Hepatocellular carcinoma presenting as polymyositis: a paraneoplastic syndrome

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Polymyositis as a paraneoplastic syndrome associated with hepatocellular carcinoma is quite rare; only a few cases have been reported. We report a case of a 50-year-old female who presented with subacute quadripareisis, neck muscle weakness, elevated creatinine phosphokinase, a myogenic pattern on the EMG and was diagnosed as having polymyositis, a paraneoplastic syndrome associated with hepatocellular carcinoma with negative hepatic viral markers and a positive ANA. Improvement in patient symptoms and reduction in creatinine phosphokinase, which occurred after lobectomy, supports this rare association.

A nd autoimmune inflammatory myopathy is characterized by nonsuppurative chronic inflammation of the muscle and lymphocytic infiltration. There are few reports on dermatomyositis and polymyositis presenting as a paraneoplastic syndrome, commonly associated with breast and lung malignancy.\(^1\) Paraneoplastic syndromes like erythrocytosis, hypercalcemia, hypercholesterolemia and porphyria cutanea tarda have been reported with hepatocellular carcinoma (HCC), but acute polymyositis as a paraneoplastic syndrome in association with hepatocellular carcinoma is rarely reported.\(^2\)-\(^4\) The pathophysiology of the association of polymyositis with HCC is poorly understood. We present a case of acute polymyositis as a paraneoplastic syndrome associated with HCC having a negative hepatic viral marker and positive antinuclear antibody.

CASE

A 50-year-old nondiabetic, nonalcoholic and nonsmoking woman presented to our outpatient department with a history of difficulty in climbing stairs and lifting objects above her head for 2 1/2 months, and difficulty in lifting her head over off the pillow and keeping her head straight for 1 1/2 month. The weakness progressed rapidly and resulted in her being bedridden during the 15 days prior to presentation. There was no history of diplopia, dysphagia, dysarthria, drooling of saliva, deviation of the angle of the mouth, exertional fatigue, cold intolerance, hypertrophy of muscle, skin rash or joint pain. The past history was unremarkable; she never had jaundice. She denied recent use of any medicine or exposure to toxin.

Physical examination revealed an afebrile bedridden patient with a pulse rate of 72/min and blood pressure of 122/76 mm Hg. She had bilaterally symmetrical quadripareisis with muscle power of grade 3 in the lower limb and grade 4 in the upper limb (proximal weakness more than distal); and truncal and neck muscle weakness (both flexor and extensor muscle groups). All deep tendon reflexes were normally elicited with normal contraction and relaxation phases. Sensory, cerebellar and cranial nerve examinations were unremarkable. Abdominal examination revealed firm, nontender hepatomegaly, palpable up to 2 cm below subcostal margin in the midclavicular line. Cardiac and respiratory examinations were unremarkable. We decided on a working diagnosis of subacute-onset symmetrical quadripareisis without bowel and bladder involvement with the possibility of inflammatory muscle disease.

