A case presentation of widespread macular amyloidosis associated with dual hepatitis B and hepatitis C infection

Jihan Muhaidat[1], Saleh A Ba-Shammakh[2], Hasn M Haj-Freej[2], Enas Abdullah Al Haje[1]

Affiliations: [1]Department of Dermatology, Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan, [2]Faculty of Medicine, Jordan University of Science and Technology, Irbid, Jordan

Corresponding Author: Jihan Muhaidat, Department of Dermatology, Faculty of Medicine, Jordan University of Science and Technology, PO Box 3030, Irbid 22110, Jordan, Tel: 962-790835525, Email: jmmuhaidat@just.edu.jo

Abstract

Macular amyloidosis is a variant of primary localized cutaneous amyloidosis in which amyloid protein is believed to be derived from keratinocytes. The care of this variant generally focuses on addressing the associated symptoms without the need to assess for underlying disease. However, an increasing number of cases of primary localized cutaneous amyloidosis have been reported in association with systemic diseases, particularly autoimmune diseases. A few cases of biphasic primary localized cutaneous amyloidosis have been reported in association with chronic hepatitis C infection. Herein, we report an unusual patient, a 38-year-old man with widespread macular amyloidosis concurrently presenting with dual hepatitis B virus and hepatitis C virus infections. Collecting similar cases can further validate this uncommon association.

Keywords: hepatitis, macular amyloidosis

Introduction

Macular Amyloidosis represents a distinct subtype of primary localized cutaneous amyloidosis, characterized by the aberrant accumulation of amyloid derived from degenerated keratinocytes within the dermis; it is devoid of systemic involvement [1]. This disorder is more prevalent among individuals from Asian, Middle Eastern, and South American ethnicities [2]. Clinically, it is identified by the presence of hyperpigmented, pruritic macules exhibiting a rippled linear distribution, typically observed on the upper back and extensor surfaces of the upper extremities. The current case under discussion brings to light an extraordinarily rare association between macular amyloidosis and hepatitis B and C virus infections.

Case Synopsis

A 38-year-old apparently healthy man presented with a ten-year history of progressive skin hyperpigmentation associated with itching localized to the areas of involvement only. The patient wasn't known to have any atopic diseases and denied skin rubbing with a loofah or nylon brush. Family history was notable for chronic viral hepatitis in his father. Upon physical examination, diffuse confluent hyperpigmented patches with a prominent rippled pattern were present over his back and proximal extremities (**Figure 1**). Eczematous rash, lichenification, or papules were not seen.

A punch biopsy from his back showed a pigmented basal layer with pigment incontinence and eosinophilic bodies in the papillary dermis (**Figure 2**), staining positive with Congo red (**Figure 3**).

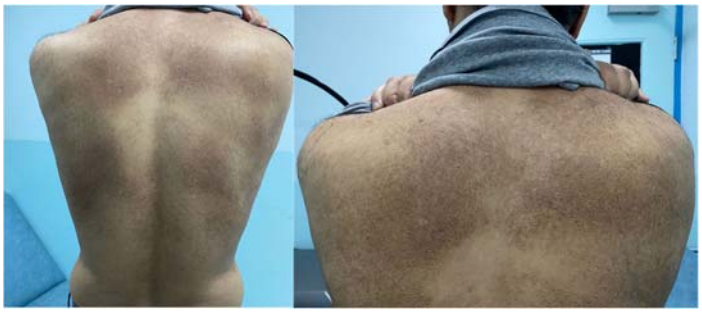

Figure 1. *Distant and closer images show widespread rippled hyperpigmentation over the back.*

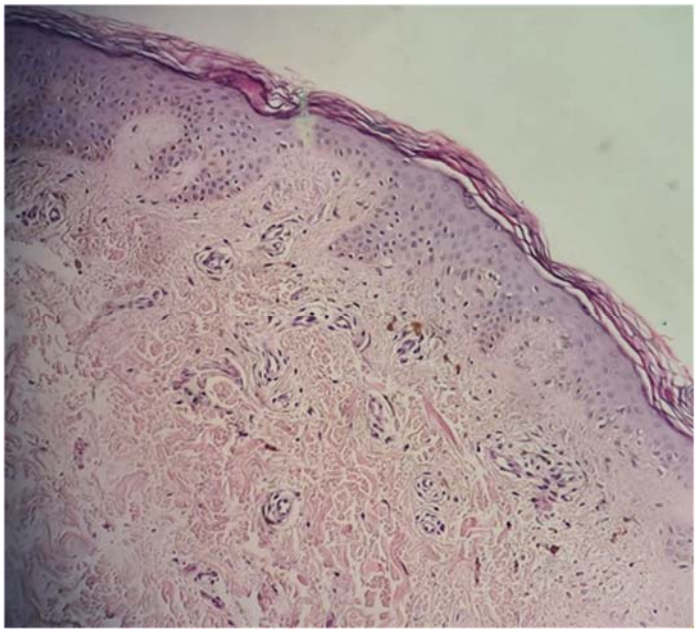

Figure 2. *Pigmented basal layer, melanophages with perivascular lymphohistiocytic infiltrate, and subtle eosinophilic deposits within the papillary dermis. H&E, 20×.*

