INTERNAL MEDICINE

□ CASE REPORT □

Dermatomyositis Induced by Hepatitis B Virus-related Hepatocellular Carcinoma: A Case Report and Review of the Literature

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Abstract

Dermatomyositis or polymyositis as a paraneoplastic syndrome of hepatocellular carcinoma (HCC) is an uncommon event. Few cases have been reported in the literature. We herein report the case of a 55-year-old man with chronic hepatitis B and alcoholism who presented with skin rash. Abdominal computed tomography revealed multiple hypervascular liver tumors consistent with HCC. He subsequently developed dysphagia with proximal limb weakness. Laboratory tests and electromyography demonstrated inflammatory myopathy. We therefore diagnosed the patient with HCC-induced dermatomyositis. Prednisolone and anti-viral therapy were administered; however, the patient died two months later due to the progression of the disease. We review the cases of HCC-induced dermatomyositis and polymyositis in the literature.

Key words: dermatomyositis, hepatitis B virus, hepatitis C virus, hepatocellular carcinoma, paraneoplastic syndrome, polymyositis

Introduction

Dermatomyositis and polymyositis are idiopathic inflammatory myopathies that are associated with muscle weakness and inflammatory infiltration within the skeletal muscle. The pathogenesis and etiology of both diseases are still unclear. It has been suspected that viral and autoimmune factors may be involved, and that an immune response against cancer may trigger an attack against the muscle components (1). The muscle damage associated with dermatomyositis is believed to be mediated by humoral factors directed against the endomysial capillary endothelial cells, while in polymyositis, cytotoxic T-cells mediate muscle fiber injury. Although the factors causing dermatomyositis or polymyositis remain to be elucidated, the relationship between inflammatory myopathies and viral infections or cancer has been reported in the literature (2-18). The tumors associated with dermatomyositis include ovarian cancer, breast cancer, melanoma, colon cancer and non-Hodgkin lymphoma (19); it is rarely associated with hepatocellular carcinoma (HCC). We herein report the case of a 55-year-old man of dermatomyositis induced by hepatitis B virus (HBV)-related HCC in Taiwan and review some cases of HCC-induced dermatomyositis and polymyositis in the English literature.

Case Report

A 55-year-old man with a history of alcoholism and who also was an HBV carrier, presented to our hospital due to tea-colored urine and yellow skin for 3 days. Moreover, he had exertional dyspnea and a poor appetite, but denied having weight loss. He had a family history of HCC and chronic hepatitis B (CHB).
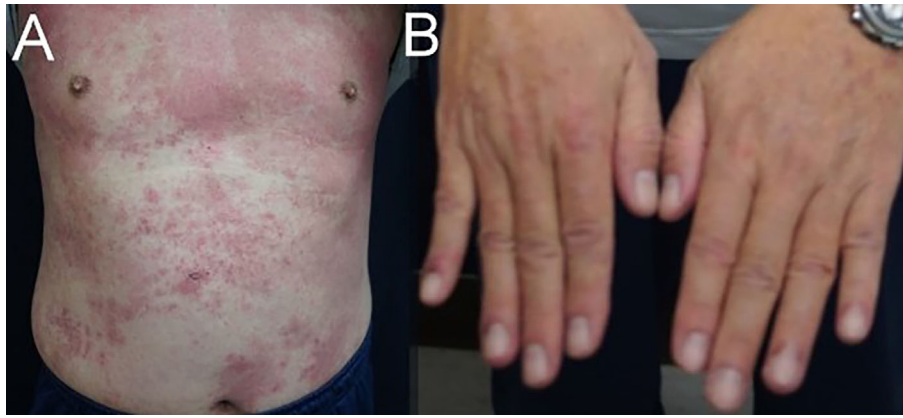
Two weeks prior to his admission, he visited our dermatology clinic because of a generalized skin rash. A skin examination showed multiple erythematous patches over his

Figure 1. Skin examination showed multiple erythematous patches over his trunk, four limbs, scalp, and face.

Table 1. Laboratory Findings on Admission.

