Unusual association of diseases/symptoms

Pseudo-ischaemic ECG in a patient with amyotrophic lateral sclerosis surviving for a decade

Jian Zhang,¹ Shi-Wei Yang,² Zheng Wang,² Guang-Ru Wei,³ Yu-Jie Zhou²¹Cardiology Department, General Hospital of Beijing Military Command, Beijing, China;²Cardiology Department, Beijing Anzhen Hospital Affiliated to Capital Medical University, Beijing, China;³Neurology Department, People's Hospital Affiliated to Peking University, Beijing, China**Correspondence to** Professor Yu-Jie Zhou, jackydang@163.com**Summary**

A 58-year-old female with no history of heart disease was admitted to our hospital for abnormal ECG mimicking myocardial ischaemia. The ECG revealed persistent T-wave inversion in almost all leads, especially in precordial leads V₂–V₆. The patient had no complaints of chest pain, chest distress, short of breath or other atypical myocardial ischaemia symptoms. She had a history of amyotrophic lateral sclerosis (ALS) with a disease course more than 20 years. Examinations help rule out other diseases causing persistent T-wave inversion. Importantly, cardiac catheterisation showed nearly normal coronary arteries that could rule out myocardial ischaemia. Accordingly, the authors presumed that the pseudo-ischaemic ECG was associated with ALS in this patient. The findings of the present case provide new evidence that autonomic nervous system may involve in the pathophysiological progress of ALS.

BACKGROUND

Amyotrophic lateral sclerosis (ALS) is a rare but fatal disease, also known as a form of motor neuron disease caused by the degeneration of neurons located in the ventral horn of the spinal cord and the cortical neurons that provide their afferent input.^{1, 2} ALS has not revealed dysfunction of the autonomic nervous system or disturbed cardiovascular regulation in previous studies.^{2–4} Accordingly, although some central nervous system disorders can cause certain ECG abnormalities including ST-T wave changes and QT interval prolongation, there are few reports indicating these abnormalities in patients with ALS.⁵ Prognosis is poor in most cases because of the progressive nature of the condition and the eventual respiratory failure.^{6, 7} Cases of slowly progressing ALS with disease courses lasting over 20 years have only rarely been reported. We describe a pseudo-ischaemic ECG in a patient with ALS surviving for a decade.

CASE PRESENTATION

A 58-year-old female with no history of heart disease was admitted to our hospital for abnormal ECG mimicking myocardial ischaemia. The ECG on admission revealed T-wave inversion in almost all leads, especially in precordial leads V₂–V₆ (figure 1). And 24 h Holter ECG showed that there were no significant dynamic changes in ST-segment and T-wave (figure 2). Previous ECGs were available for comparison and demonstrated no changes in the tracing during a 3-year period (figure 3). The patient had no complaints of chest pain, chest distress, short of breath or other atypical myocardial ischaemia symptoms. She had a history of ALS with a disease course more than 20 years. Initially, there was mild weakness with atrophy in her right lower limb. A few months later she experienced paroxysmal spasticity in the limb, which caused her to stumble frequently. And that she required a walking

Figure 1 ECG on admission revealed T-wave inversion in almost all leads, especially in precordial leads V2–V6 mimicking myocardial ischaemia.

Figure 2 The 24 h Holter ECG showed that there were no significant dynamic changes in ST-segment and T-wave.

Figure 3 Previous ECGs were available for comparison and demonstrated no changes in the tracing during a 3-year period.

aid. Muscle weakness and atrophy increased slowly and spread to both lower limbs as the disease progressed. Six years ago, the neurological findings showed a paresis of the upper extremities with bilateral atrophy of the hand muscles. Then she became fully wheelchair-dependent. Now there are no sensory, swallowing, or visual issues, and she has not any breathing difficulties. After a series of examinations the diagnosis of ALS involving both upper and lower motor neuron was made according to the revised El Escorial criteria for definite ALS. The patient had no history of hypertension, diabetes mellitus, hyperlipidaemia and other traditional cardiovascular risk factors. And she had no history of prior myocardial infarction, myocarditis, cardiomyopathy, pericarditis, hyper/hypothyroidism and hypocalcemia, which could cause persistent T-wave inversion. The patient had no history of drinking or smoking. And she denied any history of toxicant exposure or illicit drug use. The patient was not

taking any prescription medication before admission and had no known allergies.

On examination, her pulse was regular at 56 beats per min and her blood pressure was 120/64 mm Hg. She had no visible external chest injuries, and we could not find cardiac enlargement on cardiorespiratory examination. She is alert and oriented to person, place and situation. Her language is normal. Fund of knowledge is normal. Fundoscopic examination is normal, with normal optic discs visualised. Motor examination is 4/5 in the arms and 3/5 in the legs bilaterally. There is spasticity in the legs and no drift. Fasciculations are not noted in the arms and legs bilaterally. Reflexes are 3/4 symmetrically bilaterally, with toes up going. Sensory is intact to light touch, pinprick and vibration bilaterally. Romberg is negative. The coordination is intact to finger to finger and heel to shin. Laboratory values showed: troponin I of 0.03 ng/ml (normal range 0–0.05 ng/ml), low-density lipoprotein

Figure 4 Echocardiogram revealed a normal left ventricular cavity and a left ventricular ejection fraction without segmental wall-motion abnormalities.

