Michael Babich, MD, Series Editor

Beyond Jaundice Part 2: Recognizing Dermatologic Findings in Chronic Liver Diseases

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Chronic liver disease is often accompanied by cutaneous findings indicative of underlying pathology. However, in addition to the many widely-known and recognizable dermatologic manifestations, there exists a multitude of subtle, lesser-known findings which warrant increased attention. Recognition of these dermatologic findings is invaluable, as they contribute to the diagnostic picture and can aid in prioritization of the differential diagnosis. It is vital for providers across specialties to be able to recognize and describe such lesions in order to help reduce diagnostic delay and hasten time to treatment. In this article, we present the associated cutaneous findings for common liver diseases including autoimmune hepatitis, Wilson's disease, hemochromatosis, alpha-1 antitrypsin deficiency, primary biliary cholangitis, primary sclerosing cholangitis, and metabolic dysfunction-associated steatotic liver disease.

INTRODUCTION

Liver disease continues to have a significant impact on public health, both in the United States and globally.[1] In the United States, chronic liver disease and cirrhosis represent the 10th leading cause of death, just behind kidney disease and diabetes, and continue to account for a significant portion of overall healthcare expenditures.[2–4] Given the pathophysiology of liver diseases, dermatologic manifestations are both common and multitudinous. These cutaneous findings are crucial to identify, given that they may represent some of the earliest indicators of underlying dysfunction.[6] For providers outside of the specialty of dermatology, learning how to both recognize and accurately describe lesions is paramount to ensuring timely diagnosis. In this review, we present associated cutaneous findings of

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several common forms of chronic liver disease with discussion of lesion description, etiopathogenesis, and significance. Also included are brief summaries regarding appropriate management of dermatologic lesions.

Autoimmune Hepatitis

Vitiligo

In patients with autoimmune hepatitis (AIH), there is significant overlap with other autoimmune disorders. Following autoimmune thyroid disease, skin diseases are most commonly-reported.[7,8] Vitiligo is the most well-known of these associations, as ~23% of patients with vitiligo have a comorbid autoimmune disease. Patients with more extensive vitiligo tend to have a greater likelihood of being diagnosed with at least one comorbid autoimmune disease.[9] Multiple case reports have documented AIH occurring in association with vitiligo, and a 2017 systematic review identified vitiligo as having a particularly strong association with type 2 AIH.[10–12] Vitiligo presents as depigmented, coalescing macules and patches with well-defined borders, more common in sun-exposed areas or regions prone to repetitive trauma such as intertriginous skin **[Figure 1]**. Vitiligo treatment is varied and may include topical treatments such as corticosteroids, calcineurin inhibitors, ruxolitinib cream, UVB phototherapy, depigmentation therapy, or surgical approaches involving grafting.[13]

Pyoderma gangrenosum

Pyoderma gangrenosum is a neutrophilic dermatosis which occurs in association with systemic disease in at least 50% of cases. Upregulation of several proinflammatory and chemotactic cytokines including interleukin-8 have been identified in affected skin.[14] Lesions begin as single, small papules/pustules before rapidly developing into large, painful ulcers with violaceous, undermined borders and surrounding erythema. Ulcers often feature a purulent, exudative base which can develop into exuberant granulation tissue over several weeks **[Figure 2]**. Multiple case reports have described the association of pyoderma gangrenosum with AIH, noting its development even in periods of quiescent disease.[15–17] Recommended laboratory investigations in pyoderma patients consequently include liver function tests and a full hepatitis panel.[18] Treatment requires expert wound care and pain management. Early, uncomplicated wounds may be treated with topical corticosteroids or tacrolimus ointment. As lesions progress, systemic steroids as well as biologics may be utilized. Patients should be referred to dermatology for optimal management.[19]

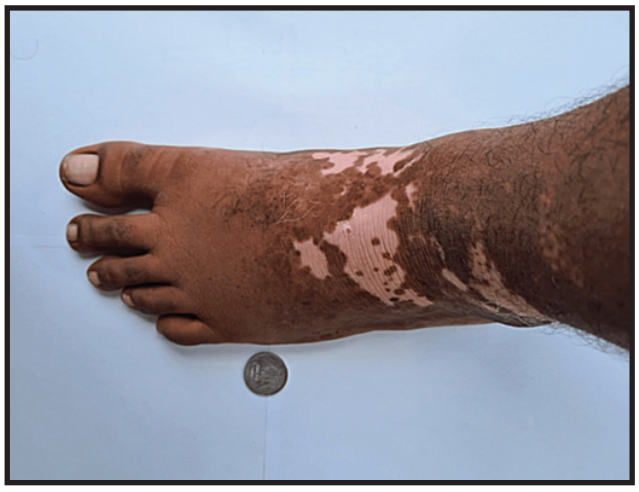

Figure 1. Vitiligo
Figure from Nimkar P, Wanjari A. Vitiligo and the Role of Newer Therapeutic Modalities. Cureus 2022;14(11): e31022. doi:10.7759/cureus.31022 (CC BY 4.0).
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Hemochromatosis