Complete blood count/ Differential count								
Item (unit)	WBC (×10³/μL)	Neu. (%)	Lym. (%)	Mono. (%)	Eos (%)	Baso. (%)	Hb (g/dL)	RDW (×10³fl)	PLT (×10³/μL)
Normal range	3.6-11.2	43.3-76.6	16-43.5	4.5-12.5	0.6-7.9	0.2-1.4	12-16	130-140	12.3-17
Result	13,600	70.7	10.3	10.9	7.5	0.6	10.3	22.8	274

Blood biochemistry								
Item (unit)	ALT (IU/L)	AST (IU/L)	T. bilirubin (mg/dL)	D. bilirubin (mg/dL)	γ-GT (IU/L)	Albumin (g/dL)	LDH (IU/L)	AFP (ng/mL)
Normal range	5-34	5-40	0.2-1.3	0.0-0.4	8-50	3.8-5.3	98-192	<9
Result	147	351	1.4	0.3	356	2.7	506	792.6
Item (unit)	BUN (mg/dL)	Cr (mg/dL)	Na (mmol/L)	K (mmol/L)	APTT (second)	PT (second)	Ammonia (μg/dL)	hsCRP (mg/dL)
Normal range	5-26	0.5-1.3	135-147	3.5-4.9	24.3-32.7	9.5-11.7	<70	<0.08
Result	18	0.68	130	3.8	31.7	11.4	68	1.47

Viral hepatitis markers				
Item	HBsAg	HBeAg	Anti-HBe Ab	Anti-HCV Ab	HBV DNA
Normal range	Nonreactive	Nonreactive	Nonreactive	Nonreactive	Nonreactive
Result	Reactive 21.72	Nonreactive 0.33	Reactive 0.60	Nonreactive 0.05	5.19×10⁸ IU/mL

WBC: white blood cell, RBC: red blood cell, Hb: hemoglobin, PLT: platelet, RDW: red cell distribution width, Neu: neutrophils, Lym: lymphocytes, Mono: monocytes, Eos: eosinophils, Baso: basophils, AST: aspartate aminotransferase, ALT: alanine aminotransferase, T. bilirubin: total bilirubin, D. bilirubin: direct bilirubin, γ-GT: γ-glutamyl transferase, BUN: blood urea nitrogen, Cr: creatinine, Na: sodium, K: potassium, AFP: α-fetoprotein, LDH: lactate dehydrogenase, hsCRP: high sensitivity C-reactive protein, APTT: activated partial thromboplastin time, PT: prothrombin time, HBsAg: hepatitis B surface antigen, HBeAg: hepatitis B e antigen, anti-HBeAb: anti-hepatitis B e antibody, anti-HCV Ab: anti-hepatitis C virus antibody

scalp, face, trunk and four limbs. Moreover, gottron rash, and erythematous to violaceous raised papules overlying the metacarpals were noted (Fig. 1). Initially, delayed-type hypersensitivity, drug eruptions, and urticarial vasculitis were suspected. A skin biopsy was performed due to his poor response to treatment. A pathological examination of the skin biopsy specimen revealed mild vacuolar interface, mild superficial lymphohistiocytic and eosinophilic dermatitis consistent with an allergic cutaneous reaction or drug eruption without significant depositions of immunoglobulin (Ig) G,

IgM, IgA, or C3. He was referred to our gastrointestinal clinic due to an impaired liver function. The serological examinations for viral hepatitis showed HBV surface antigen reactivity with a high viral load level of $5.19×10^8$ IU/mL (Table 1). He visited our emergency department due to his severe weakness and poor appetite.

