulcers. In addition, she had fever up to 39°C, arthralgias and pustules on her back and buttocks (fig 1). Blood tests revealed an erythrocyte sedimentation rate (ESR) of 44 mm/h, C-reactive protein (CRP) of 65 mg/l and leucocytes of 13×10^9/litre. Blood, urinary and stool cultures as well as chest *x* ray did not reveal an infectious cause of the fever. Withdrawal of the 6-MP had no effect on the fever. The fistulas were not active upon magnetic resonance imaging (MRI). Joints were tender but not swollen. Dermatological investigation showed multiple purulent pustules. Cultures of the pustules were negative whereas skin biopsy showed a predominantly neutrophilic infiltrate of the dermis with admixture of histiocytes and lymphocytes.

QUESTIONS

(1) What skin lesions are shown here?
(2) What is the diagnosis?
See page 1564 for the answer

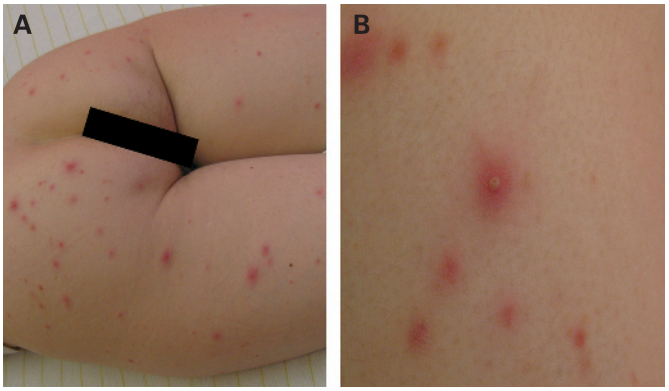

Figure 1 Pustular skin lesions (A); detail (B).

G Bouma,[1] S Neve,[2] N C T van Grieken,[3] C J Mulder,[1] T J Stoof[2]

[1] Department of Gastroenterology, Vrije Universiteit Medical Center, Amsterdam, The Netherlands; [2] Department of Dermatology, Vrije Universiteit Medical Center, Amsterdam, The Netherlands; [3] Department of Pathology, Vrije Universiteit Medical Center, Amsterdam, The Netherlands

Correspondence to: Dr G Bouma, Department of Gastroenterology, Vrije Universiteit Medical Center, De Boelelaan 1117, 1081 HV Amsterdam, The Netherlands; g.bouma@vumc.nl

Competing interests: None.

Patient consent: Obtained.

Provenance and peer review: Not commissioned; externally peer reviewed.

Gut 2009;**58**:1537. doi:10.1136/gut.2008.172205

88. **Watanabe I,** Tomita A, Shimizu M, *et al*. A study to survey susceptible genetic factors responsible for troglitazone-associated hepatotoxicity in Japanese patients with type 2 diabetes mellitus. *Clin Pharmacol Ther* 2003;**73**:435–55.
89. **Simon T,** Becquemont L, Mary-Krause M, *et al*. Combined glutathione-S-transferase M1 and T1 genetic polymorphism and tacrine hepatotoxicity. *Clin Pharmacol Ther* 2000;**67**:432–7.
90. **Senior J.** Regulatory perspectives, In: Kaplowitz N, ed. *Drug induced liver diseases*. New York: Marcel Dekker, 2003:739–54.
91. **Kaplowitz N.** Rules and laws of drug hepatotoxicity. *Pharmacoepidemiol Drug Saf* 2006;**15**:231–3.
92. **L Graham DJ,** Drinkard CR, Shatin D, *et al*. Liver enzyme monitoring in patients treated with troglitazone. *JAMA* 2001;**286**:831–3.
93. **Nolan CM,** Goldberg SV, Buskin SE. Hepatotoxicity associated with isoniazid preventive therapy: a 7 year survey from a public health tuberculosis clinic. *JAMA* 1999;**281**:1014–8
94. **Lee WM.** Acetaminophen toxicity: changing perceptions on a social/medical issue. *AASLD Public Policy* 2007;**46**:966–70.
95. **Hawkins LC,** Edwards JN, Dargan PI. Impact of restricting paracetamol pack sizes on paracetamol poisoning in the United Kingdom: a review of the literature. *Drug Safety* 2007;**30**:465–79.
96. **Krivoy N,** Taer M, Neuman MG. Antiepileptic drug-induced hypersensitivity syndrome reactions. *Curr Drug Safety* 2006;**1**:289–99.
97. **Hagley MT,** Benak RL, Hulisz DT. Suspected cross-reactivity of enalapril- and captopril-induced hepatotoxicity. *Ann Pharmacother* 1992;**26**:780–1.
98. **Andrejak M,** Davion T, Gineston JL, *et al*. Cross hepatotoxicity between non-steroidal anti-inflammatory drugs.*Br Med J (Clin Res Ed)* 1987;**295**:180–1.
99. **Keeffe EB,** Reis TC, Berland JE. Hepatotoxicity to both erythromycin estolate and erythromycin ethylsuccinate. *Dig Dis Sci* 1982;**27**:701–4.
100. **Remy AJ,** Larrey D, Pageaux GP, *et al*. Cross-hepatotoxicity between tricyclic antidepressants and phenothiazines. *Eur J Gastroenterol Hepatol* 1995;**7**:373–6.
101. **Larrey D,** Rueff B, Pessayre D, *et al*. Cross-hepatotoxicity between tricyclic antidepressants. *Gut* 1986;**27**:726–7.

