Case Report

Rigid Spine Syndrome Associated with Cardiomyopathy: Clinical and Nosological Considerations

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We report observations in a 32-year-old man with the following characteristics of rigid spine syndrome: humero-peroneal muscular atrophy and weakness; bradycardia, dilated cardiomegaly and complete cardiac conduction block; and severe fatty degeneration of the paravertebral and calf muscles. The latter showed a predominance of type 1 fibers, a deficiency of type 2A fibers, and an increase in type 2C fibers.

The patient had no familial background of the disease. There was no contracture of the elbows. These findings, especially the severe cardiac involvement, suggest that the rigid spine syndrome can be difficult to distinguish from the Emery-Dreifuss form of muscular dystrophy.

Key words: Rigid spine syndrome, Cardiomyopathy

Rigid spine syndrome was first described by Dubowitz (1) in 1971. Since then more than 10 cases have been reported in the medical literature world wide (1-14). However, some authors doubt it is a distinct clinical syndrome, pointing out its resemblance to some X-linked myopathies, particularly the Emery-Dreifuss form of muscular dystrophy. That is, there is a benign clinical course with involvement of the spine, elbows, or ankles (7, 12, 13, 15). Rowland et al (15) and Goto et al (14), however, hold there are differences between the rigid spine syndrome and Emery-Dreifuss muscular dystrophy, pointing out that the rigid spine syndrome is neither inherited nor does it show cardiac conduction defects. In this paper we report a 32-year-old man with rigid spine syndrome associated with severe cardiac failure.

Our purpose is to illustrate the clinical features in this patient and discuss the rigid spine syndrome as a diagnostic entity.

CASE REPORT

A 32-year-old man was admitted to the Yamaguchi University Hospital for evaluation of weakness in the upper extremities. His development had proceeded normally until he was 7 years old when it was noted he was unable to run fast in athletic activities. At the age of 17 he noticed that he was standing and walking on his toes. These symptoms progressed until at the age of 29, he was unable to lift a hair drier with one arm and had severe atrophy in both limbs. The weakness and atrophy continued to progress gradually.

Physical examination on admission revealed a blood pressure of 140/70 mmHg and a pulse rate of 48 beat/min. There was a 3/6 systolic murmur at the apex of the heart. There was no enlargement of the liver or spleen. There was no ophthalmoplegia or abnormal pigmentation of the retina. Color vision was normal. There were flexion contractures of the neck, spine, and ankle joints. The patient was able to walk on his toes but not on his heels, and showed a waddling gait. He was able to rise from a squatting position without difficulty. The facial muscles were normal. The supraspinati, infraspinati, and deltoid muscles were strong, but he had
a slight winged scapula. There was marked wasting and weakness of the brachial biceps and brachial triceps, with slight weakness of the wrist flexors and extensors. The leg muscles were strong except for a moderate weakness of the anterior tibialis and peroneals. Deep tendon reflexes could not be elicited. Radiographic evaluation of the cervical, thoracic and lumbar spine showed there was no scoliosis or hypoplastic bodies, but there was limitation of the neck flexor and extensor mobility. However, the chest radiograph demonstrated an increase in the cardio-thoracic ratio of up to 64% (Fig. 1). CT scan (Fig. 2) showed a severe fatty change of the following muscles: neck extensors, paravertebral muscles, brachial biceps, brachial triceps, hamstrings, and posterior crural muscles. In the hamstrings, the caput longus of the biceps femoris were selectively and severely affected. Evaluation of blood and serum electrolytes was normal. Serum creatine kinase activity was 402 U/l (N, 44 to 260), with 15 U/l of MB isoenzyme; lactate dehydrogenase was 303 U/l (N, 103 to 220); aldolase 6.6 U/l (N, 0.7 to 4.4). The glutamic oxaloacetic transaminase and glutamic pyruvic transaminase were normal. Urine creatine was 0.7 g/day (N, 0 to 0.6). Serum pyruvate and lactate activity were normal; these values increased normally during ischemic exercise testing. Diabetes mellitus, collagen disease, and syphilis were ruled out. Thyroid activity and routine examination of the cerebrospinal liquor were normal. An electrocardiogram showed atrial flutter or fibrillation, complete atrio-ventricular block, right axis deviation, and high voltage (Fig. 3). An echocardiogram demonstrated a markedly dilated left ventricle with moderately severe systolic mitral regurgitation. The cardiac wall was mildly and diffusely hypokinetic, especially the left ventricle. Analysis of blood flow by color mapping method of echocardiogram showed second degree mitral regurgitation. A radioisotope scintigram showed a decreased accumulation of the isotope in the anterior wall, septum and left ventricular wall. Motor and sensory nerve conduction velocities were normal. An electromyogram showed either neurogenic or myogenic patterns, or both, in the left deltoid, brachial biceps, and anterior tibial muscle. A biopsy of the right anterior tibial muscle (Figs. 4, 5) showed increased...
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Fig. 3. ECG showing complete atrio-ventricular block, fibrillation, right axis deviation, and high voltage.

Fig. 4. Muscle biopsy specimen stained with haematoxylin and eosin showing fiber size variability, splitting fibers, central nuclei, and an increase in the interstitial fibrous tissue (×250).