Hyperpigmentation/bronzing

Hemochromatosis is an autosomal recessive condition involving mutations to the HFE gene which ultimately leads to iron overload with deposition in tissues. Over 90% of patients with hemochromatosis develop skin hyperpigmentation. This pigmentation has a particular bronze hue, leading to coining of the term "bronze diabetes" to describe hemochromatosis. Hyperpigmentation often develops several years prior to other disease features, and may be the only sign of disease. Pigmentation is common on sun-exposed skin, and may be most evident on the face and dorsal hands **[Figure 3]**.[20] Treatment for pigmentary changes is the same as treatment for hemochromatosis as a

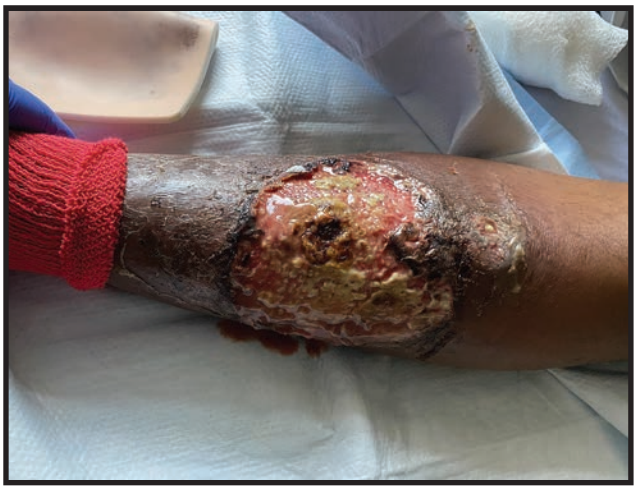

Figure 2. Pyoderma Gangrenosum
Figure from Wallace C E, Sharma A. Pyoderma Gangrenosum in an African American Male Initially Presenting as Sepsis. Cureus 2022;14(1): e21592. doi:10.7759/cureus.21592 (CC BY 4.0).
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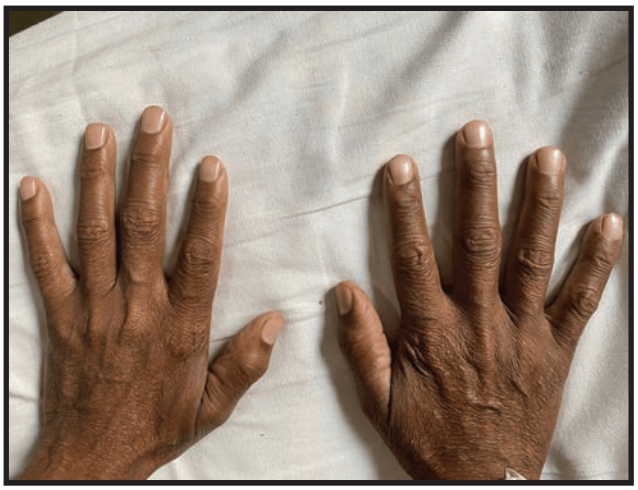

Figure 3. Cutaneous Bronzing
Figure from Batool M, Ehsan N, Imran M, et al. The Quiet Burden of Iron: A Rare Case of Hereditary Hemochromatosis in Pakistan. Cureus 2025;17(7): e88355. doi:10.7759/cureus.88355 (CC BY 4.0).
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whole; regular phlebotomy/venesection has been shown to gradually reverse cutaneous bronzing.[21]

Alopecia

Cases of alopecia areata, alopecia universalis, and scarring alopecia have all been reported in patients with hemochromatosis. In one study, 62% of patients reported partial hair loss while 12% noted complete hair loss.[22] Alopecia areata involves acute-onset, focal hair loss in well-demarcated round patches. Broken hair strands that appear to thin as they enter the scalp, or "exclamation point hairs", may be observed at the periphery of bald patches **[Figure 4].** It may be advantageous to collect iron studies in alopecia patients at greater risk for hemochromatosis such as those with a family history and the typical demographic profile.[23] Regarding treatment, topical immunotherapies such as diphenylcyclopropenone, topical or intralesional corticosteroids, and/or phlebotomy have been shown to provide satisfactory results in hemochromatosis patients.[21]

