



Editorial

Skin manifestations of liver diseasesA. Koulaouzidis;¹ S. Bhat;² J. Moschos³**Introduction**

Both acute and chronic liver disease can manifest on the skin. The appearances can range from the very subtle, such as early finger clubbing, to the more obvious such as jaundice. Identifying these changes early on can lead to prompt diagnosis and management of the underlying condition. In this pictorial review we will describe the skin manifestations of specific liver conditions illustrated with appropriate figures.

General skin findings in liver disease

Chronic liver disease of any origin can cause typical skin findings. Jaundice, spider nevi, leuconychia and finger clubbing are well known features (*Figures 1 a, b and 2*). Palmar erythema, “paper-money” skin (*Figure 3*), rosacea and rhinophyma are common but often overlooked by the busy practitioner. More subtle signs include scratch marks, loss of axillary hair and gynaecomastia. Ascites can lead to striae (*Figure 4*) and an umbilical hernia (*Figure 5*).

Skin findings in Primary Biliary Cirrhosis (PBC)

Xanthelasmas are collections of lipid-laden histiocytes deposited in the upper and lower eyelids (*Figure 6*). They can be florid and are usually idiopathic. There is a firm connection between PBC and hypercholesterolemia, which can explain the tendency of these patients to de-

velop both xanthelasmas and cutaneous xanthomas (5%) (*Figure 7*).¹ Other disease-associated skin manifestations, but not as frequent, include the sicca syndrome and vitiligo.² Melanosis and xerodermia have been reported. PBC may also rarely present with a cutaneous vasculitis (*Figures 8 and 9*).³⁻⁵

Alcohol related liver disease

Dupuytren’s contracture was described initially by the French surgeon Guillaume Dupuytren in the 1830s. Although it has other causes, it is considered a strong clinical pointer of alcohol misuse and its related liver damage (*Figure 10*).⁶ Therapy options other than surgery include simvastatin, radiation, N-acetyl-L-cysteine.^{7,8} Facial lipodystrophy is commonly seen as alcohol replaces most of the caloric intake in advanced alcoholism (*Figure 11*).

Porphyria cutanea tarda (PCT) is the commonest of the porphyrias and results from deficiency of the enzyme uroporphyrinogen decarboxylase (UROD).⁹ The terms porphyrin and porphyria are derived from the Greek word “*πορφύρεος*” which means purple. The blistering rash develops in sun-exposed areas and increased local hair growth eventually appears (*Figure 12*). Alcohol remains the best known trigger factor –especially in patients with concurrent HCV infection- and complete abstinence is advisable.

Viral hepatitis

HCV association with extrahepatic manifestations can occur in one third of patients with chronic infection and is generally seen in the late stages of the disease.¹⁰ Cryoglobulinemia, polyarthritis nodosa (*Figure 8*), leucocytoclastic vasculitis (*Figure 13*), urticaria and porphyria cutanea tarda (*Figure 12*) are the classic skin manifestations of chronic HCV and less frequently HBV infection.^{11,12}

Hemochromatosis

Iron is deposited in multiple organs including the skin. ‘Slate grey’ skin is often used to describe the typical skin manifestation of hemochromatosis. The term

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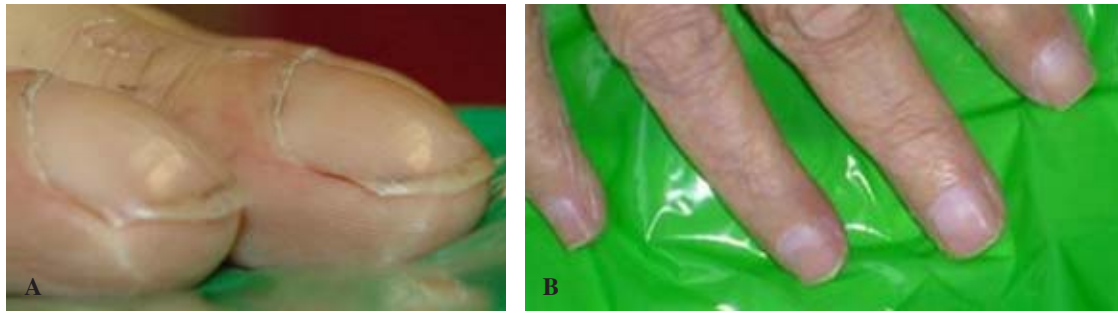


Figure 1. A. Gross clubbing in patient with alcohol-related liver cirrhosis (Koulaouzidis A, Said E. Clubbing in a patient with liver disease. Saudi Med J 2007 Mar; 28: 481-2, with permission). B. (amendum) – Terry's nails or half-and-half nails/associated with hypoalbuminaemia in patient with cirrhosis.



Figure 2. Close up view of the central arteriole (punctum) of a spider naevus (from Color Atlas & Synopsis of Clinical Dermatology, 4the, Fitzpatrick et al., with permission).



Figure 4. Dilated superficial veins network and stretch marks in patient with ascites.



