· CASE ANALYSES · · 临床病例讨论 ·

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Coexistence of systemic sclerosis and ankylosing spondylitis: A case report and literature review

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ABSTRACT Systemic sclerosis (SSc) is an autoimmune disease characterized by thickening of the skin and organ fibrosis. Ankylosing spondylitis (AS) is a type of arthritis with long-term inflammation of the axial joints. Previous studies presented 5 cases of concomitant AS and SSc. However, there was only 1 patient of those 5 cases complaining of muscle weakness while all patients had approximately normal creatine kinase (CK). Here we reported a young male who met the criteria for SSc and AS while showing significantly elevated CK. Human leukocyte antigen (HLA) typing results indicated the genetic susceptibility to these two diseases. The patient was prescribed prednisone (30 mg/d) and cyclophosphamide. After 2 months, the patient's skin became soft with normal CK.

KEY WORDS systemic sclerosis; ankylosing spondylitis; creatine kinase

系统性硬化症合并强直性脊柱炎1例及文献复习

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[摘要] 系统性硬化症是一种以皮肤增厚和纤维化为特征的自身免疫性疾病，强直性脊柱炎是一种以中轴关节受累为主的关节炎，强直性脊柱炎极少与弥漫性结缔组织病合并存在。既往文献报道了5例强直性脊柱炎合并系统性硬化症的病例，其中仅1例患者诉有肌无力，且5例患者的血清肌酸激酶水平均无明显异常。本文报道1例青年男性患者符合系统性硬化症与强直性脊柱炎的诊断标准，同时出现肌无力、肌酸激酶水平明显增高。人类白细胞抗原(human leukocyte antigen，HLA)分型检测发现该患者携带这两种疾病的HLA易感基因。对该患者予以强的松30 mg/d及环磷酰胺治疗，2个月后皮肤增厚好转，肌酸激酶降至正常。

[关键词] 系统性硬化症；强直性脊柱炎；肌酸激酶

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Ankylosing spondylitis (AS) is a highly heritable disease mostly involving the axial joints, which is strongly associated with HLA-B27. The prevalence rate of AS in China is about 0.25%. AS rarely coexists with other rheumatic diseases. Systemic sclerosis (SSc) is one of the diffuse connective tissue diseases characterized with skin sclerosis and multi-organ dysfunction. Previous studies[1-5] presented 5 cases of concomitant AS and SSc, while all these patients had approximately normal creatine kinase (CK). Here, we report a young male who met the criteria for SSc and AS, with significantly elevated muscle enzymes.

1 Case report

A 28-year-old man was referred to our hospital for Raynaud's phenomenon and diffuse skin thickness with muscle weakness for 2 months in 2017. The patient developed low back pain in 2001 and was diagnosed as AS in 2005. He underwent total hip replacement for bilateral femoral head necrosis in 2012 and has suffered from deformity of the spine since 2015. He had no family history of rheumatic diseases. Physical examination showed kyphosis; skin induration in the face, extremities and trunk with dotted depigmentation; weakness of all four limbs (proximal limb muscle strength: 4–). The harden skin involved the face, proximal and distal limbs, protothorax and abdomen, which was consistent with diffuse cutaneous systemic sclerosis (dcSSc). The modified Rodnan skin score (mRSS) was 42. The laboratory results showed creatine kinase (CK) 1 208.5 U/L, creatine kinase isoenzyme (CK-MB) 45.9 U/L, myoglobin 147.7 μg/L, ESR 55 mm/h, CRP 40.1 mg/L, HLA-B27 (+), anti-nuclear antibody (ANA) 1:160 (cytoplasmic granule pattern), extractable nuclear antibody spectrum anti-SSA (+) and anti-Ro-52 (+). SSc specific autoantibodies were negative, including anti-Scl 70, anticentromere and anti-RNA polymerase III. Myositis specific autoantibodies were negative, including anti-Ku, anti-PM-Scl 75 and anti-PM-Scl 100. Sacroiliac joint X-ray displayed bilateral artificial femoral head replaced with bilateral sacroiliac joint space disappeared. Chest high resolution CT (HRCT) did not indicate interstitial lung disease. Electromyography showed myogenic injury in the extremities. The skin biopsy showed collagen hyperplasia. The light microscopy of muscle biopsy showed the muscle fibers were unequal in size with visible scattered necrotic and regenerated muscle fibers. Immunohistochemistry results exhibited that some muscle fibers around the muscle bundle were MHC-I positive and many CD68 positive macrophagocytes infiltrated the endomysium, without CD4, CD8 positive lymphocytes or CD20, CD303 positive lymphocytes infiltration. Human leukocyte antigen (HLA) typing test showed DQA1*0104, DQA1*0505, DQB1*0503, DQB1*0301, DPA1*0103, DPA1*0202, DPB1*0402, DPB1*0501, DRB1*1101, and DRB1*1454. The patient was diagnosed as AS and dcSSc. He was prescribed prednisone (30 mg/d) and cyclophosphamide. At the 2-month follow-up, the patient's skin became soft (mRSS: 19) with normal CK. After 3 months, the patient felt energetic and his skin was softer (mRSS: 14).

