



Chronic hepatitis in a patient with rigid spine myopathy: Cause or just an association?

To the Editor,

Rigid spine syndrome (RSS) is a congenital, axial, muscular dystrophy due to a mutation in the gene on chromosome 1p36 coding for selenoprotein N1 (SEPN1) (1,2). Up to date, no case of hepatic dysfunction has been reported in the literature. The following is a case report of a patient with rigid spine syndrome and coexistent chronic hepatitis.

An 18-year-old male patient was referred to the hepatology department due to persistent elevation in liver enzymes. His major complaint was fatigue. He was a child of consanguineous parents. The family history was otherwise insignificant. Physical examination revealed several facial and skeletal deformities as well as choreiform head and foot movements. Further neurological examination revealed no deep tendon reflexes except for the patella. Laboratory tests are shown in Table 1. Drug, alcohol, herbal, and toxic substance screening was insignificant. Initial investigation against liver dysfunction revealed that serological studies for hepatitis B (HBs-Ag, anti-HBc IgM/IgG, HBeAg, anti-Hbe) and hepatitis C antibody (anti-HCV) were all negative, with hepatitis B surface antibody positivity consistent with vaccine immunization. HCV-RNA PCR was negative. Serum ceruloplasmin level was in the lower limit (0.19 g/L), with slightly low serum copper level (53 µg/dL) and elevated urinary copper excretion (210 µg/day), which was elevated insignificantly after D-penicillamine challenge (215.8 µg/day). In the ophthalmologic evaluation, there was no Keiser-Fleicher ring, and a neurological investigation excluded Wilson's Disease. Serum iron, ferritin, and tumor marker levels were all within the normal range. Serological studies for anti-nuclear, anti-smooth muscle, anti-mitochondrial, liver/kidney microsomal-1, soluble liver antigen, and anti-SP100 antibodies were all negative. Serum immunoglobulin G, A, and M; alpha-1 anti-trypsin; and protein electrophoresis

were also normal. In the ultrasonographic evaluation, there was no sign of steatosis, vascular pathology, or chronic parenchymal liver disease. Echocardiography was normal with no sign of respiratory or cardiac insufficiency. Electromyography represented primary muscle involvement. The muscle biopsy was compatible with inflammatory myopathy (Figure 1-3). Genetic testing resulted in a characteristic mutation. Due to chronic elevation in liver enzymes, liver biopsy was performed. The lobullary architecture was protected and had mild inflammation in intralobullary spaces, consistent with chronic hepatitis. Neither fatty change nor any virological or autoimmune signs were defined in hepatocytes, and copper was all negative (Figure 4). As a result of 5 years of follow-up, 2-3-fold elevation of liver enzymes persisted, without any cirrhotic change.

Congenital muscular dystrophy with early RSS is a rare disease characterized by several skeletal and muscular abnormalities and chronic respiratory failure (3-5). Our patient presented clinical, histological, and genetic alterations consistent with RSS.

For the evaluation of liver dysfunction, all the markers of viral, autoimmune, and metabolic liver diseases were

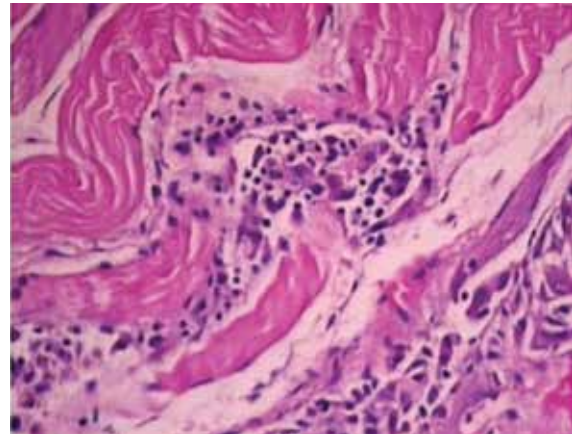


Figure 1. Lymphocytic infiltration around the necrotic muscle fibers (HE x400).