Figure 3. Fine "paper-money" skin appearance of cheeks and nasolabial folds, hypertrichosis and bilateral parotid enlargement in patient with alcohol-related liver disease.



Figure 5. Umbilical hernia in patient with gross ascites.



Figure 6. Bilateral xanthelasmata of upper eyelids (Macias-Rodriguez RU, Torre-Delgadillo A. Xanthelasmas and xanthomatas striatum palmare in primary biliary cirrhosis. *Ann Hepatol.* 2006 Jan-Mar; 5: 49, with permission).



Figure 9. Pustular vaculitis – discrete, red papules and pustules in a patient with primary biliary cirrhosis (Koulaouzidis et al., from *Annals of Hepatology* 2006; 5(3), with permission).



Figure 7. Papular eruptive xanthomas—multiple, discrete, papules becoming confluent at the level of elbow (from *Color Atlas & Synopsis of Clinical Dermatology*, 4the, Fitzpatrick et al., with permission).



Figure 10. Dupuytren's contracture (Macias-Rodriguez RU, Torre-Delgadillo A. Xanthelasmas and xanthomatas striatum palmare in primary biliary cirrhosis. *Ann Hepatol.* 2006 Jan-Mar; 5: 49, with permission).



Figure 8. Polyarteritis nodosa – multiple, confluent, dermal and subcutaneous nodules with ulceration on the medial aspect of the lower legs (from *Color Atlas & Synopsis of Clinical Dermatology*, 4the, Fitzpatrick et al., with permission).



Figure 11. Marked facial lipodystrophy in patient with alcohol-related liver disease due to protein-energy malnutrition.



Figure 12. Porphyria cutanea tarda – periorbital and malar violaceous coloration, hyperpigmentation and hypertrichosis on the face with bullae and scars on the dorsum of the hands (from Color Atlas & Synopsis of Clinical Dermatology, 4the, Fitzpatrick et al., with permission).

“bronze diabetes” was also used to describe the classic presentation. With the advent of blood testing for the diagnosis of hemochromatosis the term has become obsolete. Multiple organ involvement is seen less commonly now that genetic screening of relatives is commonplace. Treatment with venesection in the presymptomatic stage of the disorder is advocated.

Conclusion

The skin is the largest organ in the body and if examined too briefly this will lead to subtle changes that can be missed. In the modern era, where laboratory and radiological investigations are close at hand, the art of clinical medicine is practiced less often. Identifying these fascinating clinical signs not only aids in making a diagnosis but provides satisfaction to the clerking physician.

References

1. Macias-Rodriguez RU, Torre-Delgadillo A. Xanthelasma and xanthomas striatum palmare in primary biliary cirrhosis. *Ann Hepatol* 2006; 5(1): 49.
2. Zauli D, Crespi C, Barzagli M, et al. Vitiligo and biliary cirrhosis. *Am J Gastroenterol* 1986; 81(1): 91.
3. Terkeltaub R, Esdaile JM, Bruneau C, Danoff D, Watters AK. Vasculitis as a presenting manifestation of primary biliary cirrhosis: a case report. *Clin Exp Rheumatol* 1984; 2(1): 67-73.



Figure 13. Leucocytoclastic vasculitis-discrete red/purple plaque with fine scales on its surface.

4. Diederichsen H, Sorensen PG, Mickley H, Hage E, Schultz-Larsen F. Petechiae and vasculitis in asymptomatic primary biliary cirrhosis. *Acta Derm Venereol* 1985; 65(3): 263-6.
5. Koulaouzidis A, Campbell S, Bharati A, Leonard N, Azurdia R. Primary biliary cirrhosis associated pustular vasculitis. *Ann Hepatol* 2006; 5(3): 177-8.
6. Sanderson PL, Morris MA, Stanley JK, Fahmy NR. Lipids and Dupuytren's disease. *J Bone Joint Surg Br* 1992; 74(6): 923-7.
7. Kopp J, Seyhan H, Muller B, Lanczak J, Pausch E, Gressner AM, Dooley S, et al. N-acetyl-L-cysteine abrogates fibrogenic properties of fibroblasts isolated from Dupuytren's disease by blunting TGF-beta signalling. *J Cell Mol Med* 2006; 10(1): 157-65.
8. Adamietz B, Keilholz L, Grunert J, Sauer R. Radiotherapy of early stage Dupuytren disease. Long-term results after a median follow-up period of 10 years [Article in German]. *Strahlenther Onkol* 2001; 177(11): 604-10.
9. Rossmann-Ringdahl I, Olsson R. Porphyria cutanea tarda in a Swedish population: risk factors and complications. *Acta Derm Venereol* 2005; 85(4): 337-41.
10. García-Carrasco M, Escárcega RO. Extrahepatic autoimmune manifestations of chronic hepatitis C virus infection. *Ann Hepatol* 2006; 5(3): 161-3.
11. Sterling RK, Bralow S. Extrahepatic manifestations of hepatitis C virus. *Curr Gastroenterol Rep* 2006; 8(1): 53-9.
12. Han SH. Extrahepatic manifestations of chronic hepatitis B. *Clin Liver Dis* 2004; 8(2): 403-18.