Correlating these findings with the clinical picture established a diagnosis of macular amyloidosis. An initial work-up revealed abnormal liver function tests with elevated levels of gamma-glutamyl transferase (266U/l, normal 5 to 40U/l), direct bilirubin (8.76μmol/l, normal <5.1μmol/L), total bilirubin (30.07μmol/l, normal 1.71-20.5μmol/l), aspartate aminotransferase (65.67U/l, normal 8-33 U/), and alanine aminotransferase (49U/l, normal 4-36U/l). Thrombocytopenia was also identified, with a platelet count of 115,000/μl.

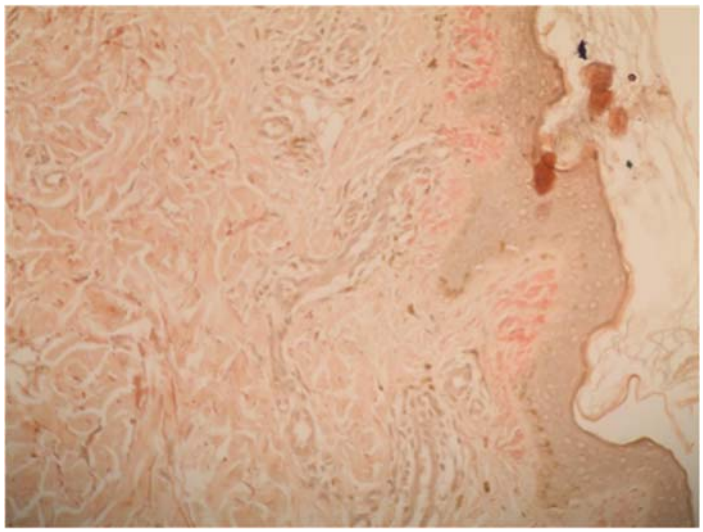

Figure 3. *Amyloid deposits highlighted by Congo red stain, 20×.*

Further investigations showed reactivity for hepatitis B surface antigen and hepatitis C virus antibodies. Quantitative hepatitis C virus PCR results showed a viral load of 2.21×10^4IU/ml, indicative of an active hepatitis C virus infection. In addition, a comprehensive abdominal assessment by ultrasonography images revealed a heterogeneously textured liver, slightly irregular borders, and multiple small variable-sized hyperechoic nodules in both lobes, with the long axis of the liver measuring 11.3cm. An abdominal magnetic resonance imaging suggested potential portal hypertension, possible micronodular cirrhosis, and splenomegaly, with the spleen measuring 20cm in maximum diameter.

Following these diagnoses, the patient has been prescribed a therapeutic regimen of sofosbuvir-ledipasvir for hepatitis C virus, tenofovir alafenamide for hepatitis B virus, and a topical corticosteroid for macular amyloidosis. After six months of follow-up, the liver function tests indicated some improvement, with a reduction in gamma-glutamyl transferase levels (165U/l), normalization of total bilirubin (11μmol/l), and a decrease in aspartate aminotransferase (41U/l). The alanine aminotransferase level had returned to normal (34U/l). However, the patient's erythrocyte sedimentation rate was still elevated. A noteworthy reduction in hepatitis C virus viral load to ≤53IU/ml was detected and a hepatitis B virus PCR outcome of 81×10^2IU/ml indicated a favorable response to the treatment. However, the patient's latest complete blood count analysis revealed a continuous reduction in the platelet count, measuring 99,000/μl; his cutaneous eruption and itching did not ameliorate after the treatment.

The patient's complex diagnostic and treatment journey continues, with persistent thrombocytopenia, slightly elevated aspartate aminotransferase levels, and an increased erythrocyte sedimentation rate requiring further monitoring and management.

Case Discussion

The skin is frequently the sole organ of primary localized cutaneous amyloidosis. The precise

etiopathogenesis of primary localized cutaneous amyloidosis has yet to be determined. Many studies have linked primary localized cutaneous amyloidosis to various autoimmune illnesses like systemic sclerosis, autoimmune hepatitis, primary biliary cirrhosis, Sjogren syndrome, and sarcoidosis, suggesting involvement of an underlying immune-mediated mechanism [3-6].

