

Kennedy Disease Misdiagnosed as Polyneuropathy, Organomegaly, Endocrinopathy, Monoclonal Gammopathy, and Skin Changes (POEMS) Syndrome: A Case Report

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Key Words

Kennedy disease · POEMS syndrome · Gynecomastia · Gene analysis

Abstract

Objective: The aim of this paper was to report the first case of Kennedy disease misdiagnosed as polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome. **Clinical Presentation and Intervention:** A 58-year-old Chinese man presented with limb numbness, progressive limb proximal weakness, lymph node and thyroid enlargement, edema, pigmentation in the lower limb, and obvious gynecomastia, which was initially diagnosed as POEMS syndrome and was treated with dexamethasone and small doses of cyclophosphamide without any improvement after 6 months. Finally, the patient diagnosis was confirmed as Kennedy disease (KD) by gene analysis. **Conclusion:** This case suggests that clinicians should pay more attention to the differential diagnosis between KD and POEMS syndrome. Gene analysis was helpful in detecting this rare confusing disease in this patient.

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Introduction

Kennedy disease (KD), also known as X-linked spinal bulbar muscular atrophy, is a lower motor neuron degenerative disease with onset in adulthood and is characterized by slowly progressive proximal weakness, medullary involvement, muscle atrophy, and widespread muscle bundle fibrillation accompanied by postural tremor and nonneurological symptoms, such as gynecomastia [1, 2]. Gene analysis can provide a diagnostic basis for this disease. Polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes (POEMS) syndrome is a rare paraneoplastic syndrome caused by an underlying plasma cell disorder [3]. The disorder may have overlapping clinical manifestations with KD. It is necessary for clinicians to have a high index of suspicion to distinguish them. Here we present a case of KD initially misdiagnosed as atypical POEMS syndrome.

roneal nerve sensory potentials did not elicit positive records. F waves obtained from stimulation of the median nerve appeared lower than 50%. Electromyography (EMG) showed a large number of normal-phase fibrillation potentials when the muscles relaxed; with mild muscle contraction, the reaction time of motor units extended, and the amplitude increased, and when the muscles vigorously contracted, the number of motor units decreased, rendering it as a simple phase. In conclusion, EMG showed widespread neuropathic damage. The results of gene analysis also suggest that the androgen receptor gene in exon 1 of the CAG trinucleotide repeat number is 47, confirming the suspected diagnosis of KD (fig. 1, 2).

Discussion

This case highlights the difficulties involved in the differential diagnosis of KD from POEMS syndrome through the patient's clinical symptoms and physical examination. Gene analysis is essential for the diagnosis of KD due to the high rate of misdiagnosis in practical clinical work, as has been previously reported [4, 5]. POEMS syndrome is a rare paraneoplastic syndrome associated with plasma cell dyscrasia that has overlapping clinical manifestations with KD. At first, we were confident that the above case fulfilled the diagnosis of atypical POEMS syndrome, so a bone marrow biopsy was not performed after the onset of his symptoms. Although the M-protein was not detected in the blood and urine of the patient, we found the serum γ -globulin ratio of the patient was significantly higher, and studies have shown that the incidence of M-proteins in patients with POEMS syndrome is not 100%. We know now, however, that the initial diagnosis was not appropriate, and we hope that clinicians will pay more attention and thus prevent the occurrence of such phenomena in the future.

KD is an X-linked recessive disorder due to a dynamic mutation in the androgen receptor gene [2]. Although KD has overlapping clinical manifestations with POEMS syndrome, there are distinguishing characteristics. The major mandatory criteria of KD include progressive proximal weakness, medullary involvement, asymmetrical muscle weakness, muscle atrophy, gynecomastia, and sexual dysfunction [1, 2]. This is different from POEMS syndrome that mainly involves symptoms of polyneuropathy and monoclonal plasma proliferative disorders [3]. Furthermore, the EMG in KD often shows widespread neuropathic damage. Muscle fibrillation potentials appear, with positive sharp waves in the resting state. Motor nerve conduction velocity is normal, but the sensory nerve action potential amplitude often decreases, as does the sensory nerve conduction velocity. The muscle biop-

sy usually shows neurogenic damage and occasionally muscle damage [1, 6].

Studies have found that the pathogenesis of KD is androgen receptor mutations, which are caused by an expansion of the CAG trinucleotide repeat in the androgen receptor gene on chromosome Xq11–12 [6], making androgen receptor protein in polyglutamine regional augmentation [7]. Its toxicity and abnormal degradation eventually cause cell dysfunction and transgender deaths [1, 8]. Most of the patients are male, and the gold standard for diagnosis is gene analysis. In healthy people, the CAG repeat range of gene analysis is from 17 to 26; the new European Neuroscience Association (EFNS) guidelines show that patients can be diagnosed with Kennedy disease if the CAG repetitive sequence number ≥ 35 [9]. In this study, the patient's CAG repetitive sequence number is 47, which is consistent with the diagnostic criteria of KD. However, the patient has a son who has no similar symptoms, and whose CAG repetitive sequence number is 27, which may indicate that KD is a rare X-linked recessive disorder.

As we all know, currently, there is no specific treatment for KD and it is still dominated by symptomatic treatment [6]. Studies have shown an inhibition of abnormal protein accumulation, and applications with androgen deprivation are the basic treatment strategies for polyglutamine disease. As KD is androgen dependent, one study has suggested that blocking androgen action may be an effective treatment [10], but the effects have not been clearly proven in clinical trials [7]. Therefore, the specific pathogenesis and treatment methods of KD are worthy of further study and need more research to confirm.

Conclusion

This was a case of initial misdiagnosis: of POEMS syndrome instead of KD. This suggests that clinicians should pay more attention to the differential diagnosis of KD and POEMS syndrome and that gene analysis is essential to differentiate these rare confusing diseases.

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