

## Complete heart block in a patient with POEMS syndrome: A case report

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### Case Report

#### Abstract

**BACKGROUND:** Polyneuropathy, organomegaly, endocrinopathy, monoclonal syndrome (POEMS) is a rare paraneoplastic syndrome associated with plasma cell dyscrasia.

**CASE REPORT:** A 48-year-old man presented with a 1-year history of paresthesia and progressive weakness of extremities. Diagnosis of POEMS syndrome was made for him on the basis of clinical presentation, additional physical findings, typical sclerotic bone lesion, and bone marrow findings. In last admission, he explained episodes of dyspnea and chest pain that associated with frequent premature ventricular contraction in his electrocardiograph. Patient heart monitoring showed some episodes of complete heart block. Infra-His atrioventricular block in electro-physiologic study was detected. He had no history of ischemic heart disease. His cardiopulmonary findings on examination were normal. All results of cardiac biomarkers and serum electrolytes and repeated echocardiography were within normal range. Congo red staining of rectal fat pad biopsy was negative. After pacemaker insertion radiation of sclerotic bone, lesion started for him, but radiotherapy was ineffective, and he expired with respiratory failure. Complete heart block in POEMS syndrome has not been reported previously, and it is the first POEMS case with complete heart block.

**CONCLUSION:** Complete heart block is a cardiac manifestation of POEMS syndrome.

**Keywords:** Complete Heart Block, POEM Syndrome, Multiple Meloma

*Date of submission:* 31 Aug 2013, *Date of acceptance:* 16 Feb 2014

#### Introduction

POEMS syndrome is a rare paraneoplastic syndrome associated with plasma cell dyscrasia. The acronym POEMS refers to several, but not all, of the features of the syndrome: polyneuropathy, organomegaly, endocrinopathy, monoclonal gammopathy, and skin changes.<sup>1</sup> There are two points related to this acronym. First, all of the features within the acronym are not required to make the diagnosis.<sup>2</sup> Second, there are some other features such as sclerotic bone lesion, thrombocytosis, erythrocytosis, papilledema, and extravascular volume overload that are not included in the acronym POEMS.<sup>2,3</sup> The diagnosis of POEMS syndrome is confirmed when both of the mandatory major criteria (polyneuropathy and plasma cell gammopathy), and at least one of the minor criteria (sclerotic bone lesions, Castleman disease, organomegaly, edema, endocrinopathy, skin changes, and papilledema) are present.<sup>3</sup>

Polyneuropathy and plasma cell dyscrasia are the most common features in patients and seen in all of them.<sup>4</sup> Cardiopulmonary manifestation of POEMS syndrome consist of pulmonary hypertension,<sup>5</sup> cardiomyopathy,<sup>3,6</sup> heart failure,<sup>3</sup> pericarditis,<sup>3</sup> and myocardial infarction.<sup>3,7</sup> Kanda et al. reported five patients with POEMS syndrome and cardiomyopathy. In all patients, diffuse hypokinesia of left ventricular wall motion was seen on echocardiograms. In one case cardiac amyloidosis was diagnosed by Congo red staining of the myocardium biopsy, but the etiology of the cardiomyopathy was not determined in the other four cases.<sup>6</sup> Myocardial infarction in POEMS syndrome has rarely been reported. Manning et al. reported a 27-year-old man with POEMS syndrome and extensive myocardial infarction and ulcerative proctitis. The patient had no significant risk factor for coronary arterial disease.<sup>7</sup> Manning et al.

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hypothesized that an abnormal immunoglobulin (or fragment) is responsible for these findings.<sup>7</sup>

Despite variable manifestation of cardiac disease in POEMS syndrome, complete heart block has not been reported previously. Herein, we present a case of POEMS syndrome with cardiac involvement, characterized by complete heart block.

### Case Report

A 48-year-old man presented with numbness and weakness in lower extremities 1 year before admission in our center. Progressive proximal weakness had been developed in 3 weeks, and he was not able to walk and became wheelchair dependent. No abnormalities in urination and bowel habit were detected. In history he has had a history of low back pain since last year that had been diagnosed as a discopathy and medical treatment had been advised. In the physical examination, his muscle strength was 2/5 in proximal lower extremities and 3/5 in proximal of upper extremities. Deep tendon reflexes were decreased. Touch and pain sensation were also impaired, but anal sphincter tone and cranial nerves were normal.