Upon admission, a physical examination revealed anicteric sclerae, pink conjunctivae and the patient's abdomen was distended. His skin had multiple rashes on his trunk and limbs. The results of the patient's laboratory tests, including
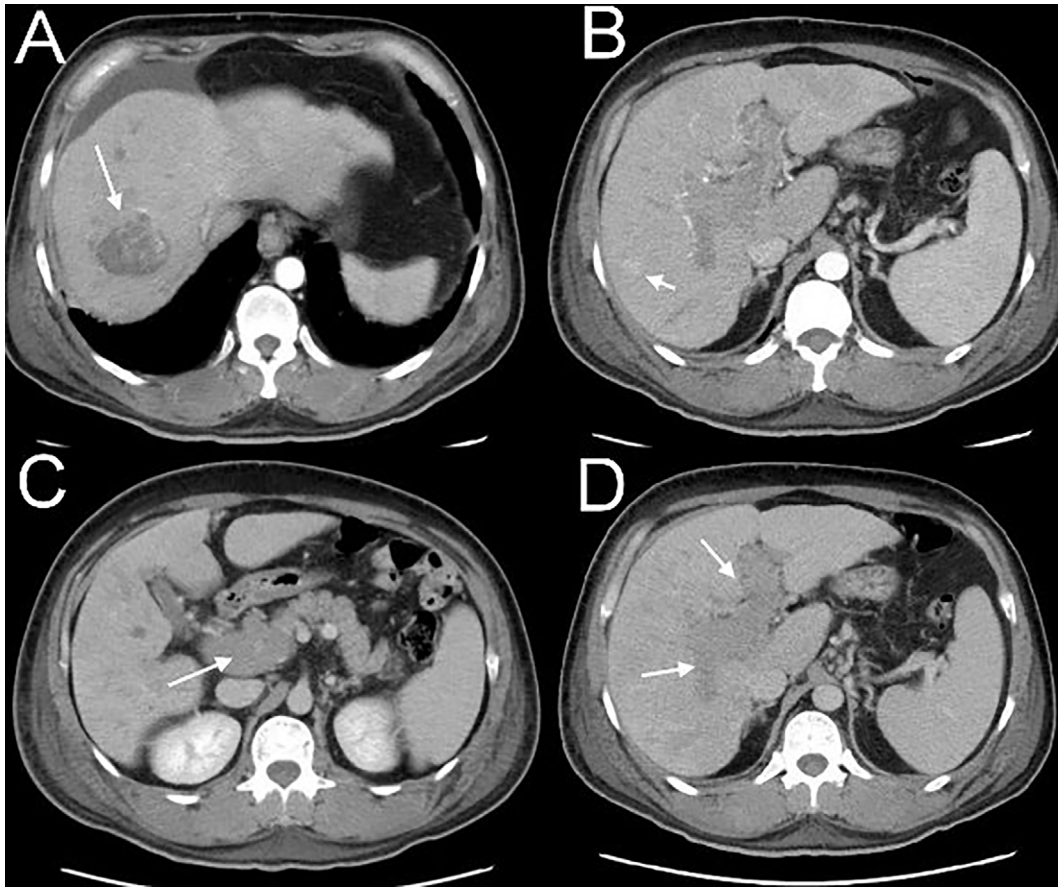
Figure 2. Contrast-enhanced abdominal computed tomography. A: A 5-cm sized hypervascular tumor on the right lobe of the liver (arrow). B: A small hypervascular nodule was also identified on the right lobe of the liver (arrow). C: The tumor invaded the main portal vein (arrow). D: The tumor invaded the bilateral portal veins (arrows).

complete blood tests and a biochemistry analysis are shown in Table 1. Contrast-enhanced abdominal computed tomography revealed cirrhosis with multiple hypervascular tumors of up to 5 cm in diameter on both lobes of the liver (Fig. 2A and B). Moreover, tumors invading the main portal vein and bilateral portal veins were also identified (Fig. 2C and D). We therefore made a clinical diagnosis of HCC with a staging of T3bN0M0. The patient's skin symptoms improved after topical steroid treatment, but he complained of difficulty swallowing and muscle weakness. He had difficulty lifting his proximal limbs, limited squatting ability, and choking episodes, but denied slurred speech, double or blurred vision, sensory abnormalities, neck stiffness or headache. We consulted both a neurologist and a rheumatologist. A neurological examination revealed decreased proximal muscle tone and a lack of bilateral deep tendon reflexes. No muscle wasting or fasciculation was detected. A motor conduction study showed increased spontaneous activity with fibrillation, complex repetitive discharges, and positive sharp waves (Fig. 3). The voluntary motor units consist of low-amplitude polyphasic units of short duration. These findings were consistent with inflammatory myopathy. The patient's highly elevated serum level of myoglobin and the results of other rheumatological tests

are shown in Table 2. According to the Bohan and Peter criteria (1988), our patient was diagnosed to have dermatomyositis, favoring HCC-induced paraneoplastic syndrome. We initially prescribed intravenous hydrocortisone (200 mg, daily), then shifted to oral prednisolone (30 mg, daily). However, we tapered the prednisolone dose progressively due to the worsening of his liver function. In addition, we also prescribed an anti-viral agent, telbivudine (600 mg, daily). We advised the patient to undergo a liver biopsy and target therapy, but he refused. He developed profound jaundice, ascites, and hepatic encephalopathy. Two months later, the patient died due to the progression of his disease (Fig. 4).