Primary localized cutaneous amyloidosis has also been reported to co-occur with chronic hepatitis C infection in at least three cases, suggesting it may represent an additional extrahepatic manifestation. Hepatitis B infection has only been linked to systemic amyloidosis [7,8]. Based on this, we believe our patient's macular amyloidosis. might be related to his hepatitis C infection rather than hepatitis B.

It is possible that pruritus associated with liver disease, including viral hepatitis, could potentially contribute to amyloid genesis. However, hepatic pruritus is generalized, more pronounced at the hands and feet, and tends to worsen at nighttime [9]. According to this patient, itching has been localized to the hyperpigmented patches that have progressively appeared on his torso and shoulders. Furthermore, interestingly, there have been no reported cases of cutaneous amyloidosis associated with chronic renal disease, a common cause of generalized pruritus.

This case presented a clinical dilemma because of a potential link between macular amyloidosis and an underlying hepatitis C infection. Hyperbilirubinemia has been shown to have a toxic effect on keratinocytes leading to the formation of amyloid [10]. This patient's macular amyloidosis has been present for over a decade and his hepatitis was also chronic, with some recognizable manifestations of cirrhosis. In addition, macular amyloidosis is considered a rare condition among different populations and hepatitis C infection is rare in the patient's community [11], arguing against a mere coincidence. However, more similar cases are required to support this association.

Conclusion

In this case, we detailed the unusual coexistence of macular amyloidosis and dual hepatitis B and C infections in a single patient. Despite the patient's slight improvements post-antiviral treatment, persistent skin symptoms and declining platelet count highlight the need for continuous monitoring and potential regimen alterations. This report underscores the importance of exploring systemic diseases in macular amyloidosis patients, particularly those with a family history of liver disorder. Our tentative association between macular amyloidosis and hepatitis, especially hepatitis C virus, encourages further investigation and collective data from similar cases. Ultimately, such a comprehensive approach could lead to improved diagnostics and therapeutics for patients afflicted by these conditions.

Potential conflicts of interest

The authors declare no conflicts of interest.

References

1. Fernandez-Flores A. Cutaneous amyloidosis: a concept review. *Am J Dermatopathol*. 2012;34:1-14. [PMID: 22257835].
2. Rasi A, Khatami A, Javaheri SM. Macular amyloidosis: an assessment of prevalence, sex, and age. *Int J Dermatol*. 2004;43:898-9. [PMID: 15569011].
3. Dahdah MJ, Kurban M, Kibbi AG, Ghosn S. Primary localized cutaneous amyloidosis: a sign of immune dysregulation? *Int J Dermatol*. 2009;48:419-21. [PMID: 19335432].
4. Yan X, Jin J. Primary cutaneous amyloidosis associated with autoimmune hepatitis-primary biliary cirrhosis overlap syndrome and Sjögren syndrome: A case report. *Medicine (Baltimore)*. 2018;97:e0004. [PMID: 29465536].
5. Ogiyama Y, Hayashi Y, Kou C, et al. Cutaneous amyloidosis in patients with progressive systemic sclerosis. *Cutis*. 1996;57:28-32. [PMID: 8620682].
6. González-Moreno EI, Cámara-Lemarroy CR, Borjas-Almaguer DO, et al. Cutaneous amyloidosis associated with autoimmune hepatitis-primary biliary cirrhosis overlap syndrome. *Ann Hepatol*. 2015;14:416-9. [PMID: 25864224].
7. Abe M, Kawakami Y, Oyama N, et al. A rare co-occurrence of primary localized cutaneous amyloidosis and chronic C type hepatitis. *Int J Dermatol*. 2010;49:960-2. [PMID: 21128925].
8. Erbagci Z, Erkilic S, Tuncel AA. Diffuse biphasic cutaneous amyloidosis in an HCV-seropositive patient: another extrahepatic manifestation of HCV infection? *Int J Clin Pract*. 2005;59:983-5. [PMID: 16033625].
9. Tarikci N, Kocatürk E, Güngör Ş, et al. Pruritus in Systemic Diseases: A Review of Etiological Factors and New Treatment Modalities.

ScientificWorldJournal. 2015;2015:803752. [PMID: 26240837].

10. Kamada N, Yoneyama K, Togawa Y, et al. Toxic epidermal necrolysis with severe hyperbilirubinemia: complete re-epithelialization after bilirubin reduction therapies. *J Dermatol*. 2010;37:534-6. [PMID: 20536667].
11. Hamoudi W, Ali SA, Abdallat M, et al. HCV infection prevalence in a population recruited at health centers in Jordan. *J Epidemiol Glob Health*. 2013;3:67-71. [PMID: 23856567].