Chronic Hepatitis C Virus Infection Associated with Dermatomyositis and Hepatocellular Carcinoma

Kwong-Ming Kee, MD; Jing-Houng Wang, MD; Chuan-Mo Lee, MD; Chi-Sin Changchien, MD; Hock-Liew Eng¹, MD

Dermatomyositis is a rare and idiopathic inflammatory myopathy with characteristic cutaneous manifestations. In recent years, some researchers have showed that the cause of dermatomyositis might be due to an autoimmune response induced by viral infections. However, chronic hepatitis C virus (HCV) infection associated with dermatomyositis is very rare. In this report, we present a patient with dermatomyositis with abnormal liver function test results and elevated alfa-fetoprotein level. After excluding multiple viral infections known to cause myositis, the case was proven to be chronic hepatitis C by positive HCV-RNA in the serum. Abdominal computed tomography showed a liver tumor on the right lobe and needle biopsy proved it to be hepatocellular carcinoma. Chronic hepatitis C or hepatocellular carcinoma might cause dermatomyositis by inducing the formation of autoantibodies. Chronic hepatitis C or hepatocellular carcinoma should be considered in patients of dermatomyositis if no other cause is found. (Chang Gung Med J 2004;27:834-9)

Key words: hepatitis C virus, dermatomyositis, hepatocellular carcinoma.

CASE REPORT

A 71-year-old man had been healthy, however, he began to suffer from progressive weakness in his bilateral hips and thighs, difficulty in combing his hair, dysphagia, and erythematous changes of the skin over his face, upper chest and neck for about 3 weeks. There was history of no blood transfusion, tattooing, or intravenous drug addiction in this patient. Physical examination revealed heliotrope rash with bilateral periorbital edema, violaceous papules over the scalp, and poikiloderma on the upper chest and neck. Musculoskeletal examination showed marked weakness of all proximal muscles of the extremities symmetrically.

Laboratory data showed levels of serum creatine

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kinase (CK): 674 IU/L (15-130), lactate dehydrogenase (LDH): 215 IU/L (47-140), aspartate aminotransferase (AST): 128 IU/L (0-34), alanine aminotransferase (ALT): 68 IU/L (0-36), albumin: 2.4 g/dl (3.5-5.5), and total bilirubin: 1.3 mg/dl (0-1.3). Antinuclear antibody was positive (1:80, speckled).

Other autoantibodies, including anti-ENA, anti-double-strand DNA, anti-RNP, anti-Sm, anti-SSA, anti-SSB, anti-Scl 70 and anti-Jo-1, were all negative. The results of the complete blood count were normal. Electromyography showed a small amount of polyphasic waves with normal interference pattern in all muscles tested. Skin biopsy of the right upper arm showed a sparse lymphocytic infiltration around the blood vessels and negative results on the immunofluorescent study (Fig. 1), which is compatible with dermatomyositis.

Tumor markers were checked under suggestion of underlying malignant disease. CEA, CA199 and PSA were normal but he had marked elevation of alpha-fetoprotein of up to 21051 ng/ml. Abdominal sonography and computer tomography revealed a 6.5-cm liver tumor on the right lobe (Fig. 2) and liver cirrhosis. Liver tumor needle biopsy pathology showed hepatocellular carcinoma. Hepatitis B virus surface antigen was negative, and antibody to HCV was positive using enzyme linked immunosorbent assay. HCV infection was confirmed by the presence of HCV-RNA in the serum with reverse transcriptase polymerase chain reaction amplification. Serum antibody titers of human immunodeficiency virus (HIV), coxsackieviruses, adenovirus, influenza virus, human T leukemia/lymphoma virus type I (HTLV-1) and rubella virus were not elevated.

A total of 30 mg of oral prednisolone was given per day and his muscle power improved slightly. Prednisolone was stopped 2 weeks after beginning the administration due to active bleeding of gastroduodenal ulcers. Transcatheter arterial embolization and local injection therapy for liver tumor were not performed because of poor liver function.