Discussion

Dermatomyositis and polymyositis are idiopathic inflammatory myopathies that are characterized by muscle weakness and inflammatory infiltration within the skeletal muscle. The pathogenesis and etiology of both are still unclear. It has been suspected that viral and autoimmune factors may be involved, and that an immune response against cancer may trigger an attack against the muscle components (1). Humoral factors directed against endomysial capillary endo-
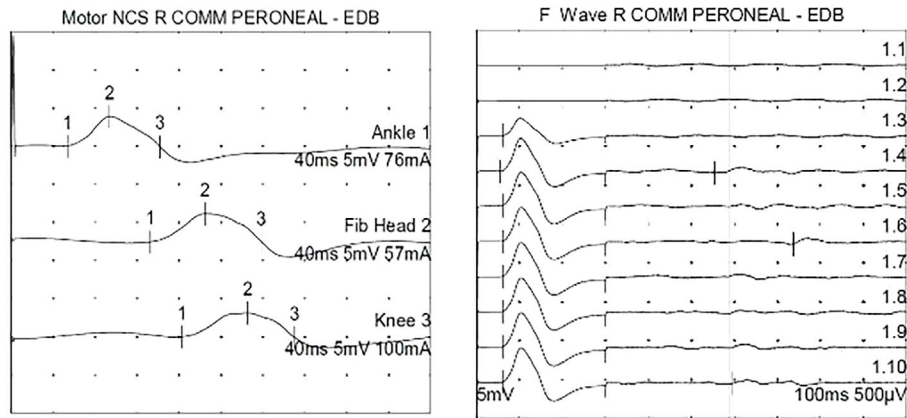
Figure 3. Motor conduction studies revealed the following abnormalities, which were consistent with inflammatory myopathy: prolonged distal latency with a reduced compound muscle action potential amplitude, a normal nerve conduction velocity and a delayed F response in the right peroneal nerve.

Table 2. Serum Rheumatological Work-up after Onset of Weakness during Hospital Course.

| Examination	Result	Normal range
ANA	Homogenous 1:160	Negative
Anti-Jo 1 antibody	<0.3 U/mL	(<7:Negative)
Anti-nDNA	1.6 IU/mL	(<10:Negative)
RA	148 IU/mL	(<20.0:Negative)
Myoglobin	629 ng/mL	(<85 ng/mL)

ANA: anti-nuclear antibody, RA: rheumatoid factor, Anti-nDNA: anti-native DNA antibody

thelial cells are believed to cause perimysial inflammation. As for polymyositis, cyotoxic T-cells mediate muscle fiber injury causing endomysial inflammation. Although the factors causing dermatomyositis or polymyositis remain to be elucidated, the relationship between inflammatory myopathies and viral infection or cancer has been reported in the literature (2-18). The tumors that are associated with dermatomyositis include ovarian cancer, breast cancer, melanoma, colon cancer and non-Hodgkin lymphoma (19); it is less commonly associated with HCC. HCC is the leading cause of cancer death in Asia, including Taiwan. Chronic HBV or hepatitis C virus (HCV) infection is an important precipitating factor for HCC (20-22). Paraneoplastic syndrome of HCC is uncommon and has various clinical manifestations, including hypercholesterolemia, hypoglycemia, hypercalcemia, and erythrocytosis (23, 24). Chronic HCV infection has been known to cause extrahepatic syndromes involving the organs, such as Grave's disease or destructive thyroiditis, glomerular and tubulointerstitial renal involvement, porphyria cutanea tarda in the skin, as well as rheumatic diseases, such as Sjogren's syndrome, rheumatoid arthritis, dermatomyositis, and polymyositis (25, 26). The extrahepatic symptoms of chronic HBV infection have also been well documented in the literature; these include renal involvement causing glomerulonephritis, membranoprolifera-

tive glomerulonephritis, and IgA nephropathy, and rheumatic diseases such as polyartertits nodosa, anti-phospholipid syndrome, multiple sclerosis, and systemic lupus erythematosus (27).