Ichthyosis

Ichthyosiform changes have been noted as a prominent skin finding in patients with hemochromatosis. A 2024 systematic review found that 46/100 hemochromatosis patients reported ichthyosis-like changes of the skin.[21] Pathogenesis involves transepidermal water loss and compensatory epidermal hyperproliferation as a result of impaired barrier function. The appearance of this cutaneous finding in hemochromatosis patients is similar to ichthyosis vulgaris, with extremely dry, thickened skin and "fish-like" scales **[Figure 5]**. Treatment may include salt water baths, exfoliation to remove scale, and moisturizing creams containing agents such as alpha-hydroxy acids, salicylic acid, or high-dose urea applied to damp skin. Topicals may be used alone or in combination with retinoids to help promote skin cell turnover.[24]

Koilonychia

Koilonychia is an upward eversion of the latero-distal nail plate with central depression. Nails are thin, brittle, and commonly referred to as "spoon-shaped" or concave **[Figure 6]**. Adult-onset koilonychia may be associated with iron deficiency anemia or hemochromatosis; this should prompt further investigation via a complete blood count and ferritin level in those without a clearly associated illness.[25] Koilonychia has been noted in approximately 49% of hemochromatosis patients,

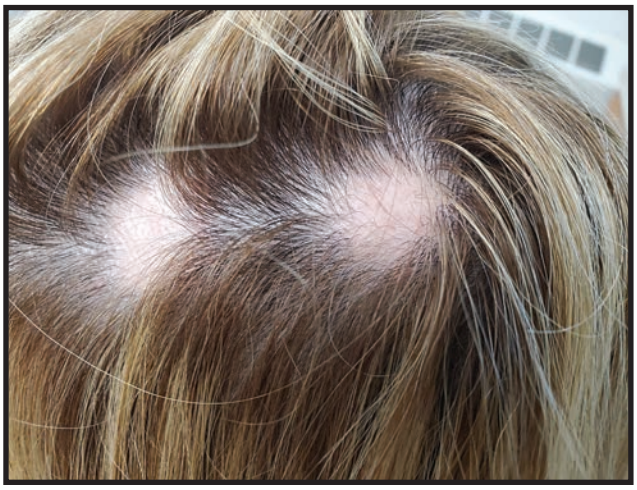

Figure 4. Alopecia Areata
Figure from Chang A H, Brownstone N D, Hsu S. Drug-Induced Alopecia Areata From Upadacitinib. Cureus 2024;16(8): e66647. doi:10.7759/cureus.66647 (CC BY 4.0).
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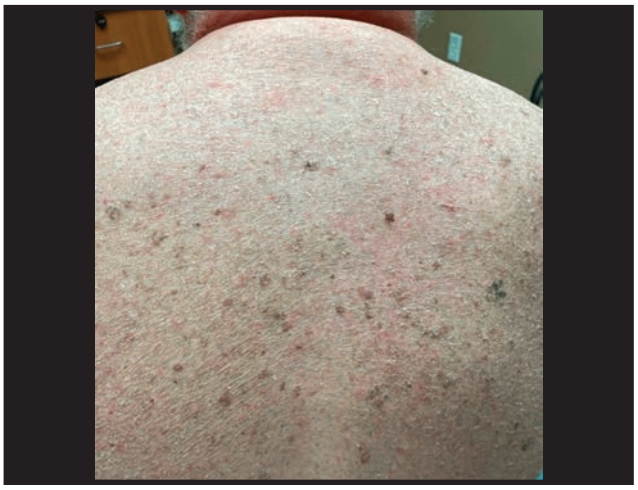

Figure 5. Ichthyosis
Figure from Arora N, Nguyen K, Hudson A, et al. Ichthyosis Skin Changes in a Patient With Hereditary Hemochromatosis. Cureus 2024; 16(1): e52823. doi:10.7759/cureus.52823 (CC BY 4.0).
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and may occur at any point during the disease course. Koilonychia is treated by addressing its underlying cause, though phlebotomy in the case of hemochromatosis does not appear to have a significant effect.[22]

Wilson's Disease

Lower extremity hyperpigmentation

Patchy hypermelanotic pigmentation has been reported as being the most distinctive cutaneous

Table 1. Liver Diseases and Associated Dermatologic Manifestations

Liver Disease	Associated Dermatologic Findings
Autoimmune Hepatitis	• Vitiligo • Pyoderma gangrenosum
Hemochromatosis	• Hyperpigmentation/bronzing • Alopecia • Ichthyosis • Koilonychia
Wilson's Disease	• Lower extremity hyperpigmentation • Azure lunulae
Alpha-1 Antitrypsin Deficiency	• Panniculitis
Primary Biliary Cholangitis	• Pruritis: excoriations, post-inflammatory hyperpigmentation, butterfly sign • Xanthomas: xanthelasma palpebrarum, tuberous, tendinous, xanthoma striata palmaris • Extrahepatic autoimmune disease: systemic sclerosis, psoriasis, Sjögren's syndrome
Primary Sclerosing Cholangitis	• Inflammatory bowel disease overlap: erythema nodosum, pyoderma gangrenosum
Metabolic Dysfunction-Associated Steatotic Liver Disease	• Psoriasis • Acanthosis nigricans