**DISCUSSION**

The criteria to define dermatomyositis were first proposed by Bohan and Peter in 1975. The etiology and pathogenesis of dermatomyositis are still unknown, but it is believed to be a disorder of the autoimmunity that is triggered by environmental factors in genetically susceptible indi-
The increased frequency of HLA-DR3 and HLA-DRw52 antigens in these patients suggests an underlying genetic predisposition.\(^{(3)}\)

The results of tests for multiple viral infections, such as coxsackieviruses, HIV, HTLV-1, echovirus, influenza, adenovirus and hepatitis B, which are known to cause myositis, were all negative in this patient. Antibodies that attack a virus or virus-enzyme complex could cross react with homologous area of host proteins and result in autoantibody production, which is called a cross-reactive phenomenon. Anti-aminoacyl-tRNA synthetases are the most commonly recognized myositis-specific autoantibodies, such as anti-Jo1 and anti-Mi2 autoantibodies. Circulating immune complexes or autoantibodies might induce dermatomyositis of this patient. HCV may interact with aminoacyl-tRNA synthetase, which is the target of several myositis specific autoantibodies.\(^{(4)}\)

Only 11 cases of dermatomyositis and HCV infection have been reported in the literature (Table 1).\(^{(5-11)}\) Some cases also had other autoimmune diseases, such as autoimmune thrombocytopenic purpura, cryoglobulinemia, collagenous colitis, acquired ichthyosis and interstitial pneumonitis. HCV was found during an endomyocardial biopsy in a patient of dermatomyositis associated with left ventricular dysfunction.\(^{(9)}\) In the cases reported in the literature, three cases had been infected with HCV before dermatomyositis was diagnosed and the other eight cases of dermatomyositis had been diagnosed with HCV infection incidentally. We speculated that these cases might also have had long-term chronic HCV infection and induced dermatomyositis by the autoantibodies. The use of immunosuppressive agents, such as steroid and azathioprine, may improve the symptoms of myositis clinically in some cases,\(^{(5,7,8,11)}\) however, hepatitis C viremia was noted to be persistent in these cases after the treatment. Long-term effects and complications of immunosuppressive agents need further investigations.

An association between malignancy and dermatomyositis has been widely reported in the literature, with an incidence ranging from 7 to 30%.\(^{(12)}\) These malignancies include ovarian cancer, breast cancer, cervical cancer, esophageal cancer, sigmoid colitis, and leukemic infiltration. 

<table>
<thead>
<tr>
<th>Case (Ref)</th>
<th>Years (years)</th>
<th>Age</th>
<th>Gender</th>
<th>Diagnosis of HCV and Derm</th>
<th>Anti-Jo-1 antibody</th>
<th>Associated disorders</th>
<th>Antinuclear antibody</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^{(0)})</td>
<td>1994</td>
<td>48</td>
<td>Male</td>
<td>Coincident</td>
<td>Not done</td>
<td>Nil</td>
<td>Negative</td>
</tr>
<tr>
<td>2(^{(0)})</td>
<td>1996</td>
<td>72</td>
<td>Male</td>
<td>Coincident</td>
<td>Positive</td>
<td>Nil</td>
<td>Negative</td>
</tr>
<tr>
<td>3(^{(0)})</td>
<td>1996</td>
<td>70</td>
<td>Male</td>
<td>Coincident</td>
<td>Positive</td>
<td>AIDS</td>
<td>Negative</td>
</tr>
<tr>
<td>4(^{(0)})</td>
<td>1996</td>
<td>65</td>
<td>Male</td>
<td>Coincident</td>
<td>Positive</td>
<td>Interstitial pneumonitis; Raynaud phenomenon</td>
<td>Negative</td>
</tr>
<tr>
<td>5(^{(0)})</td>
<td>1996</td>
<td>-</td>
<td>Female</td>
<td>Coincident</td>
<td>Positive</td>
<td>Liver cirrhosis, Hepatitis B, Cryoglobulinemia</td>
<td>Negative</td>
</tr>
<tr>
<td>6(^{(0)})</td>
<td>1996</td>
<td>68</td>
<td>Male</td>
<td>Coincident</td>
<td>Positive</td>
<td>Hepatitis B</td>
<td>Negative</td>
</tr>
<tr>
<td>7(^{(0)})</td>
<td>1997</td>
<td>73</td>
<td>Male</td>
<td>Coincident</td>
<td>Positive</td>
<td>HCC</td>
<td>Positive</td>
</tr>
<tr>
<td>8(^{(0)})</td>
<td>1998</td>
<td>65</td>
<td>Female</td>
<td>4 years earlier of HCV</td>
<td>Positive</td>
<td>Autoimmune thrombocytopenic purpura</td>
<td>Positive</td>
</tr>
<tr>
<td>9(^{(0)})</td>
<td>2000</td>
<td>60</td>
<td>Female</td>
<td>6 years earlier of HCV</td>
<td>Negative</td>
<td>Left ventricular dysfunction Myocardial biopsy: HCV positive</td>
<td>Negative</td>
</tr>
<tr>
<td>10(^{(0)})</td>
<td>2001</td>
<td>51</td>
<td>Male</td>
<td>7 years earlier of HCV</td>
<td>Negative</td>
<td>HCC, Acquired ichthyosis</td>
<td>Positive</td>
</tr>
<tr>
<td>11(^{(0)})</td>
<td>2002</td>
<td>40</td>
<td>Female</td>
<td>Coincident</td>
<td>Negative</td>
<td>Collagenous colitis</td>
<td>Negative</td>
</tr>
<tr>
<td>Our case</td>
<td>2003</td>
<td>71</td>
<td>Male</td>
<td>Coincident</td>
<td>Negative</td>
<td>HCC, Liver cirrhosis</td>
<td>Positive</td>
</tr>
</tbody>
</table>
cancer, lung cancer, and nasopharyngeal carcinoma. Anti-Mi2 autoantibodies were found in a few cases of dermatomyositis (20%) and cancer-associated myositis.\(^{(13)}\) In an animal study, a 169bp cDNA product, which was isolated from H4IIE rat hepatoma cells, was 88% homologous to the human Mi2 autoantigen. At the protein level, there was 100% homology. Anti-Mi2 autoantibodies may be cross reactive with rat hepatoma cells and cause dermatomyositis.\(^{(14)}\)