Fig. 5. Histochemical staining shows type 1 fiber predominance. Type 1 fibers show decreased activity (arrow). Myosin ATPase, pH 10.8 (×200).

variability in muscle fiber size due to hypertrophy and atrophy of both type 1 and type 2 fibers. Mild to moderate increases in endomysial and perimysial connective tissues, necrotic fibers, splitting fibers, regeneration fibers, and central nuclei were present. No specific abnormalities in mitochondria, lipid, or glycogen were observed in the analysis of Gomori-trichrome, oil red O, and periodic acid-Schiff stains respectively. ATPase stain did not show type grouping. The fiber type distribution was 85% type 1, 2% type 2B, 12% type 2C and 0% type 2A fibers. NADH-tetrazolium stain showed the disturbance of the intermyofibrillar network pattern in almost all fibers. Electron microscopic examination provided no additional information.

DISCUSSION

This patient presented with myopathy characterized by mild to moderate weakness of muscular power, limitation of spinal flexion, and contractures of the Achilles tendons. The onset was in early childhood with a mild but steady progression of weakness and atrophy of the muscles, especially humero-distal. Thus, this patient meets the criteria for the rigid spine syndrome as described by Dubowitz (1). However, the variety of clinical and genetic findings of the rigid spine syndrome reported in the literature (2–14) make its delineation difficult.

Recently the differentiation of rigid spine syndrome from the Emery-Dreifuss form of muscular dystrophy has been disputed. They share similar clinical characteristics, making it difficult to distinguish them with assurance. However, Goto et al (14) and Rowland et al (15) argue that the Emery-Dreifuss muscular dystrophy has a hereditary basis and has evidence of a cardiac conduction defect, clearly distinguishing it from the rigid spine...
syndrome. The cases of Emery-Dreifuss muscular dystrophy and similar myopathies with a hereditary basis reported in the literature (16–18) to date were almost all X-chromosome linked genetic types except for the patient described by Rowland et al (15). The rigid spine syndrome shows a predominance among males with few reports in females, suggesting that most of these conditions may be X-chromosome linked. Powe et al (5) and Serratrice et al (6) described cases of rigid spine syndrome with familial occurrence. Thus, Mussini et al (2) and Powe et al (5) propose that the rigid spine syndrome might be an autosomal recessive disorder with variable penetrance, and that some cases might represent a sex-linked expression. In this respect, the majority of cases of rigid spine syndrome, including ours, without evidence of definitive heredity, may be of autosomal or X-linked recessive origin. Thus, it is not easy to distinguish the rigid spine syndrome from the Emery-Dreifuss form of muscular dystrophy on the basis of heredity.

Further, it has been stated that the characteristic presence of cardiomyopathy is important in classifying both myopathies. Rowland et al (15) and Goto et al (14) suggested that the rigid spine syndrome could be distinguished from the Emery-Dreifuss muscular dystrophy by the absence of severe cardiac involvement. However, Powe et al (5) reported a patient with the rigid spine syndrome having fatal cardiomyopathy; the present patient showed dilated cardiomegaly, conduction defects, circulatory insufficiency, and hypokinetic movement of the heart. Some of the patients reported by Emery and Dreifuss (16), Thomas et al (17) and Rotthauwe et al (18), with a genetic basis and cardiomyopathy, also resemble our case. Nevertheless, it is very difficult to distinguish two, and it is possible that they do in fact represent the same disorder. Therefore, it is important that myopathies with humero-peroneal distribution and the clinical features described above are evaluated clinically in detail and analyzed genetically using biochemical analyses.

There is no distinguishing histological pattern observed in muscle biopsy specimens in patients with rigid spine syndrome. Dubowitz et al (1) reported that interstitial fibrosis is a characteristic finding of muscle biopsies in the rigid spine syndrome. However, several patients did not show definite interstitial fibrosis (2, 6–8). Thus, the presence of interstitial fibrosis may perhaps depend upon the disease stage. Several authors suggest that the rigid spine syndrome is a type 1 fiber myopathy (2, 4, 7, 9, 10). In our patient histochemical staining also showed a type 1 fiber predominance, but the marked type 2A fiber deficiency and the increase in type 2C fibers observed in this case have not been described in previous reports on this syndrome. However, these findings are typical of chronic progressive muscular dystrophy and are not specific for rigid spine syndrome. Some patients with rigid spine syndrome reported by Powe et al (5) and Colver et al (8) exhibited a predominance of type 2 fibers with atrophy of some type 1 fibers. Moreover histochemical studies of several cases reported in the literature did not show selective atrophy of any one fiber type (1, 6, 11, 12). Uehara et al (10), who histologically and histochemically examined muscle biopsy specimens of different stage muscles in rigid spine syndrome, concluded that type 1 fibers become predominant as muscle alteration progresses, and that type 1 predominance and atrophy are not specific for rigid spine syndrome. Thus, there appears to be no characteristic muscle biopsy finding in this syndrome.

Recently, computed tomography (CT) has been performed in various myopathies, especially muscular dystrophies, and appears to be useful in evaluating the site or stage of the lesion (19). In the present case, muscle CT showed a prominent decrease in radio density, which was interpreted as infiltration of the fatty tissue of the neck, paravertebral, hamstrings, and posterior crural muscles (Fig. 2). These findings are compatible with the clinical manifestations: limitation of neck and trunk flexion and contracture of the Achilles tendons. It is possible that the previously reported cases of rigid spine syndrome and Emery-Dreifuss muscular dystrophy show similar patterns.

The etiology of rigid spine syndrome and Emery-Dreifuss muscular dystrophy are unknown, and their exact nosological position remains uncertain. We have presented a case of rigid spine syndrome associated with cardiac involvement. Several patients with X-linked inheritance similar to our case have been previously reported. Therefore, detailed genetic studies are necessary to definitely determine the type
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of myopathy.

REFERENCES