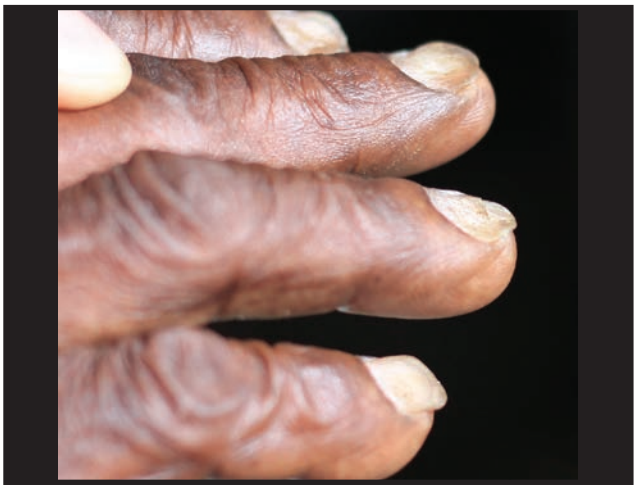

Figure 6. Koilonychia
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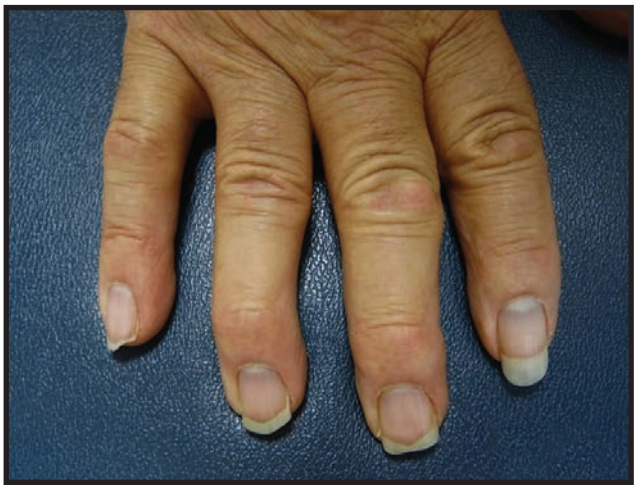

Figure 7. Azure Lunulae
Figure from Slater K, Sommariva E, Kartono F. A Case Study of Argyria of the Nails Secondary to Colloidal Silver Ingestion. Cureus 2022;14(10): e30818. doi:10.7759/cureus.30818 (CC BY 4.0).
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manifestation of Wilson's disease. A prospective study of patients with Wilson's disease found that ~30% developed hyperpigmentation.[26] This form of hyperpigmentation presents as grey-brown, coalescing macules/patches with a rippled appearance over the anterior aspect of the lower extremities, though more diffuse hyperpigmentation has also been reported.[27–29] Cutaneous changes are found more frequently in patients with hepatic Wilson's disease, and histopathological analysis shows increased melanin deposition with normal iron and copper content.[30] A 2022 paper by Tiwari at al. suggests that hyperpigmentation could be an early sensitive marker for Wilson's disease. Cutaneous lesions may improve with chelating agents, though most case reports note persistent hyperpigmentation despite treatment.[31]

Azure lunulae

Azure lunulae, or "blue nails", were first described in 1958 by Drs. Beam and McKusick as a distinctive and diagnostic sign of Wilson's disease.[32] While no longer considered "diagnostic", azure lunulae are reported to occur in ~10% of patients with Wilson's disease, and may aid in its detection.[33] Azure lunulae describes a bluish, non-blanching discoloration that is restricted to the nail lunula, the visible part of the distal nail matrix that extends past the proximal nail fold **[Figure 7]**. In a 2020 case report, the authors noted that these nail changes served as an important diagnostic clue which led them to consider and ultimately diagnose a 24-year-old patient with Wilson's disease.[34] The exact pathophysiology behind azure lunulae is unclear, and there is no specific treatment.

Alpha-1 Antitrypsin Deficiency

Panniculitis

In the 1930s, the first association was made between panniculitis and alpha-1-antitrypsin deficiency (A1AD). While rare, over 120 additional cases have since been reported.[35] This association may be explained by the same protease/antiprotease imbalance that causes A1AD lung disease, wherein increased activity of proteolytic enzymes leads to localized tissue destruction. Supporting this claim is the fact that A1AD panniculitis has been shown to improve with intravenous alpha-1 antitrypsin augmentation therapy (IV-AAT), plasma exchange, and liver transplant.[36,37] A1AD panniculitis is considered "necrotizing panniculitis", and begins with painful, erythematous nodules – typically

