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CASE REPORT

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Amyloid myopathy mimicked with idiopathic inflammatory myopathy diagnosed using Congo red staining: a case report

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Abstract

Amyloid myopathy often occurs in the context of systemic amyloidosis, as a rare manifestation of "light chain" (AL) amyloidosis, accounting for 1% of its incidence. A 58-year-old man with two years history of weakness and edema of lower extremity, elevated creatine kinase (CK), and inflammatory lesions from muscle biopsy which was misdiagnosed as inflammatory myopathy. After immunotherapy, the original symptoms worsened. We later confirmed the disease through MRI, Congo red staining and bone marrow puncture results. Our purpose is that to increase awareness of amyloid myopathy to minimize the risk of misdiagnosis and emphasize the importance of Congo red staining in diagnosing similar conditions.

Keywords Amyloid myopathy, Inflammatory myopathy, Congo red staining, M proteinemia

Introduction

Idiopathic inflammatory myopathy (IIM) is a heterogeneous group of systemic autoimmune diseases that affect skeletal muscle and may also involve skin, joints, lungs, and heart, with an incidence of about 0.2 to 2 cases per 100,000 people [1]. Systemic amyloidosis is a rare disease characterized by the deposition of insoluble amyloid fibers in organs or tissues, occurring in 5 to 13 cases per million people, and its main subtype is considered "light chain" (AL) amyloidosis, which accounts for 68% of systemic amyloidosis [2, 3].

Amyloid myopathy(AM) often occurs in the context of systemic amyloidosis, as a rare manifestation of "light chain" (AL) amyloidosis, accounting for 1% of its incidence [4], whereas isolated amyloid myopathy is rarer, accounting for 27% of AM [5]. Marcus [6] et al. analyzed 14 patients with isolated amyloidosis myopathy, revealing that 10 of them carried mutations in the anoctamin-5 gene (ANO5), while the remaining 2 patients carried mutations in the dysferlin gene (DYSF). Transthyretin(ATTR) [7] amyloidosisis the third most common cause of amyloid myopathy, following AL amyloidosis and ANO5-related amyloidosis. AM patients frequently exhibit symmetrical limb weakness, elevated CK levels, as well as petechiae, diarrhea, autonomic neuropathy, and renal and cardiac dysfunction [4, 8]. Distinctive pathological changes in muscle biopsy are amyloid

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deposits in Congo-Red stains that reveal apple-green birefringence under polarized light [9]. Due to similar clinical features, it is very simple to misdiagnose AM as IIM or muscular dystrophy [10]. Therefore, we describe a case of amyloid myopathy that was misdiagnosed as IIM or myotonic dystrophy. We aim to raise awareness of AM to minimize the risk of misdiagnosis.

Case presentation

A 58-year-old male patient presented to our hospital with the chief complaint of progressive bilateral limbs weakness for two years with edema, manifested as difficulty walking up and down stairs and difficulty lifting both upper limbs, which was failed to improve even after therapy. Upon physical examination, he had grade 3 proximal and grade 4 distal muscle strength in both upper extremities and grade 2 proximal and grade 4 distal muscle strength in both lower extremities.

The patient underwent evaluations at two hospitals, revealing elevated CK levels, inflammatory lesions in biopsy of right thigh muscle, abnormal results in a echocardiography, leading to a diagnosis of IIM and hypertrophic cardiomyopathy in December 2017. In 2018, MRI results for the left upper arm indicated diffuse signal abnormalities in the anterior muscles, suggestive of inflammatory changes. A biceps muscle biopsy confirmed inflammatory lesions. Despite a recommendation for a genetic test to rule out muscular dystrophy, the patient declined.

The patient had no history of hypertension, diabetes, hepatitis, or tuberculosis, and denies any trauma history. Formerly a smoker and drinker for 20 years, the patient has since quit these habits.

Investigations

At our hospital, a series of tests were conducted: high-sensitivity cardiac troponin I 270.8 pg/mL(normal range: ≤0.01 ng/mL), myoglobin 306.5 ng/mL(normal range: ≤154.9 ng/mL), creatine kinase MB-type isoform 13.8 ng/mL(normal range: ≤7.2 ng/mL), creatine kinase 388U/L(normal range: ≤190 U/L), lactate dehydrogenase 377U/L(normal range: 135 ~ 225U/L), and urine protein +(normal range: negative). Unremarkable test results were as follow: myositis antibody spectrum(including anti-Ro52/Ku/Scl100/PM-Scl75/SRP/PL7/PL12/EJ antibodies), erythrocyte sedimentation rate (ESR) (normal range: 0 ~ 15mmHg), Rheumatism test(including ANA, anti-dsDNA, ANA spectrum).