Figure 5 Cardiac catheterisation showed nearly normal coronary arteries (A–D, left coronary arteries; E and F, right coronary artery).

cholesterol of 2.16 mmol/l, creatinine of 72 μ mol/l, fasting plasma glucose of 5.28 mmol/l, postprandial (2 h) plasma glucose of 9.1 mmol/l, haemoglobin A1c (HbA1c) of 5.2%, brain natriuretic peptide of 31.3 pg/ml (normal range 0–125 pg/ml), erythrocyte sedimentation rate of 2 mm/h, high-sensitivity C reactive protein of 1.20 mg/l. Her thyroid hormone levels were normal. Antigens/antibodies screening tests for Epstein–Barr virus, cytomegalovirus, hepatitis B virus, HIV and *Treponema pallidum* were all negative. Immunofluorescence assays for antinuclear antibodies, antiextractable-nuclear-antigen antibodies, antidouble-stranded DNA antibodies and anticardiolipin antibodies were all normal. An transthoracic echocardiogram (figure 4) revealed a normal left ventricular cavity (left ventricular end-diastolic dimension 46 mm, left ventricular end-systolic dimension 35 mm) and a left ventricular ejection fraction of 53% without segmental wall-motion abnormalities.

Suspected of prior anterior myocardial ischaemia due to the characteristics of his ECG, the patient was

scheduled for chronic atrophic gastritis (CAG). Cardiac catheterisation showed nearly normal coronary arteries (figure 5). There was no coronary artery spasm, coronary artery dissection, muscular bridge or thrombus. Multi-slice CT was used to complement CAG in the diagnosis and characterisation of coronary artery anomalies.⁸ And no significant anomalies were found. After gadolinium-diethylenetriamine pentaacetic acid contrast injection, delayed enhancement cardiovascular MRI was performed to assess necrotic myocardium⁹ and the result was normal too. After all the tests, diseases causing persistent T-wave inversion, including hypertension, myocardial infarction, myocarditis, cardiomyopathy, pericarditis, hyper/hypothyroidism and hypocalcaemia were ruled out. And we presumed that the pseudo-ischaemic ECG was associated with ALS.

OUTCOME AND FOLLOW-UP

The patient was discharged and she has shown ischaemic symptom-free at follow-ups.

DISCUSSION

ALS is the most common degenerative disease of the motor neuron system^{1 2} and it is a fatal disease, with median survival of 3–5 years.^{6 7} The prolonged course of the disease is unusual. Cases of slowly progressing ALS with disease courses lasting over 20 years have only rarely been reported, the most prominent example being that of the famous physicist, Stephen Hawking. Pointing out the existence of well-documented cases with a prolonged course over a decade can provide hope to the patients, especially younger ones, when informing them of the diagnosis of ALS. Current research of ALS focus mainly on postponing the progress of respiratory muscles atrophy and failure as most affected patients are dying of respiratory compromise several years after onset. The impact of ALS on cardiovascular system has less been studied, and there are few reports describing the ECG characteristics of the disease.⁵ We report the case fulfilling the El Escorial criteria for a definite ALS, and these criteria have been found to predict with 100% sensitivity the diagnosis of ALS at postmortem.¹⁰ Meanwhile, examinations help rule out other diseases causing persistent T-wave inversion, including hypertension, myocardial infarction, myocarditis, cardiomyopathy, pericarditis, hyper-/hypothyroidism and hypocalcemia, etc. Importantly, cardiac catheterisation showed nearly normal coronary arteries that could rule out myocardial ischaemia. Accordingly, we presumed that the pseudo-ischaemic ECG was associated with ALS in this patient.

The underlying mechanism of the abnormal ECG manifestations is not well understood, but there is evidence suggesting that these manifestations may be related to an autonomic system dysfunction.^{11–13} ALS has not revealed dysfunction of the autonomic nervous system or disturbed cardiovascular regulation in previous studies. However, anatomical studies have cast some doubt whether or not the autonomic nervous system is spared in ALS.^{11–14} Chida *et al*¹⁵ demonstrated that in patients with ALS, sub-clinical sympathetic hyperfunction and parasympathetic (vagal) hypofunction probably result in cardiovascular dysfunction. The alteration in autonomic function and cardiovascular regulation in ALS probably reflect anatomical, metabolic and heart electrical activity disturbance. Similar electrocardiographic findings have been reproduced in dog models by stimulating the hypothalamus, the stellate ganglion or unilateral ganglionectomy.¹⁶ Such findings could be abolished by contralateral ganglionectomy. The findings of the present case provide new evidence that autonomic nervous system may involve in the pathophysiological progress of ALS.

Learning points

- ▶ ALS may cause pseudo-ischaemic ECG of persistent T-wave inversion, which provides new evidence of autonomic nervous system involvement in the pathophysiological progress of ALS.

Competing interests None.

Patient consent Obtained.

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