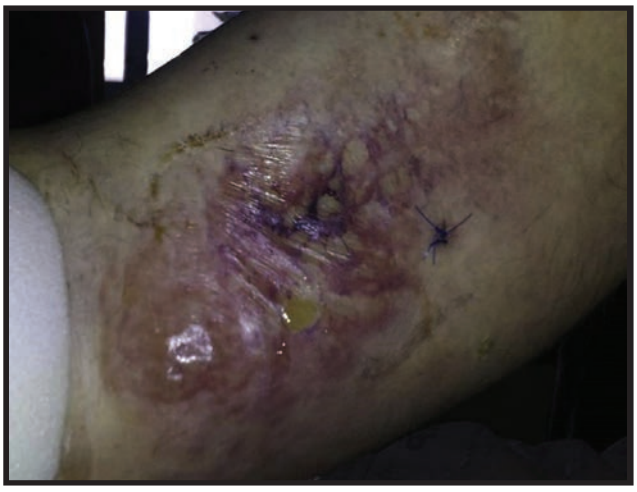

Figure 8. Necrotizing Panniculitis
Figure from Franciosi AN, Ralph J, O'Farrell NJ, et al. Alpha-1 antitrypsin deficiency-associated panniculitis. J Am Acad Dermatol. 2021;87:825-832. (CC BY 4.0).
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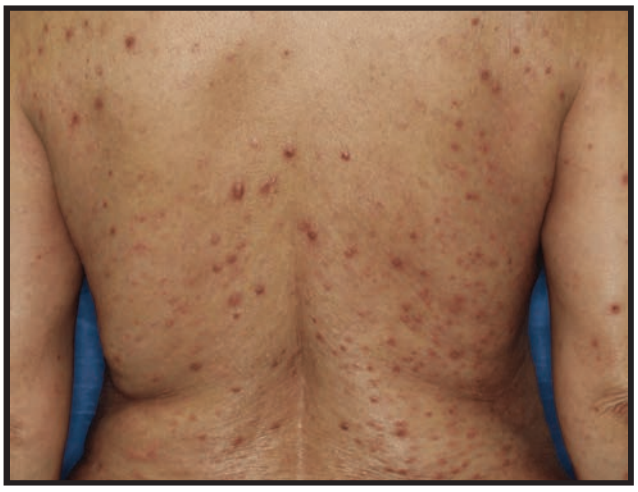

Figure 9. Butterfly Sign
Figure from Ogawa H, Izumi K. Dupilumab-Induced Psoriasis in a Patient With Prurigo Nodularis: A Case Report. Cureus 2025;17(4): e81636. doi:10.7759/cureus.81636 (CC BY 4.0).
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of the proximal extremities – which develop into large, ulcerated lesions that produce an oily, yellow exudate **[Figure 8]**. A1AD panniculitis possesses distinct histopathological features, and analysis of plasma alpha-1 antitrypsin levels in all cases of necrotizing panniculitis has been recommended. Patients should be referred to dermatology for histopathologic investigation and clinical correlation.[38] Dapsone is widely recommended as first-line therapy given its efficacy and affordability, though tetracycline antibiotics – specifically doxycycline or minocycline – may also be effective given their anti-collagenase activity. Still, IV-AAT remains the most efficacious overall treatment, especially in severe or refractory cases.[35]

Primary Biliary Cholangitis

Pruritis: excoriations, post-inflammatory hyperpigmentation, butterfly sign

Pruritis is noted by 50-75% of patients with primary biliary cholangitis (PBC) as being their first or most prominent symptom. Pruritis can lead to several cutaneous findings including excoriations, post-inflammatory hyperpigmentation, and the classic "butterfly sign."[39] Post-inflammatory hyperpigmentation is a temporary pigmentation that follows injury to the skin. It is primarily observed in darker skin types, and takes on the size/shape of the original injury, such as excoriations from excessive scratching. The "butterfly sign" was first described by hepatologist Dr. Telfer Reynolds when he noticed a butterfly-shaped sparing of skin on the back of a patient with PBC who had generalized pruritus. This rash is actually the result of post-inflammatory hyperpigmentation, as the butterfly-shaped area of relative hypopigmentation represents a region of the back that the patient is unable to scratch **[Figure 9]**.[40] Beyond treatment of underlying PBC, daily application of SPF 50+ sunscreen is important for minimizing further darkening. A variety of topical treatments are also available to lighten hyperpigmented lesions, including hydroquinone, tretinoin cream, and corticosteroids. For severe or refractory cases, consider chemical peels or laser therapy.[41]

Xanthomas: xanthelasma palpebrarum, tuberous, tendinous, xanthoma striata palmaris

Dyslipidemia is a common feature of PBC, seen in 75% of patients as a result of multiple factors