Bohan established the diagnostic criteria for dermatomyositis and polymyositis in 1988 (28). Four of the five criteria were related to muscle disease (progressive, proximal, symmetrical weakness, an increased concentration of muscle enzymes, an abnormal electromyogram, and an abnormal muscle biopsy sample); the fifth was compatible with cutaneous disease. Over the years, modifications to the diagnostic criteria for idiopathic inflammatory myopathies have been proposed (29); however, there is still no formal international consensus. As of today, the diagnosis is based on the clinical and laboratory features, such as the characteristic muscle features, skin lesions, elevated levels of muscle enzymes such as creatine kinase, and myopathic changes on electromyography. The definitive diagnostic test is a muscle biopsy showing results that are consistent with the immunopathological findings of idiopathic inflammatory myopathy (29), and skin biopsy is recommended but not required. Gottron's sign and mechanic's hand are also considered diagnostic signs for dermatomyositis (30). Positive autoantibodies are helpful markers, but they are not required for the diagnoses of dermatomyositis or polymyositis. Anti-Jo 1 antibody has been found to be related to adenocarcinoma, particularly in the lung and breast (3). It is therefore highly specific but has low sensitivity for dermatomyositis (31). Our patient developed symmetrical proximal muscle weakness and skin rashes that were consist with the classic clinical features of dermatomyositis. Electromyography showed increased spontaneous activity with fibrillation, complex repetitive discharges, and positive sharp waves. The voluntary motor units consist of low-amplitude polyphasic units of short duration. Both findings were consistent with inflammatory myopathic change. Although the patient refused to undergo muscle biopsy and the definitive diagnostic criteria
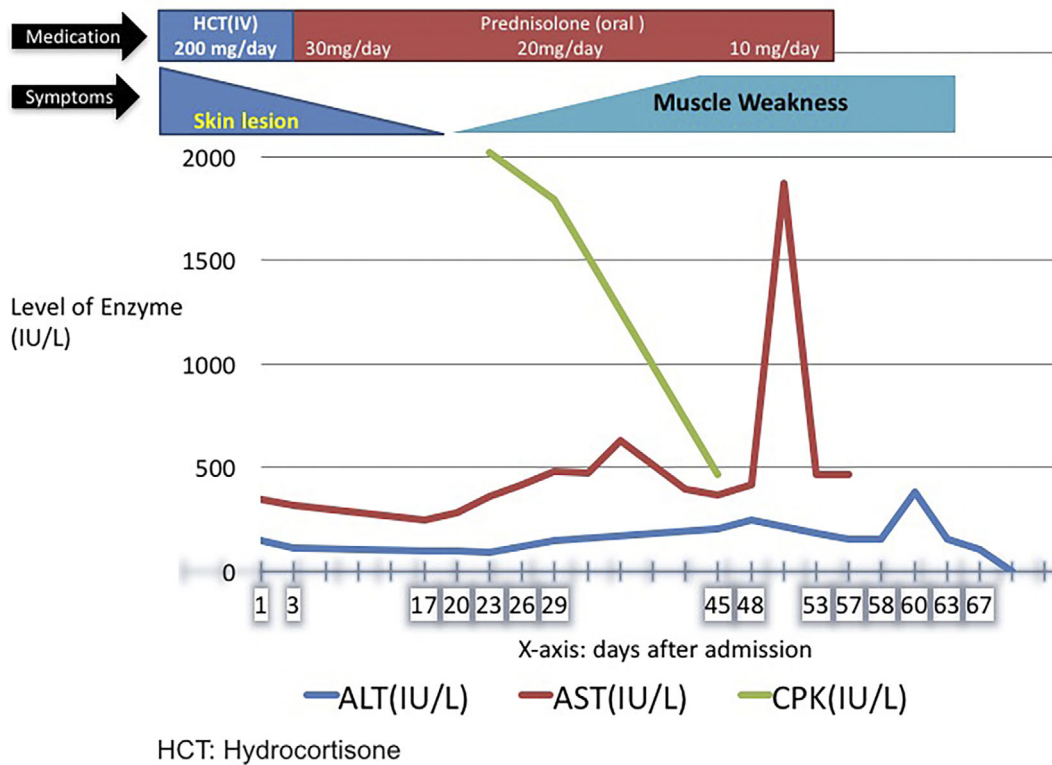
Figure 4.   **The patient's clinical course with the clinical changes in liver and muscle enzymes.**

could not be fulfilled, the other clinical and laboratorial findings in the patient were consistent with the above-mentioned criteria.

The first-line treatment for dermatomyositis or polymyositis is corticosteroids. Most authors suggest the initial use of an high-dose oral steroid with prednisolone 0.5 mg/kg per day or 60 mg per day, but variable response rates and complications may be seen (32-34). For refractory cases, pulsed intravenous methylprednisolone, immunosuppressants, intravenous immunoglobulin, and plasmapheresis are all advocated therapies for inflammatory myopathy. In our present case, the patient's skin symptoms of dermatomyositis responded to treatment with intravenous, oral and topical steroids, but his muscle symptoms did not. Finally, we discontinued steroid treatment due to the worsening of his liver function.