In lab data except elevated cerebrospinal fluid protein (90 mg/dl), there were no other abnormalities. Due to ascending and distal sensory motor polyneuropathy, Guillain-Barre syndrome was diagnosed, and plasmapheresis and intravenous immunoglobulin (IVIG) were administered. About 2

weeks after hospitalization thrombocytosis (1,120,000/ $\mu$ l) was detected in lab data, which was associated with splenomegaly and para aortic lymphadenopathy in abdominopelvic computed tomography (CT) scan. Peripheral adenopathy was not detected. Bone marrow aspiration and biopsy reported normal. Splenectomy was performed, but patient had no symptom relief. Finally, after 2 weeks, he discharged with chronic inflammatory demyelinating polyneuropathy diagnosis and advised receiving IVIG monthly. Despite receiving IVIG monthly, his neurological symptoms were aggravated, and he became bedridden. Plasmapheresis was administered, but it had no effect. About 10 months after symptoms onset he was referred to hematology the ward for evaluation of thrombocytosis. He complained of overt weight loss, low back pain, nasal speech and pedal, and hand edema. He had no cardiac or respiratory symptoms. In physical examination, the patient was quadriplegic and deep tendon reflexes were absent. In ophthalmoscopy bilateral papilledema were present. Other abnormal physical examination findings were clubbing and whitening of nails, pedal and hand edema, bilateral gynecomastia and hypertrichosis. Peripheral lymph nodes were not palpable. The cranial nerves were normal. Table 1 shows the patient lab data. Serum protein electrophoresis was normal, but in serum immunofixation immunoglobulin G (IgG) lambda and IgA lambda biconal gammaglobuline were seen.

**Table 1.** Laboratory data

Variable	Reference range	Result
White-cell count (/mm <sup>3</sup> )	4500-11000	12500
Differential count (%)		
Neutrophils	55.0-75.0	45
Lymphocytes	22.0-44.0	51.9
Mix	0.0-10.0	3.1
Platelet count (/mm <sup>3</sup> )	150000-350000	1019000
Hematocrit (%)	41.0-53.0 (men)	48.0
Hemoglobin (g/dl)	13.5-17.5 (men)	14.5
Mean corpuscular volume	80.0-100.0	89.6
Testosterone (ng/ml)	3.0-12.0	0.4
Albumin (mg/dl)	3.4-5.0	2.9
Creatinine (mg/dl)	0.6-1.5	0.5
BUN (mg/dl)	8.0-25.0	13.0
aPTT (s)	22.1-34.0	28.0
PT (s)	10.3-13.2	14.2
INR	1.00	1.16
TSH ( $\mu$ g/dl)	0.3-50.0	2.4
T4 ( $\mu$ U/ml)	4.0-12.0	5.5
FBS (mg/dl)	< 100	78

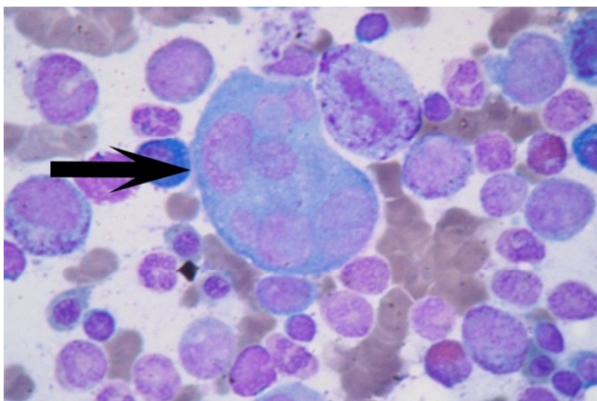
BUN: Blood urea nitrogen; aPTT: Particle thromboplastin time; PT: Prothrombin time

INR: International normal ratio; TSH: Thyroxin stimulating hormone; T4: Tetraiodo-thyronine