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including accumulation of lipoprotein X. As a result, patients may present with similar types of xanthomas as seen in types II-III hyperlipidemia, such as xanthelasma palpebrarum, tuberous xanthomas, tendinous xanthomas, or xanthoma striatum palmare.[42] Xanthelasma palpebrarum are most common, seen as soft, yellow-orange macules, papules, or plaques around the medial canthus of the upper eyelid **[Figure 10]**. Palmar xanthomas (xanthoma striata palmaris) present as yellow-orange accentuations of the palmar and wrist creases. Tuberous xanthomas are firm, painless, red-yellow single nodules or multilobulated masses that develop over the knees, elbows, or heels. Tendinous xanthomas present as slowly enlarging subcutaneous nodules typically attached to extensor tendons on the dorsal hands or on the achilles tendons. They are smooth, firm, and mobile, with normal overlying skin **[Figure 11]**. Xanthomas may improve with treatment of underlying hypercholesterolemia. However, other treatments can include topical trichloroacetic acid, electrodessication, cryotherapy, laser vaporization, or excision.[42,43]

Extrahepatic autoimmune disease: systemic sclerosis, Sjögren's syndrome, psoriasis

Up to 73% of patients with PBC report having one or more extrahepatic autoimmune diseases. Liver function abnormalities observed during treatment of extrahepatic autoimmune disease should prompt consideration of comorbid PBC.[44] Many papers have demonstrated an association between PBC and autoimmune conditions with characteristic dermatologic findings.[45–49] Up to 25% of systemic sclerosis patients are positive for PBC-specific antimitochondrial antibodies, 13% of psoriasis patients have concurrent PBC, and up to 73% of patients with Sjögren's syndrome develop comorbid PBC.[46,50,51] Systemic sclerosis can manifest with numerous cutaneous findings including sclerodactyly (thickening and tightness of the skin of the digits) **[Figure 12]**, microstomia, or digital calcinosis. Patients should be referred to dermatology for management. Cutaneous manifestations of Sjögren's syndrome include xerosis, hypohidrosis, and small vessel/urticarial vasculitis of the lower extremities. Dermatologic

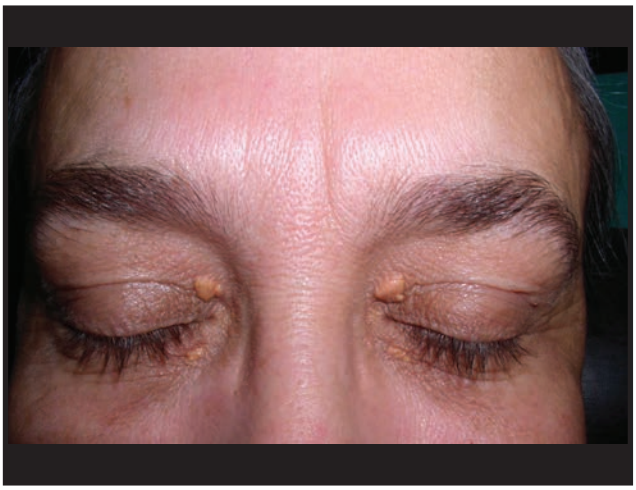

Figure 10. Xanthelasma Palpebrarum
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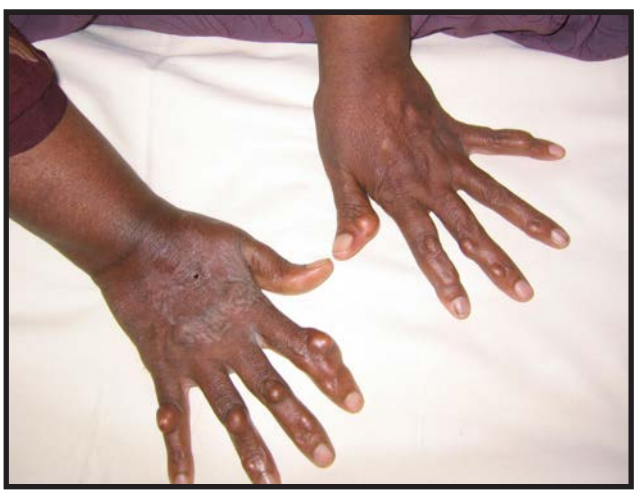

Figure 11. Tendinous Xanthomas
Figure from "Multiple hand xanthomas 18 yo case report" by Anita A Kumar, Ghanshyam Palamaner, Subash Shantha, Yadav Srinivasan, N Senthil, K Rajkumar, Neeta Paunikar, and MK Sudhakar, licensed under CC BY 2.0.
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treatment is limited to soap and detergent avoidance, with emollients and humectants for xerosis. Plaque psoriasis involves symmetrically distributed, pink-red plaques with silvery scale and well-defined borders, typically on extensor surfaces **[Figure 13]**.