Cardiac evaluations indicated significant left ventricular hypertrophy and a small amount of pericardial effusion (EF: 63%) in a cardiac ultrasound. Cardiac magnetic resonance (CMR) findings suggested cardiac amyloidosis, involving both chambers, both atria, the interatrial septum, and the chest wall (Fig. 1A-F).

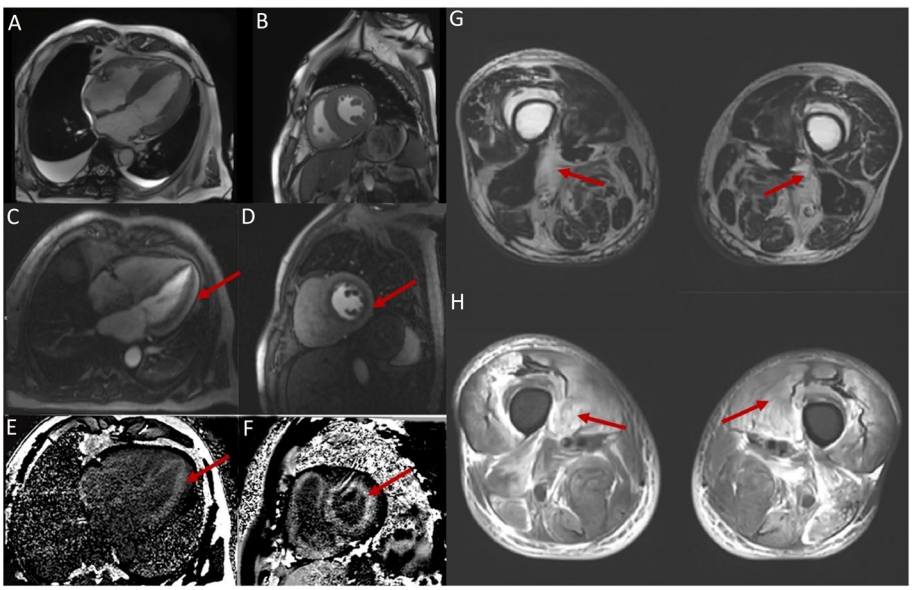

Fig. 1 Heart and thigh muscle MRI. The CMR results considered myocardial amyloidosis (involving bilateral, bilateral atria, atrial septum, and chest wall). Magnetic resonance cine sequences (A-D) showed significant left ventricular myocardial thickening (arrow) and reduced overall systolic motion. Cardiac perfusion (E, F) indicated annular low-signal filling defects in the subendocardial myocardium of the left ventricle after first perfusion, delayed enhancement in the subendocardial of both ventricle, dust-like enhancement in the walls of both atria and the atrial septum (arrow), and enhancement in the pericardium. MRI of the thigh shows diffuse muscle atrophy and fat deposition in both thigh muscles (arrow). Relaxed long T2(G) and short T1 (H) signals are seen in both thigh muscles and surrounding subcutaneous soft tissues

Muscle MRI revealed multiple abnormal signals in the thigh muscles, diffuse muscle atrophy, and fatty deposits (Fig. 1G-H).

Blood immunofixation electrophoresis identified an IgG-κ type M protein. Bone marrow aspiration showed myeloid primordial cells at 3%, normal myeloproliferative activity, and the presence of megakaryocytes. Bone marrow cytology revealed about 1.0% plasma cells, of which approximately 98.4% expressed CD38, CD138, c kappa, but not CD56, CD19, CD20, and c lambda, indicating the possibility of monoclonal abnormal plasma cells.

In consideration of the patient's muscle weakness, amyloid myopathy was explored. A review of the original hematoxylin and eosin (H&E) stained sections from the patient's muscle biopsies showed minor inflammatory cell infiltration, mostly nonspecific abnormalities (Fig. 2A). Congo red staining indicated a small amount of amyloid deposition in perivascular areas, displaying apple green birefringent alterations under a polarized light microscope (Fig. 2B-C). Conventional immunohistochemical(IHC) results showed no specific findings(Fig. 2D-I).