Editor's quiz: GI snapshot

ANSWER

From the question on page 1537

The patient was diagnosed with the bowel-associated dermatosis arthritis syndrome (BADAS). It was first described in patients undergoing ileojejunal bypass surgery for morbid obesity[1] and since then in various other intestinal disorders,[2] including occasionally in inflammatory bowel disease (IBD).[3 4] Clinical presentation is heterogeneous, but is usually characterised by sterile pustular skin lesions, fever, diarrhoea, arthritis, and eye inflammation. The symptoms generally disappear once the intestinal manifestations ameliorate. Skin lesions characteristically consist of small erythematous lesions with a perivascular neutrophilic infiltrate and dermal oedema (fig 1). Histological features however are non-specific and clinical history is essential for a correct diagnosis. The aetiology is believed to be related to bacterial overgrowth leading to the formation and deposition in skin and synovia of circulating immune complexes and subsequent activation of neutrophilic granulocytes.[5]

As in this patient, BADAS usually responds well to high-dose steroids. It may also respond to antibiotics. Antibiotics have been reported to be beneficial in up to 50% of patients with BADAS after bypass surgery, although the response has been inconsistent.[6] As far as we know, the therapeutic effect of antibiotics in patients with IBD and BADAS has not been evaluated. Since the pathophysiology is presumed to be similar in both disease entities, a course of antibiotics could be tried in patients with IBD and BADAS. The patient presented here had no clinical manifestations that might predispose her to bacterial overgrowth; however, she was not formally tested to exclude this possibility. Given the severity of her symptoms, treatment was initiated with high-dose corticosteroids (40 mg prednison/day). The fever disappeared instantly while the skin manifestations completely resolved within 1 week. Steroids were slowly tapered and symptoms have not recurred since then.

In conclusion, it is important to consider the possibility of a BADAS in patients with IBD who have unexplained fever and skin lesions because treatment may lead to prompt resolution of the symptoms and prevent an exhaustive search for other causes of fever.

Gut 2009;**58**:1564. doi:10.1136/gut.2008.172205a

REFERENCES

1. **Dicken CH,** Seehafer JR. Bowel bypass syndrome. *Arch Dermatol* 1979;**115**:837–9.
2. **Jorizzo JL,** Apisarnthara P, Subrt P, *et al*. Bowel-bypass syndrome without bowel bypass. Bowel-associated dermatosis arthritis syndrome. *Arch Intern Med* 1983;**143**:457–61.
3. **Delaney TA,** Clay CD, Randell PL. The bowel -associated dermatosis–arthritis syndrome. *Australas J Dermataol* 1989;**30**:23–7.
4. **Ashok D,** Kiely P. Bowel associated dermatosis–arthritis syndrome: a case report. *J Med Case Reports* 2007;**1**:81.
5. **Ely PH.** The bowel bypass syndrome: a response to bacterial peptidoglycans. *J Am Acad Dermatol* 1980;**2**:473–87.
6. **Stein HB,** Schlappner OL, Boyko W, *et al*. The intestinal bypass: arthritis–dermatitis syndrome. *Arthritis Rheum* 1981;**24**:684–90.

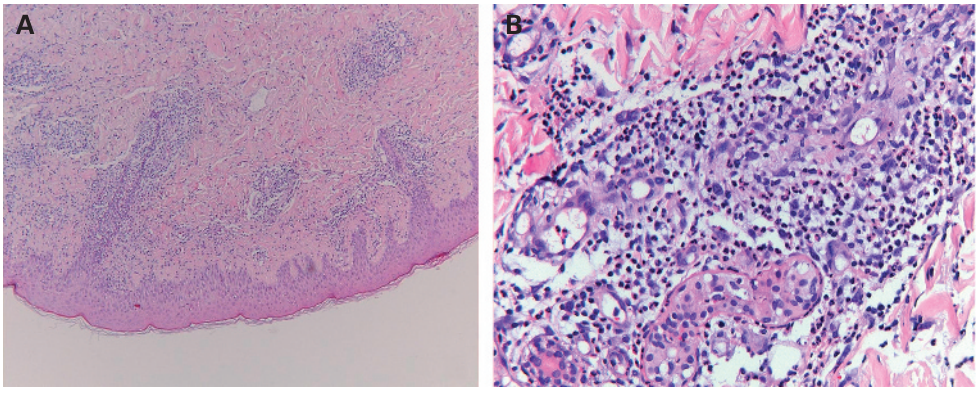

Figure 1 Haematoxylin & eosin stained photomicrograph of the dermis and epidermis demonstrating a perivascular and perifollicular neutrophilic infiltrate. Magnification: (A) ×2.5; (B) ×20.