Patients with CHB may undergo HBV reactivation, and their conditions are associated with potential morbidity and mortality during systemic glucocorticoid therapy if the therapy lasts for more than 6 months (18). In addition, a previous report recommends that such patients be monitored for an exacerbation of HBV during glucocorticoid therapy (35). In another case report of dermatomyositis induced by HBV-related HCC, the patient was treated with anti-viral therapy using lamivudine for the prevention of viral reactivation and high-dose steroids were used to treat the patient's dermatomyositis symptoms. Anti-viral therapy is recommended in patients who are HBV carriers and who require long-term steroid therapy (18). However, the role of prophylactic anti-viral therapy in patients with CHB who require short-term

steroid therapy remains unclear. In our case, we prescribed an anti-viral agent for the patient along with steroid therapy.

We reviewed sixteen cases (including the present case) of HCC-related dermatomyositis or polymyositis in the English literature. Our results are summarized in Table 3. The ratio of a synchronous diagnosis of dermatomyositis or polymyositis to HCC is 81%. The mean age of these patients was 56.3 years (range, 14 to 79 years). The ratio of dermatomyositis to polymyositis was 2.2:1 in these patients. The ratio of HBV to HCV infection in the documented case reports was 5:4. With regard to gender distribution, the ratio of males to females was 4.3:1 with a male predominance (81%). This lopsided gender ratio can be attributed to the difference in exposure to risk factors. Men are more likely to be infected with HBV and HCV, more frequently consume alcohol and cigarettes, and have a higher body mass than women. According to our results, we found that patients with HBV-related HCC had a significantly greater prevalence of dermatomyositis or polymyositis than those with HCV-related HCC. Moreover, patients with HCC-induced dermatomyositis or polymyositis had greater tumor volumes; the average tumor size in nine HCC patients with known data was 7.7 cm. In our study, we also reviewed the HCC staging of these patients according to the Barcelona-Clinic Liver Cancer (BCLC) classification. The percentages of patients with each of the BCLC stages were as follows: stage A, 6%; stage B, 44%, and stage C, 38%. There was a predominance of intermediate- and late-stage HCCs among these cases, indicating that the occurrence of dermatomyositis or polymyositis is a poor prognostic sign for HCC pa-

Table 3. Previous Case Reports of Hepatocellular Carcinoma-induced Dermatomyositis or Polymyositis Compared with Our Case Report.

References	Age/Sex	Causes of HCC	Related inflammatory myopathy	ANA	Anti Jo-1	Diagnosis of DM/PM and HCC	HCC size and number	BCLC stage**	Management	Outcome
8	56/F	ND	DM	ND	ND	Synchronous	ND	ND	Steroid, chemotherapy	Died 15 months after diagnosis with DM
6	36/M	Not found	DM	Negative	ND	5 weeks before diagnosis of HCC	ND	ND	High dose steroid	Died
14	14/M	Not found	DM	Positive	ND	Synchronous	ND	At least C (portal vein thrombosis)	Steroid, chemotherapy, hepatectomy	Died 14 months after diagnosis with DM
5	73/M	HCV	DM	Positive	Positive	Synchronous	8cm, 1	At least B	Steroid, azathioprine, TACE	Died a few months later
9	51/M	HCV	DM	Positive	Negative	Synchronous	mutiple	At least C (N1)	High dose steroid	Died
4	50/M	HBV	DM	ND	ND	4 months after the diagnosis of HCC	10cm, 1	At least B	Steroid, TACE, hepatectomy	Died 21 months after diagnosis with DM
7	70/M	ND	PM	Negative	Negative	Synchronous	8 cm, 1	At least B	TACE, Systemic resection	ND
10	71/M	HCV	DM	Positive	Negative	Synchronous	6.5cm, 1	At least B	Steroid	ND
17	79/F	HCV	DM	Positive	Negative	9 months after the diagnosis of HCC	6 cm, 1	At least B	50mg prednisolone/day then taper down, TACE	Died 3 months after diagnosis with DM
11	58/M	HBV	DM	Positive	Negative	Synchronous	7 cm, 1	At least C (portal vein thrombosis)	High dose steroid, IVIG, TACE	Died a few months later
13	50/F	Not found	PM	Positive	Negative	Synchronous	4.8cm, 1	At least A	High-dose steroid, liver lobectomy	Died 2 months after diagnosis with PM
15	72/M	Not found	PM	ND	ND	Synchronous	12 cm, 1	At least B	Steroid, NSAID	Died 2 months after diagnosis with DM
18	55/M	HBV	DM	Positive	Negative	Synchronous	6.5 cm, 1	At least B	High-dose steroid, Antiviral therapy	Died 4 months after diagnosis with DM
16	56/M	HBV	PM	Negative	Negative	Synchronous	(largest)12cm, 3	C(ECOG:2, Child-Pugh B, left main portal vein thrombosis)	Steroid, lamivudine and TACE	Died 5 months after diagnosis with PM
12	55/M	Not found	PM	Negative	Negative	Synchronous	(largest)6cm, 3	At least C(N1)	Steroid	Died 2 months after diagnosis with PM
Our case	55/M	HBV	DM	Negative	Negative	Synchronous	5 cm, multiple	C (portal vein thrombosis)	Steroid	Died 2 months after diagnosis with DM