2 Discussion

A thorough literature review indicated that AS rarely coexists with other diffuse connective tissue diseases. Previous studies[1-5] reported 5 cases of concomitant AS and SSc (Table 1). Three patients (Patient 1, 3, 4 in Table 1) suffered from AS for varying periods and developed SSc later. Patient 2 and 5 were diagnosed as SSc first and then developed AS. And 2 patients (Patient 2 and 3) showed rapidly progressive skin involvement within 1–3 months, which was similar to our patient. Muscle involvement in our case was confirmed by increased levels of muscle enzymes and abnormal muscle biopsy. Although the muscle biopsy in patient 4 showed nonspecific inflammation, his CK was not elevated. The association between HLA alleles and SSc varies depending on the population and ethnic groups[2]. Two of the 5 previously reported cases had the same susceptibility genes as our patient: DRB1*11 and DQB1*03, which are known to be related to SSc[6-7]. DRB1*11 has a particularly strong link with patients who have positive anti-Scl-70 antibody[8]. DRB1*11 allele group is most consistently described in association with SSc in caucasians[2, 9], while DRB1*15 and DQB1*06 are associated with SSc in Asians[2]. However, neither DRB1*15 nor DQB1*06 was detected in our case. In conclusion, we described a case of very rare coexistence of AS and SSc, perhaps partially due to the presence of susceptible genes.

Table 1 Characteristics of patients reported in the literature and our case

Patient	Studies (Authors)	Age/years	Sex	Raynaud's phenomenon	Dysphagia	Pulmonary fibrosis	Anti-Scl 70	ANA	Muscle biopsy	HLA typing
1	O'Hare, et al[1]	67	Male	+	–	–	NA	+	–	A2, A28, B7, B27
2	Kayser, et al[2]	42	Male	+	–	+	+	+	–	A*03, A*74, B*27, B*35, DRB1*11, DRB1*15, DRB3 (DR52), DRB5 (DR51), DQB1*03, DQB1*06
3	Ouédraogo, et al[3]	41	Male	+	+	–	–	+	–	A24(9), A11/B27, B35, DRB1*11, DQB1*03
4	Soledade, et al[4]	47	Male	+	+	+	+	NA	+	B*2705
5	Witt, et al[5]	64	Male	+	+	–	NA	+	–	B27
6	Our case	28	Male	+	–	–	–	+	+	B27, DQA1*0104, DQA1*0505, DQB1*0503, DQB1*0301, DPA1*0103, DPA1*0202, DPB1*0402, DPB1*0501, DRB1*1101, DRB1*1454

ANA: Antinuclear antibodies; NA: Not available; +: Positive; –: Negative

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