Case Report

D-Penicillamine Induced Polymyositis Causing Complete Heart Block

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Summary

We describe a 63-year-old female patient with rheumatoid arthritis who developed complete heart block and features of polymyositis within a few weeks of starting treatment with D-penicillamine. We believe she is one of only three published patients in whom complete heart block accompanies penicillamine-induced polymyositis. The literature on penicillamine myositis is reviewed with special emphasis on cardiac problems. Patients taking D-penicillamine who develop features suggestive of polymyositis may develop insidious, but potentially life-threatening cardiac involvement and must be carefully monitored.

Key words

D-penicillamine, Rheumatoid Arthritis, Polymyositis, Complete Heart Block.

INTRODUCTION

Polymyositis is a recognized but uncommon complication of treatment with D-penicillamine. Although cardiac involvement is rare, serious cardiac damage may occur. We report a patient with rheumatoid arthritis, treated with D-penicillamine who developed polymyositis with complete heart block requiring external venous pacing. This potentially fatal complication suggests that patients suspected of D-penicillamine induced polymyositis should have close cardiac and ECG monitoring.

CASE REPORT

A 63-year-old lady with a 10-year history of sero-positive erosive rheumatoid arthritis presented with increasing pain and stiffness in her shoulders, knees and hips. Two months previously she had described a short prodromal illness characterised by shivering and malaise. On examination she had chronic rheumatoid deformities in both hands, with clinical evidence of synovitis in her shoulders, and wrists. She had a fixed flexion deformity of her left knee. Cardiovascular and neurological examination was unremarkable. Investigations revealed RA latex positive with a Rose Waaler titre of 1:20,490; C-reactive protein (CRP) level 108mg/l (normal range <10); ESR 134 mm/hr (Westergren); haemoglobin 9.9/dl. Biochemical analysis was normal including creatinine kinase. She had an antinuclear antibody IgM titre of 320; IgG ANA -ve; double stranded DNA titre 1:4; pANCA titre 320, anti-myeloperoxidase antibody negative. She was commenced on D-penicillamine 250 mg/day and prednisolone 30mg/day. Two weeks later there was considerable improvement, her ESR had fallen to 74mm/hr and CRP to 38rag/l. D-penicillamine was then increased to 375mgs daily. Four days later she complained of nausea and tiredness and had a low grade pyrexia; examination was otherwise unremarkable. Urine and blood cultures were sterile. She continued to have intermittent pyrexia and complained of abdominal discomfort. Full blood picture was normal with a normal differential WCC, ESR was 102mm/hr. D-penicillamine was discontinued. Two days later she complained of shortness of breath on exertion. Chest X-ray revealed left basal atelectasis. ECG suggested right ventricular strain pattern with evidence of right ventricular conduction delay. Pulmonary embolism was suspected and intravenous heparin commenced. Six hours later she had developed severe dyspnoea associated with chest pain. On examination she was cyanosed with a pulse rate of 90/min; blood pressure 170/80; JVP ele-
vated at 2 cms. Her chest was clear to auscultation. Blood gas analysis showed a pO2 of 9.2kPa, pCO2 4.6 Pa, pH 7.43 and total CO2 24.2 mm/l. Her creatinine kinase was 1771 u/l (with MB fraction of 0.1%), LDH 611 u/l and AST 85 u/l. ECG showed left bundle branch block. She then developed complete heart block with idioventricular rhythm and required external transvenous pacing. Right heart catheterisation showed no evidence of pulmonary embolism.