Treatment may include topical corticosteroids, phototherapy, or biologic agents. Biologic agents can be particularly effective in cases of severe disease; etanercept may actually reduce AST:ALT, improve insulin sensitivity, and reduce hepatic fibrosis risk. Adalimumab and ustekinumab are also safe for use, however, infliximab should be used with caution in patients with liver failure.

Primary Sclerosing Cholangitis

Inflammatory bowel disease overlap: erythema nodosum, pyoderma gangrenosum

Primary sclerosing cholangitis (PSC) has a strong association with inflammatory bowel disease (IBD), with approximately 60%-80% of patients having coexisting ulcerative colitis (UC).[52] Conversely, PSC is diagnosed in 2-14% of patients with IBD. The two most common cutaneous manifestations of IBD, also seen in PSC patients, are erythema nodosum and pyoderma gangrenosum. Erythema nodosum presents as tender, erythematous nodules, 1-5cm in diameter, on the bilateral anterior tibia **[Figure 14]**. Pathogenesis is considered to involve a form of hypersensitivity reaction. Most lesions resolve within 8 weeks, though treatment of underlying IBD may lead to accelerated improvement. Pain management with colchicine, NSAIDs (with caution in patients with IBD, as they may trigger disease flare-up), and venous compression therapy may be helpful. Additionally, oral potassium iodide can be given to reduce lesion inflammation. Pyoderma gangrenosum is the second-most common cutaneous manifestation of IBD. See the section on "Autoimmune Hepatitis" above for specifics regarding clinical features and management of pyoderma lesions **[Figure 2]**.[53]

Metabolic Dysfunction-Associated Steatotic Liver Disease

Psoriasis

Metabolic Dysfunction-Associated Steatotic Liver Disease (MASLD) affects 20-30% of the general population, but has been reported to affect up to 50% of patients with psoriasis.[54] Notably, higher PASI scores (indicating greater extent and severity of psoriasis) have been associated with a greater likelihood of comorbid MASLD. This association

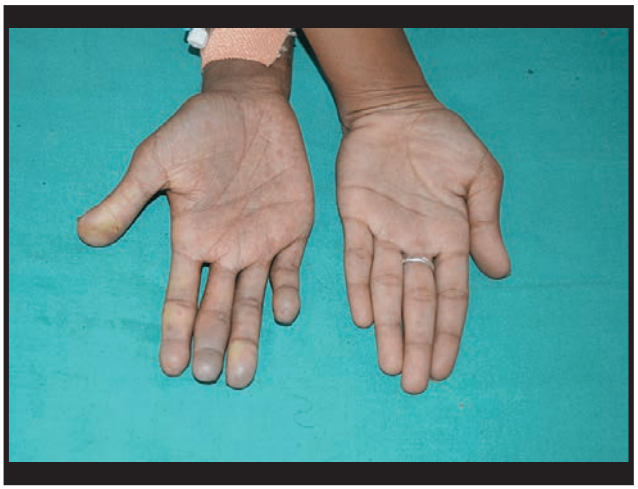

Figure 12. Systemic Sclerosis
Figure from Ganjre S, Madke B, Prakashey A, et al. Systemic Sclerosis Presenting With Frank Exhibition of Mizutani's Sign. Cureus 2023;15(9): e45387. doi:10.7759/cureus.45387 (CC BY 4.0).
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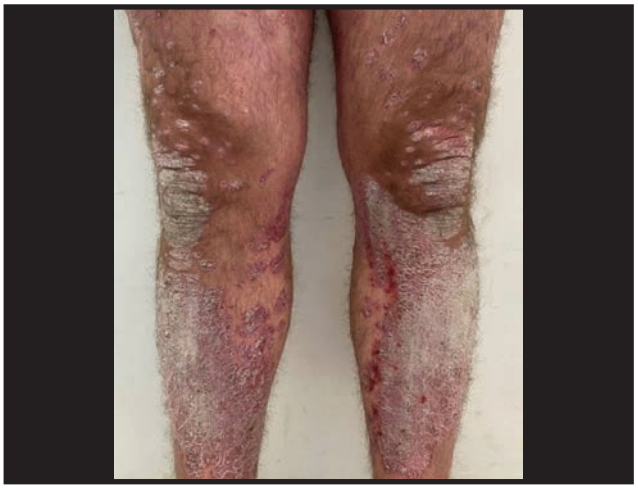

Figure 13. Plaque Psoriasis
Figure from Bellinato F, Chiricozzi A, Piaserico S, Targher G, Gisondi P. Could Targeted Pharmacotherapies Exert a "Disease Modification Effect" in Patients with Chronic Plaque Psoriasis? Int J Mol Sci. 2022; 23(21):12849. https://doi.org/10.3390/ijms232112849 (CC BY 4.0).
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has been hypothesized to relate to a "hepato-dermal axis" wherein hepatic inflammatory cytokines stimulate keratinocyte hyperproliferation in the skin and/or pro-inflammatory cytokine release