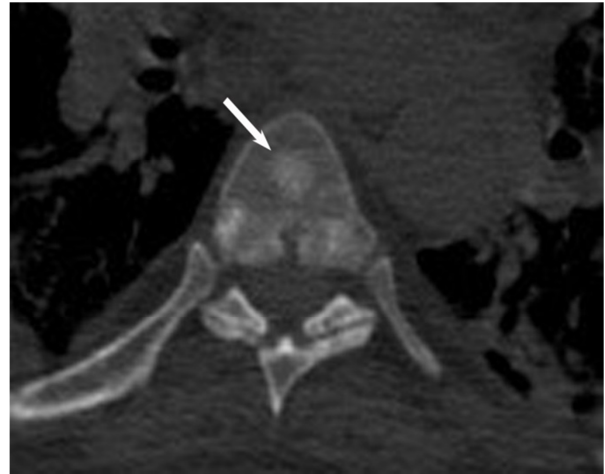
FBS: Fasting blood sugar

In urine immunofixation, free kappa and lambda light chain were detected. In bone marrow aspiration large clumps of platelets suggestive of severe thrombocytosis and up to 3% highly atypical plasma cells was seen. In bone marrow biopsy, although osteosclerosis was not seen, but infiltrated sheets of poorly differentiated cells were seen (Figure 1). Rectal biopsy was performed. Congo red stain of rectal biopsy was negative. Electromyography and nerve conduction velocity studies revealed axonal and demyelinating polyneuropathy. Multislice CT scan of full spine revealed a sclerotic bone lesion in the body of T5; measuring about 10 mm (Figure 2).

As the patients had most criteria, diagnosis of POEMS syndrome was considered. In last admission, he had explained episodes of chest pain and dyspnea. Results of cardiovascular and pulmonary examination were normal, evaluation of pulmonary thromboembolism was negative, his electrocardiograph (ECG) showed normal sinus rhythm, frequent premature ventricular contractions (PVC) (three geminal PVC), PR interval 160 ms, QRS interval 100 ms, and QTc interval 163 ms. To reduce PVC diltiazem 30 mg twice daily started. After 2 days heart monitoring in cardiac care unit the patient had frequent episodes of transient complete heart block in cardiac rhythm. On echocardiography, normal cardiac function with no structural abnormality was detected. After discontinuation of diltiazem, electro-physiologic study was done that showed infra-His atrioventricular (AV) block and patient candidate for permanent pace maker. After pace maker insertion, he referred to the radiotherapy ward for irradiation of sclerotic bone lesion. Unfortunately, radiotherapy was ineffective, and his neuropathy progressed and he passed away with respiratory failure.



**Figure 1.** Abnormal plasma cell infiltration in bone marrow aspiration



**Figure 2.** Sclerotic bone lesion in body of T5

### Discussion

Complete AV block has a variety of causes. Ischemic heart disease is responsible for about 40% of cases of AV block.<sup>8</sup> Infiltrative disease such as amyloidosis<sup>9</sup> and sarcoidosis<sup>10</sup> are other common causes of AV block. Some drugs such as digitalis, amiodarone, calcium channel blockers (especially diltiazem and verapamil),  $\beta$ -blockers and adenosine can impair AV conduction, leading to AV block.<sup>11</sup> Most patients with AV block who have no obvious cause except these drugs have underlying conductive disease.<sup>11</sup> Drug discontinuation can result in resolution of AV block in some patients but most of them without treatment AV block later recurred. Our patient had no history of coronary and atherosclerotic risk factors for ischemic heart disease; in serial ECG no ST-T changes were seen. An echocardiogram is the most valuable procedure to detecting decreased cardiac function in patients suspected for myocarditis, even when it is subclinical.<sup>12,13</sup> On repeated echocardiography, cardiac function was normal, and no evidence of structural disease was seen. Cardiac biomarkers were normal, and patient had no clinical suspicious for myocarditis. To exclude amyloidosis rectal fat biopsy was taken that was negative for Congo red staining. Results of thyroid function test and serum electrolytes were within normal range. Diltiazem was discontinued. However AV block was not resolved. These indicated that underlying conducting system abnormality in the patient existed that was related to primary disease.

### Acknowledgments

We would like to thank the patient for permitting the publication of this article.

### Conflict of Interests

Authors have no conflict of interests.

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**How to cite this article:** Ashrafi F, Darakhshandeh A, Nematolahy P, Khosravi A. **Complete heart block in a patient with POEMS syndrome: A case report.** *ARYA Atheroscler* 2014; 10(5): 276-9.