Laboratory test showed hemoglobin of 12 g/dL (normal range, 12-15.8 g/dL), erythrocyte sedimentation rate of 24 mm/h (normal range, 0-20 mm/h), and a total leukocyte count of 7600/μL (normal range, 5000-8000/μL) with a differential of polymorphs of 42% (normal range, 40/70%), lymphocytes of 50% (normal range, 20/50%), eosinophils of 4% (normal range, 0/4%).
range, 0-6%) and monocytes 6% (normal range, 4-8%). Blood urea and sugar (random) were 20 mg/dL (normal range, 5-20mg/dL) and 110 mg/dL (normal range, 75-125 mg/dL), respectively. Serum tests showed a total protein of 6.4 g/dL (normal range, 6-8.5g/dL), albumin of 3 g/dL (normal range, 3.2-5.5g/dL), aspartate aminotransferase of 240 IU/L (normal range, 0-45u/l), alanine aminotransferase of 146 IU/L (normal range, 0-50 IU/L), total bilirubin of 1.2 mg/dL (normal range, 0.1-1.2g/dL), alkaline phosphatase of 152 (normal range, 0-160 u/l), calcium of 9.4 mg/dL (normal range, 8.7-10.2 mg/dL), elevated creatinine kinase of 1972 IU/L (normal range, 40-150 IU/L) and elevated lactate dehydrogenase of 470 IU/L (115-220 IU/L). Renal function test, thyroid function test, urinalysis, electrocardiogram and chest x-ray were normal. Autoantibodies like anti-ds-DNA, anti-Jo, anti-neutrophilic cytoplasmic antibody were negative; however, antinuclear antibody was positive. The alpha-fetoprotein level was elevated. ELISA tests for HIV, rheumatoid factor, HBsAg, anti-HCV and anti-HAV were negative. Abdominal ultrasound showed a 4.8×3.6×4-cm heteroechoic solid mass in the left lobe of the liver (Figure 1). Computed tomography of the abdomen showed a solitary hypodense mass in the left lobe of the liver (Figure 2). An electromyograph of the deltoid and vastus lateralis showed low-amplitude, short-duration polyphasic motor unit potentials on voluntary contraction, positive sharp waves on rest and incomplete interference pattern with early recruitment; these findings were concluded as being a myopathic pattern. Sensory and motor nerve conduction studies revealed normal results. A muscle biopsy
from the thigh muscle showed myofibrillar necrosis with macrophage infiltration in regenerating fiber and lymphocytic infiltration in the endomysium, suggesting myositis (Figure 3). Ultrasound-guided biopsy of the hepatic mass showed poorly differentiated HCC. On viewing these findings, we made the diagnosis of HCC with polymyositis (PM).

Oral prednisolone was started at a dose of 1 mg/kg and a left lobe hepatic lobectomy was done. The patient showed improvement in power: grade 4+/5 in the lower limb and grade 5/5 in the upper limb; truncal and neck muscle weakness also showed marked improvement for 2 months. The creatinine kinase level was reduced to normal (Figure 4), while the level of alpha-fetoprotein was also reduced on follow-up at the clinic. Two months later, the patient was again admitted to ICU with acute-onset dyspnea, pleuritic chest pain and hemoptysis and diagnosed as having pulmonary embolism. Unfortunately, the patient died on the day of admission; her attendants denied autopsy.

DISCUSSION
The association of polymyositis to malignancy is less clear than that of dermatomyositis. The pathogenesis of polymyositis or dermatomyositis in association with HCC is not clear, but reports of a few cases with positive anti-HCV antibody have suggested that hepatitis C virus (HCV) infection could induce autoimmune phenomenon or circulating immune complexes, causing polymyositis or dermatomyositis. HCV was not positive in our case. Anti-nuclear antibodies were positive in our case. ANA-positive HCC might reflect an autoimmune response to intranuclear antigen that is perturbed in cellular transformation.

Few studies have shown antibodies to Mi-2, a component of the nucleosome remodeling-deacetylase complex, which are strongly associated with dermatomyositis and polymyositis. Another in vitro study showed that the 169-bp cDNA product, which is 88.8% homologous to the human Mi-2 beta antigen, is identified in H4IIE rat hepatoma cells, and 100% homology is found at the protein level. These studies suggest that anti-Mi-2 antibodies might be cross-reactive with HCC, an important factor causing paraneoplastic syndrome. Unfortunately, anti-Mi-2 antibodies were not examined in the present case. The patient showed improvement in power with oral steroid and hepatic lobectomy. Creatinine kinase returned to normal level in our case.

A limitation is that we did not evaluate the patient for other viral infections that may cause myositis. This case is a rare association of polymyositis as a paraneoplastic presentation with HCC. Further studies on autoantibodies cross-reacting with HCC should be done to understand the pathogenesis of polymyositis associated with HCC.

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