Treatment discussion

In addition to symptomatic supportive treatment, the chemotherapy regimen of bortezomib (protease inhibitor) plus dexamethasone was implemented at our hospital.

The CK, MB, cTnI and NT-proBNP levels of patient gradually decreased after treatment, the patient's muscle strength improved, and the edema was decreased bilaterally. When the myeloma panel was analyzed six months later, it was discovered that the blood's IgG-type M protein was reduced and showed the efficacy of the treatment.

Discussion

Amyloidosis, characterized by the deposition of fibrils in extracellular tissues, presents diverse clinical manifestations based on deposition type, location, and quantity [11]. Can be recognized through Congo red staining by showing apple green birefringence under polarized light microscopy. Amyloidosis is primarily systemic, with AL amyloidosis being the most prevalent subtype. This condition often involves the production of M protein [12], seen in multiple myeloma primary amyloidosis [13], and other lymphoproliferative diseases [9].

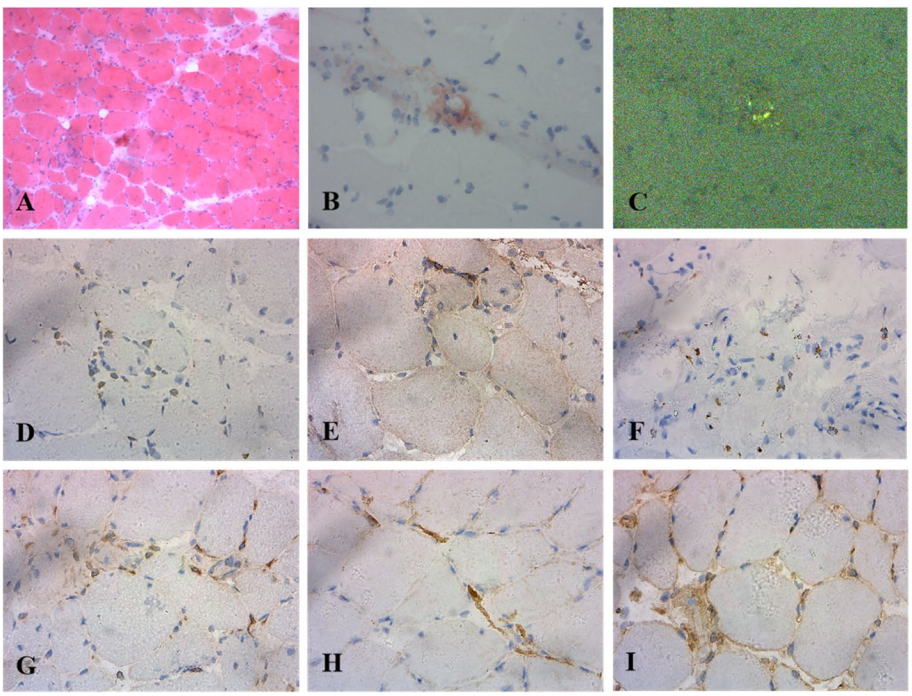

Fig. 2 HE staining and immunohistochemical results. Hematoxylin eosin staining(A) shows a small number of denatured, necrotic and regenerated muscle fibers, connective tissue hyperplasia, edema, and a small number of inflammatory cells between muscle fibers, with inflammatory cells surrounding non-necrotic muscle fibers. (Magnification X 100) Muscle Congo red staining shows small amyloid deposits around blood vessels and some muscles under a light microscope (B) and apple green birefringence changes under a polarized light microscope (C). (Magnification X 100). Immunohistochemical results： The skeletal muscle sections were positive for CD3(D), CD8(E), CD68(F), CD4(G), MAC(H) and MHC(I). (Magnification X 400)

Myopathies, classified into various types, include amyloid myopathy, a rare yet frequently overlooked cause that mimics inflammatory myopathy [14]. The Prayson reported only 16 confirmed cases of amyloid myopathy in a previous retrospective study of 3937 samples [15] .This case emphasizes the difficulty in clinically differentiating between the two, necessitating detailed assessments in order to correct diagnosis.

In 1995, Simone et al. incorporated Congo red staining into the routine of all muscle biopsy specimens and found unsuspected amyloid myopathy in all patients presenting with muscle weakness [8]. Congo red staining, despite being pivotal, is not standard practice in routine muscle biopsies in patients present with limb weakness in China. Hematoxylin staining and conventional immunohistochemical staining of the diseased muscle in this patient had no specific results.