DM: dermatomyositis, PM: polymyositis, ND: not described, IVIG: intravenous immunoglobulin, TACE: transarterial chemoembolization, HCC: hepatocellular carcinoma. ** The BCLC stages of these patients are mainly based on their image findings due to incomplete laboratory data from the majority of the articles

tients. The average survival time of 10 documented cases was seven months. However, there was one report that noted a remission from dermatomyositis after the resection of HCC (7).

In conclusion, from our experiences in this study, if a patient (especially late-stage male patients) with HCC presents with progressive proximal weakness and skin symptoms, then clinicians should consider the possibility of dermatomyositis.

The authors state that they have no Conflict of Interest (COI).

References

1. Kao LL, Chung L, Fiorentino DF. Pathogenesis of dermatomyositis: role of cytokines and interferon. Curr Rheumatol Rep **13**: 225-232, 2011.
2. Andras C, Ponyi A, Constantin T, et al. Dermatomyositis and polymyositis associated with malignancy: a 21-year retrospective study. J Rheumatol **35**: 438-444, 2008.
3. Tiniakou E, Mammen AL. Idiopathic inflammatory myopathies and malignancy: a comprehensive review. Clin Rev Allergy Immunol 2015 Oct 1 [Epub ahead of print].
4. Cheng TI, Tsou MH, Yang PS, Sung SM, Chuang VP, Sung JL. Dermatomyositis and erythrocytosis associated with hepatocellular carcinoma. J Gastroenterol Hepatol **17**: 1239-1240, 2002.
5. Gomez A, Solans R, Simeon CP, et al. Dermatomyositis, hepatocarcinoma, and hepatitis C: comment on the article by Weidensaul et al. Arthritis Rheum **40**: 394-395, 1997.
6. Gray RG, Altman RD, Gottlieb NL. Aberrant serum enzyme patterns in dermatomyositis associated with hepatoma. J Rheumatol **3**: 227-232, 1976.
7. Hasegawa K, Uesugi H, Kubota K, et al. Polymyositis as a paraneoplastic manifestation of hepatocellular carcinoma. Hepatogastroenterology **47**: 1425-1427, 2000.
8. Horie Y, Yamada M, Nakai K, et al. Combined hepatocellular-cholangiocarcinoma associated with dermatomyositis. J Gastroenterol Hepatol **4**: 101-104, 1989.
9. Inuzuka M, Tomita K, Tokura Y, Takigawa M. Acquired ichthyosis associated with dermatomyositis in a patient with hepatocellular carcinoma. Br J Dermatol **144**: 416-417, 2001.
10. Kee KM, Wang JH, Lee CM, Changchien CS, Eng HL. Chronic hepatitis C virus infection associated with dermatomyositis and hepatocellular carcinoma. Chang Gung Med J **27**: 834-839, 2004.
11. Kee SJ, Kim TJ, Lee SJ, et al. Dermatomyositis associated with hepatitis B virus-related hepatocellular carcinoma. Rheumatol Int **29**: 595-599, 2009.
12. Kim MJ, Kim JA, Sung MS, Min JK. Hepatocellular carcinoma, polymyositis, rhabdomyolysis, and acute renal failure. J Korean Med Sci **19**: 891-894, 2004.
13. Kishore D, Khurana V, Raj A, Gambhir IS, Diwaker A. Hepatocellular carcinoma presenting as polymyositis: a paraneoplastic syndrome. Ann Saudi Med **31**: 533-535, 2011.
14. Leaute-Labreze C, Perel Y, Taieb A. Childhood dermatomyositis associated with hepatocarcinoma. N Engl J Med **333**: 1083, 1995.
15. Tekaya R, Abdelghni K, Abdelmoula L, Ben Hadj Yahia C, Chaabouni L, Zouari R. Hepatocellular carcinoma with polymyositis as an initial symptom: a case report. Acta Clin Belg **66**: 53-54, 2011.