In the review of the literature, only four cases had both dermatomyositis and HCC (Table 2).\(^{(7,10,15,16)}\) Since HCV was identified in 1989,\(^{(17)}\) HCV screening tests were not performed in the case reports\(^{(15,16)}\) published before 1989. Long-term chronic HCV infection is a major risk factor for the development of HCC. Dermatomyositis of these cases might also have a strong association with HCV infection.\(^{(18)}\) There is no direct evidence showing dermatomyositis of these cases was induced by HCC through the cross-reactive phenomenon, however, the relationship between dermatomyositis and HCC needs further investigations.

In summary, dermatomyositis of our patient might have been caused by chronic HCV infection through the autoimmune mechanism. Chronic HCV infection or HCC should be considered as a cause of dermatomyositis, if there is no other etiology found.

### REFERENCES


### Table 2. Comparison of 6 Cases of Dermatomyositis Associated with Liver Cancer

<table>
<thead>
<tr>
<th>Case (Ref)</th>
<th>Year</th>
<th>Anti-HCV</th>
<th>Age (years)</th>
<th>Gender</th>
<th>Histopathology</th>
</tr>
</thead>
<tbody>
<tr>
<td>1(^{(15)})</td>
<td>1976</td>
<td>Not done</td>
<td>36</td>
<td>Male</td>
<td>HCC</td>
</tr>
<tr>
<td>2(^{(16)})</td>
<td>1989</td>
<td>Not done</td>
<td>56</td>
<td>Female</td>
<td>Combined HCC-CCC</td>
</tr>
<tr>
<td>3(^{(7)})</td>
<td>1997</td>
<td>Positive</td>
<td>73</td>
<td>Male</td>
<td>HCC</td>
</tr>
<tr>
<td>4(^{(10)})</td>
<td>2001</td>
<td>Positive</td>
<td>51</td>
<td>Male</td>
<td>HCC</td>
</tr>
<tr>
<td>Our case</td>
<td>2003</td>
<td>Positive</td>
<td>71</td>
<td>Male</td>
<td>HCC</td>
</tr>
</tbody>
</table>

Abbreviations: HCC: hepatocellular carcinoma; HCC-CCC: hepatocellular carcinoma-cholangiocellular carcinoma.

慢性C型肝炎病毒感染合併皮肌炎及肝癌

紀廣明 王景弘 李全謨 張簡吉幸 鄧福柳

皮肌炎是一種不明原因的發炎性肌肉病變合併典型的表皮特徵。近年來，有些報告顯示造成皮肌炎的原因可能與病毒感染後誘發自體免疫反應有關，但慢性C型肝炎病毒感染合併皮肌炎卻非常罕見。本篇報告一位被診斷為皮肌炎病人合併有關指數異常及胎兒蛋白上升，經排除其他已知引起皮肌炎的病毒感染後，病人血清C型肝炎病毒檢查爲陽性，證實爲慢性C型肝炎。腹部電腦斷層發現肝腫瘤，肝切片證實爲肝癌。慢性C型肝炎或肝癌可能經由誘發自體抗體的產生而造成皮肌炎，在皮肌炎的病人若找不到其他原因時，應考慮是否有慢性C型肝炎感染或是肝癌。（長庚醫誌2004:27:834-9）

關鍵字：C型肝炎，皮肌炎，肝癌。