This case underscores the diagnostic value of CMR [16], revealing heart involvement in amyloidosis. Despite lacking a heart biopsy, the patient's symptoms, including limb edema, align with amyloid cardiomyopathy [14]. Recognizing the similarity between amyloid myopathy and IIM, the diagnosis relied on comprehensive examinations, including immunohistochemical staining. The representative immunohistochemical markers of inflammatory myopathy include CD3(universal T cells), CD8(cytotoxic T cells), CD4 (helper T cells), MHC I and CD68(macrophages), but these markers lack specificity [17]. Therefore, the immunohistochemical results in this case suggest the possibility of inflammatory myopathy, but cannot correctly diagnose its classification. Especially in the case of negative myositis antibodies and lack of specific marker staining. The absence of specific findings in conventional immunohistochemistry highlighted the specificity of Congo red staining.

Emphasizing the invasive nature of muscle biopsies and the potential for confusion with other myopathies, this case advocates the early use of non-invasive CMR in patients presenting with symptoms of heart damage. In this instance, it not only suggested myocardial involvement but also guided subsequent Congo red staining. In this patient, edema of both lower limbs, moderately elevated CK, atypical IIM in muscle biopsy and poor response to hormone and immunosuppressive therapy indicated that the patient may be suffering from diseases other than IIM. It is difficult for clinicians to make a correct diagnosis because amyloid myopathy is very rare and confused with IIM and muscular dystrophy. Patients are not diagnosed in time after two years of diagnosis and treatment, which is very unfavorable to the patient's condition and economic level. Given the atypical and rare symptoms of amyloid myopathy, detailed clinical assessment is crucial to avoid mis-diagnosis and subsequent adverse outcomes. Clinicians should broaden examination scopes, differentiate symptoms from similar diseases, and consider underlying conditions to enhance amyloid myopathy diagnosis and treatment.

Follow up

In collaboration with the hematology department, we initiated a total of 8 courses of the molecularly targeted drugs bortezomib (2.5 mg, d1-d4) and dexamethasone (20 mg, d1-d4). Three months after chemotherapy and dexamethasone treatment, the muscle strength of the patient began to improve, the respiratory and swallowing function gradually recovered, and the patient was likely to walk on foot at the six-month follow-up. During the follow-up in August 2021, the patient's breathing and swallowing were normal, the ability to lie flat and raise his head was restored, and muscle strength returned to near normal levels. The degree of atrophy was obviously improved. At the same time, CK and lactate dehydrogenase (LDH) decreased progressively, and IgG-κ M protein in blood was weakened.

At the follow-up in August 2023, the patient's blood IgG-κ M protein disappeared, the symptoms of limb muscle weakness and lower limb edema improved, and he could walk with crutches at ordinary times. CMR showed that the patient's heart function was better than before.

Conclusion

To sum up, this is a typical case of systemic amyloid myopathy, with significant improvement in clinical symptoms after treatment. The patient's symptoms were initially clinically thought to be inflammatory myopathy, but amyloid lesions in the heart muscle, subtle m proteins in the blood, and muscle Congo red staining helped us make the final diagnosis of systemic amyloid myopathy. As can be seen from our case, amyloid myopathy can be similar to other types of muscle diseases, which are more difficult to distinguish. If there are atypical features of inflammatory myopathy, it is recommended to improve Congo red staining to further clarify the diagnosis. Treatment options for amyloid myopathy are significantly different from those for other types of myopathy, so it is crucial to ensure correct diagnosis, early positive diagnosis, and early treatment.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12883-024-03900-z.

Supplementary Material 1.

Authors' contributions

All members participated in the diagnosis and treatment of the patient, Xingyu Han completed the writing of the article and the production of pictures, Mohammadreza Kosari completed the graphics and production, Li Xu and Yue Li completed the collection of clinical data, Meng-geYang, Huajie Gao, HuizhenGe and others participated in the follow-up and treatment. Suqiong Ji and Bitao Bu directed the clinical diagnosis and treatment and the writing of the article.

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Data availability

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

The study involved human participants and was reviewed and approved by the Ethics Committee of Tongji Hospital of Huazhong University of Science and Technology. Patients provided written informed consent to participate in the study and to publish any potentially identifiable images or data contained in this article.

Consent for publication

Written informed consent for publication was obtained from the patients and there legal guardians for publication of identifying information and images in an online open-access publication.

Competing interests

The authors declare no competing interests.

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