16. Thanapirom K, Aniwan S, Treeprasertsuk S. Polymyositis associated with hepatitis B virus cirrhosis and advanced hepatocellular carcinoma. ACG Case Rep J **1**: 167-169, 2014.
17. Toshikuni N, Torigoe R, Mitsunaga M, Omoto A, Nakashima K. Dermatomyositis associated with hepatocellular carcinoma in an elderly female patient with hepatitis C virus-related liver cirrhosis. World J Gastroenterol **12**: 1641-1644, 2006.
18. Yang SY, Cha BK, Kim G, et al. Dermatomyositis associated with hepatitis B virus-related hepatocellular carcinoma. Korean J Intern Med **29**: 231-235, 2014.
19. Sigurgeirsson B, Lindelof B, Edhag O, Allander E. Risk of cancer in patients with dermatomyositis or polymyositis. A population-based study. N Engl J Med **326**: 363-367, 1992.
20. Huang H, Hu XF, Zhao FH, Garland SM, Bhatla N, Qiao YL. Estimation of cancer burden attributable to infection in Asia. J Epidemiol **25**: 626-638, 2015.
21. Shlomai A, de Jong YP, Rice CM. Virus associated malignancies: the role of viral hepatitis in hepatocellular carcinoma. Semin Cancer Biol **26**: 78-88, 2014.
22. Birrer RB, Birrer D, Klavins JV. Hepatocellular carcinoma and hepatitis virus. Ann Clin Lab Sci **33**: 39-54, 2003.
23. Qu Q, Wang S, Chen S, Zhou L, Rui JA. Prognostic role and significance of paraneoplastic syndromes in hepatocellular carcinoma. Am Surg **80**: 191-196, 2014.
24. Vautravers C, Rat P, Cercueil JP, Moreau T, Horiot JC, Chauffert B. Hepatocellular carcinoma presenting as paraneoplastic myasthenia gravis. Eur J Intern Med **19**: e86-e87, 2008.
25. Coccoli P, Esposito P, Cianciaruso B, et al. Hepatitis C and kidney disease. Dig Liver Dis **39** Suppl 1: S83-S85, 2007.
26. Ferri C, Antonelli A, Mascia MT, et al. HCV-related autoimmune and neoplastic disorders: the HCV syndrome. Dig Liver Dis **39** Suppl 1: S13-S21, 2007.
27. Maya R, Gershwin ME, Shoenfeld Y. Hepatitis B virus (HBV) and autoimmune disease. Clin Rev Allergy Immunol **34**: 85-102, 2008.
28. Bohan A. History and classification of polymyositis and dermatomyositis. Clin Dermatol **6**: 3-8, 1988.
29. Cox S, Limaye V, Hill C, Blumbergs P, Roberts-Thomson P. Idiopathic inflammatory myopathies: diagnostic criteria, classification and epidemiological features. Int J Rheum Dis **13**: 117-124, 2010.
30. Sultan SM, Isenberg DA. Re-classifying myositis. Rheumatology (Oxford) **49**: 831-833, 2010.
31. Satoh M, Tanaka S, Ceribelli A, Calise SJ, Chan EK. A comprehensive overview on myositis-specific antibodies: new and old biomarkers in idiopathic inflammatory myopathy. Clin Rev Allergy Immunol 2015 Sep 30 (Epub ahead of print).
32. Choy EH, Isenberg DA. Treatment of dermatomyositis and polymyositis. Rheumatology (Oxford) **41**: 7-13, 2002.
33. Aggarwal R, Oddis CV. Therapeutic advances in myositis. Curr Opin Rheumatol **24**: 635-641, 2012.
34. Bronner IM, van der Meulen MF, de Visser M, et al. Long-term outcome in polymyositis and dermatomyositis. Ann Rheum Dis **65**: 1456-1461, 2006.
35. Yang CH, Wu TS, Chiu CT. Chronic hepatitis B reactivation: a word of caution regarding the use of systemic glucocorticosteroid therapy. Br J Dermatol **157**: 587-590, 2007.