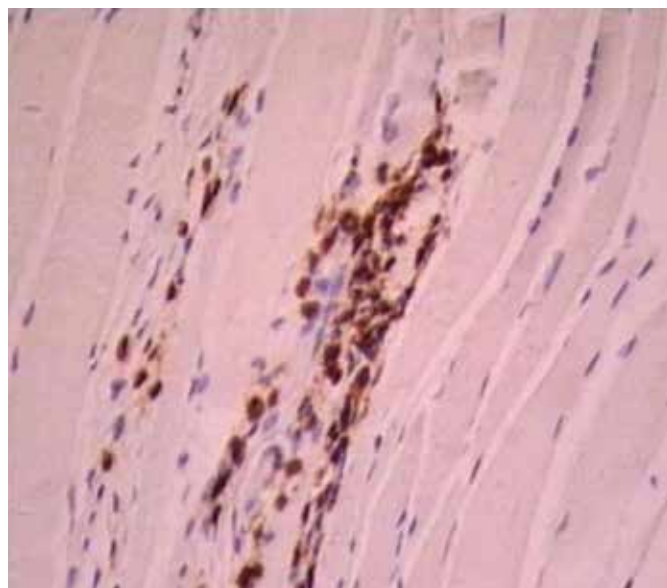
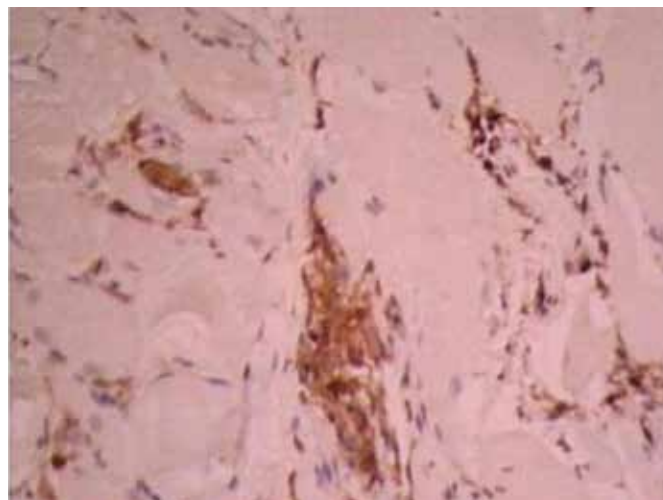
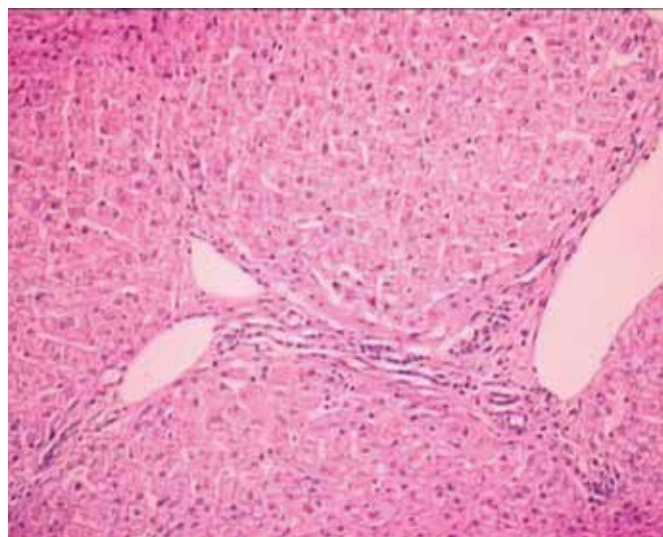
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Table 1. Results of the laboratory investigation

Test	Result	Normal Range
Hematocrit (%)	49.3	39-49
Hemoglobin (g/dL)	16.8	13.2-17.3
Leukocyte (/mm ³)	5100	4500-11,000
Platelet (/mm ³)	259,000	150,000-400,000
Prothrombin Time (sec)	11.9	9.6-13.0
Aspartate Aminotransferase (IU/L)	78	0-31
Alanine Aminotransferase (IU/L)	99	0-35
Total Bilirubin (mg/dL)	2.08	0.3-1.2
Conjugated Bilirubin (mg/dL)	0.36	<0.3
Alkaline Phosphatase (mg/dL)	74	40-129
Gamma Glutamyl Transferase (mg/dL)	8	8-61
Lactate Dehydrogenase (IU/L)	590	240-480
Serum Aldolase (U/L)	15.8	3.1-7.6
Creatine Phosphokinase (U/L)	2803	0-172
Ceruloplasmin (g/L)	0.19	0.2-0.6
Serum Copper (µg/dL)	53	95-130
Urinary Copper (µg/day)	210	3-35
D - penicillamine challenge test - Urinary Copper (µg/day)	215.8	
Immunoglobulin G (IU/mL)	11.7	7-16
Immunoglobulin M (IU/mL)	2.55	0.4-2.3
Thyroid-Stimulating Hormone (IU/L)	2.65	0.34-5.6
Free Thyroxine (ng/dL)	23.06	7-20
Erythrocyte Sedimentation Rate (mm/hr)	4	0-20

**Figure 2.** CD45-positive lymphocytes (x400).**Figure 3.** CD4-positive T lymphocytes (x400).**Figure 4.** Minimal mild inflammation in intralobular spaces (HE x400).

negative. Furthermore, there was no risk factor for toxic liver disease. In the family history, there was no other case of RSS or chronic hepatitis. He had no cardiac or respiratory insufficiency. In the literature review, there was no other association between RSS and chronic hepatitis or abnormal liver function tests.

In hepatology clinics, there are a significant number of patients in whom the etiology of liver damage can not be determined. In some of these cases, the etiological factor becomes evident during some years of follow-up. But, this is not the case in this patient after 3 years of follow-up.

In conclusion, this case is of interest, because it is the only case in the literature of RSS showing a possible association with a significant liver abnormality, like chronic hepatitis. In the management of these patients, liver functions should be followed for a possible abnormality.

Ethics Committee Approval: Ethics committee approval was received for this study.

Informed Consent: Written informed consent was obtained from patient who participated in this study.

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