Twenty-four hours later she had developed profound proximal myopathy with poor respiratory effort and her peak flow rate was 75 litres per minute. Her pO2 was maintained on 24% oxygen by mask. She then developed dysphagia associated with nasal regurgitation. CK was 5305 u/l, LDH 920 u/l, AST 276 u/l, CK(MB)4%, ESR 120mm/h (Westergren), CRP 140 mg/l, and Jo-1 antibody negative. Polymyositis was suspected and she was commenced on 500 mg hydrocortisone daily. Muscle biopsy showed variation in fibre size with a few fibres undergoing dissolution. There was a mild inflammatory reaction, with mainly macrophages in the interstitial tissue, consistent with polymyositis. Electron microscopy revealed a small focus of inflammatory cells, mostly macrophages. In addition, there was variation in fibre diameter with occasional central nuclei. Barium swallow showed oesophageal dysmotility and nasogastric feeding was instituted. Further investigations showed normal complement and immunoglobulin levels, with an IgM antinuclear antibody (1/160). Viral cultures were negative. Over the following week her cardiac function improved and she returned to sinus rhythm with occasional runs of atrial fibrillation. 12 Lead ECG showed right bundle branch block, and temporary pacing was discontinued. Oral prednisolone was re-commenced at 50mg daily. Two weeks later she had mobilised fully with normal muscle power and muscle enzymes. She was discharged home on a reducing dose of prednisolone.

**DISCUSSION**

Immune-mediated disorders attributed to D-penicillamine therapy include systemic lupus erythematosus, Goodpastures syndrome, polymyositis and dermatomyositis. To date just over 30 cases of D-penicillamine-induced polymyositis have been reported: 28 patients had rheumatoid arthritis, three had progressive systemic sclerosis or Wilson’s disease. The clinical and pathological features of D-penicillamine-induced polymyositis and idiopathic polymyositis are very similar. The pattern and severity of muscle weakness are similar, and dysphagia is present in equal proportions (about 50%) of patients with idiopathic and D-penicillamine related polymyositis. The serum muscle enzyme profiles and EMG findings are also similar and the histopathological findings are virtually indistinguishable, with necrosis of muscle fibres and perivascular inflammatory cell infiltration occurring to a similar degree in both conditions. The clinical course, however, is very different. Patients with D-penicillamine polymyositis recover rapidly when the drug is stopped and most recover completely within 6 months. In some cases corticosteroids are not required. Furthermore, patients do not spontaneously relapse. Therefore, although idiopathic and D-penicillamine polymyositis have much in common, the latter is generally more benign. Four cases, however, with cardiac involvement have been reported (1-4): three female and one male, all with rheumatoid arthritis. Fatality occurred in 2 cases; one had complete heart block, ventricular tachycardia and heart failure (1) the other patient had heart failure, premature beats and incomplete right bundle branch block (2). In one survivor the cardiac damage was minimal, with right bundle branch block with inverted T-waves in V2-3 and transient dysrhythmias responding to digoxin (3). The other survivor had complete heart block with idio-ventricular escape rhythm requiring external transvenous pacing. After withdrawal of penicillamine the cardiac rhythm normalised, only leaving right bundle branch block (4). None of these patients had symptoms or signs of cardiovascular disease prior to treatment with D-penicillamine.

We believe our patient represents the third published case of D-penicillamine-induced polymyositis with heart block and confirms that serious cardiac damage is reversible on withdrawing the drug. The history, signs, muscle enzymes and muscle biopsy confirmed the diagnosis of polymyositis. The rapid normalisation of muscle enzymes and ECG following withdrawal of D-penicillamine strongly suggests that both the complete heart block and the myositis were drug-induced events.

Takahashi et al. estimated the frequency of coexistent rheumatoid arthritis and polymyositis to be less than 0.001% (5). Carroll et al. estimated the frequency of D-penicillamine polymyositis as about 0.3% (6). Strong correlation has been observed between the discontinuation of D-penicillamine and the resolution of polymyositis. There seems, however, to be no relation between the duration of treatment, nor cumulative dose of D-penicillamine on speed of onset or severity.

It has been suggested that D-penicillamine therapy might be incidental to the development of polymyositis (7) or that other etiological agents may be present (8). However, a patient with Wilson’s disease treated with D-penicillamine, who developed polymyositis (9), recovered on withdrawal of the drug but relapsed on re-