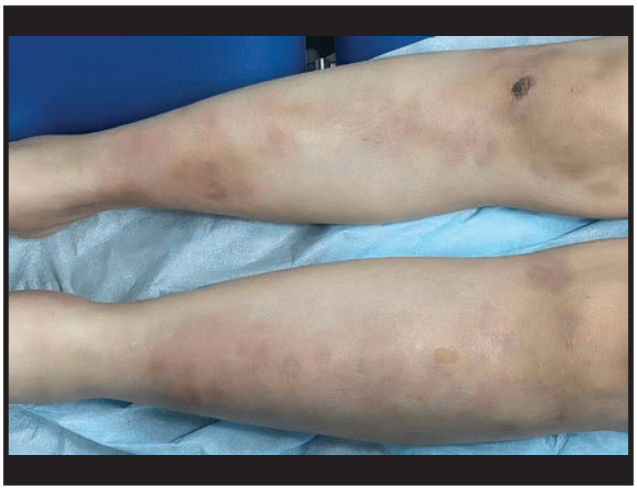

Figure 14. Erythema Nodosum
Figure from Alghamdi N, Alamrie R M, Alshafie A Y, et al. Delayed Recurrent Erythema Nodosum Following COVID-19 Vaccine: A Case Report. Cureus 2023;15(7): e42776. doi:10.7759/cureus.42776 (CC BY 4.0).
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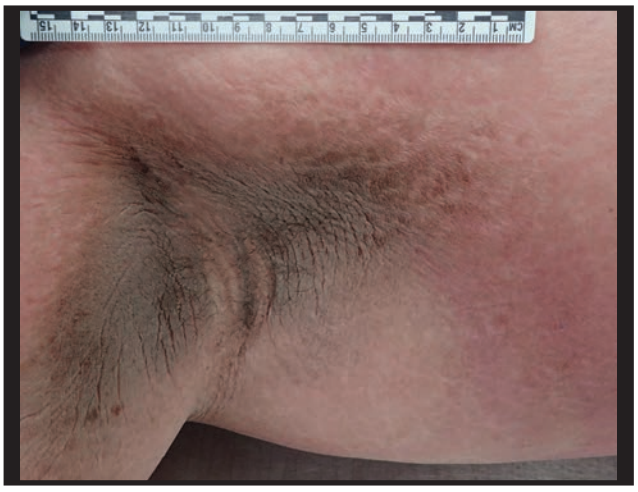

Figure from Byard, R.W., Gilbert, J. Acanthosis nigricans – a potentially useful clue to the presence of significant occult disease at autopsy. Forensic Sci Med Pathol 2025;21, 472–477. https://doi.org/10.1007/s12024-024-00815-6 (CC BY 4.0).
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from skin lymphocytes leads to insulin resistance and subsequent lipid accumulation in the liver. See the section on "Primary Biliary Cholangitis" above for specifics regarding clinical features and management of plaque psoriasis **[Figure 13]**.[55–57]

Acanthosis nigricans

The presence of acanthosis nigricans (AN), particularly in diabetic patients, may also predict hepatic steatosis and fibrosis. AN presents with symmetric, velvety, dark brown patches and plaques most commonly in intertriginous regions such as the axillae, groin, and folds of the neck **[Figure 15]**. These lesions are papillomatous overgrowths of the epidermis, often associated with insulin resistance. Notably, insulin resistance is also widely accepted as an underlying cause of MASLD. A study of 114 patients with type 2 diabetes mellitus (T2DM) found that, of the 78 patients with AN, 41 (53%) had MASLD.[58] A 2024 case-control study found evidence of an independent association between AN and the presence of both hepatic steatosis and fibrosis, indicating that AN may have some utility as a clinical marker for MASLD.[59] Another study of 3012 patients found that AN was present more frequently in those with MASLD compared to healthy male (37.9% vs. 4.8%, $p < 0.001$) and female patients (39.8% vs. 5.8%, $p < 0.001$), with a specificity of ~95%.[60] Regarding treatment, focus should remain on management of the underlying disease. Treatment for cosmetic reasons may include topical retinoids, calcipotriol, fish oil, podophyllin, keratolytic agents such as salicylic acid, glycolic acid, or trichloroacetic acid, or procedural modalities such as dermabrasion or alexandrite laser.[61]

CONCLUSION

Dermatologic findings often represent the very earliest extrahepatic signs of chronic liver disease. A consideration of cutaneous findings in conjunction with other signs and symptoms can be helpful in identification of underlying hepatic dysfunction. In order to properly recognize the cutaneous manifestations of chronic liver disease, providers should be aware of the general principles of lesion identification and description. Recognition of dermatologic findings is invaluable, as it can contribute to the diagnostic picture, aid in more rapid diagnosis, and hasten time to treatment for patients. ■

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