Case Report | Internal Medicine

Polymyalgia Rheumatica Presenting as Nocturnal Pyrexia of Unknown Origin: A Case Report

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Abstract

Background. Polymyalgia rheumatica (PMR) is a rheumatic disorder characterized by musculoskeletal stiffness and pain, primarily affecting the shoulder, neck, and hip areas. It is more common in females, with the peak incidence usually after the age of 70.

Case Report. A 74-year-old man presented with a two-month history of low-grade nocturnal fever up to 100°F (37.7°C) which did not respond to multiple courses of antibiotics. There was unintentional weight loss of 5 kg and mild shoulder stiffness. The patient had a history of Type 2 diabetes mellitus treated with 34 units of insulin (Humulin 70/30) daily and active smoking of 40 pack-years. On examination, mild tenderness of both shoulder girdle muscles and discomfort on external rotation were noted. The initial blood work-up revealed raised erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels. Serologies for syphilis, human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) were negative. Given the negative results of infective and malignancy screening, along with raised inflammatory markers and mild shoulder stiffness, a diagnosis of PMR was made and a trial of prednisolone was initiated, resulting in the resolution of symptoms.

Conclusions. The present case report highlights the importance of thoroughly investigating all differential diagnoses of pyrexia of unknown origin, regardless of the patient’s ethnic origin, to facilitate timely diagnosis.

Keywords

Polymyalgia Rheumatica; Pyrexia of Unknown Origin; Corticosteroids; Prednisolone

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Background

A chronic rheumatic disease of unknown etiology - polymyalgia rheumatica (PMR), is associated with musculoskeletal stiffness and pain affecting the shoulder, neck, and hip areas [1]. PMR is rarely seen in individuals under the age of 50; however, its incidence increases with age and females are up to three times more likely to be affected than males [2]. The incidence of PMR in population over 50 years of age is approximately 50 per 100,000 annually, with the peak incidence typically occurring after the age of 70. [3]. PMR is relatively uncommon in the South Asia region, including India and Pakistan, with a higher prevalence in Caucasians and Northern European countries, especially Scandinavia [4–6]. The diagnosis of PMR may be challenging as there are no specific diagnostic tests [3]. A thorough clinical assessment and the exclusion of other causes is essential to diagnose PMR. Clinical manifestations of PMR typically include musculoskeletal pain and stiffness, accompanied by elevated inflammatory markers such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). The initial manifestation is typically symmetrical shoulder involvement, which may extend to the neck region and hip girdles. The pain is usually worse at night, accompanied by morning stiffness lasting over 60 minutes, which may result in limitation of joint movements. On examination, the patient typically exhibits bilateral proximal muscle tenderness, which aids in diagnosis and monitoring treatment response [3]. Rarely, small joint involvement,
normal ESR and CRP levels, weight loss, fever, and anemia may also be seen [7, 8].

**Case Report**

**Patient Information**

We report the case of a 74-year-old man who presented with a two-month history of gradual-onset, low-grade nocturnal fever, documented up to 100°F (37.7°C). The fever occurred almost daily at night, ranging from 98.8°F to 100°F (37.1°C to 37.7°C), and subsided on its own by morning. The patient took oral paracetamol, analgesics, and multiple courses of antibiotics, but the fever persisted. Additionally, there was a history of unintentional weight loss of 5 kg over the last two months, decreasing from 96 kg to 91 kg. There was no history of cough, sputum, shortness of breath, chest pain, headache, vision disturbances, oral or genital ulcers, skin rashes, dysphagia, altered bowel habits, joint pain, lumps or bumps, or bleeding from any site. Additionally, the patient had a history of Type 2 diabetes mellitus for the last 30 years and was currently being treated with 34 units of insulin (Humulin 70/30) daily. The patient reported mild stiffness in both shoulders without any weakness for the last few months, for which a local general practitioner (GP) suspected adhesive capsulitis and prescribed analgesics and multiple courses of antibiotics, but the fever persisted. Additionally, there was a history of unintentional weight loss of 5 kg over the last two months, decreasing from 96 kg to 91 kg. There was no history of cough, sputum, shortness of breath, chest pain, headache, vision disturbances, oral or genital ulcers, skin rashes, dysphagia, altered bowel habits, joint pain, lumps or bumps, or bleeding from any site. Additionally, the patient had a history of Type 2 diabetes mellitus for the last 30 years and was currently being treated with 34 units of insulin (Humulin 70/30) daily. The patient reported mild stiffness in both shoulders without any weakness for the last few months, for which a local general practitioner (GP) suspected adhesive capsulitis and prescribed analgesics and physiotherapy. Additionally, the patient was an active smoker with 40 pack-years but denied alcohol intake and illicit drug use. He was married with four children and was a retired factory office worker.

**Clinical Findings**

There were no notable findings on his general, systemic, and musculoskeletal examinations, apart from mild tenderness of both shoulder girdle muscles and discomfort on external rotation.

**Investigations**

The differential diagnosis encompassed infections such as tuberculosis, malignancies including lung and prostate cancers, leukemia, and autoimmune disorders such as systemic lupus erythematosus (SLE) and vasculitis. The initial blood work-up (Table 1) did not reveal any abnormalities other than raised ESR and CRP levels. Serologies for syphilis, human immunodeficiency virus (HIV), hepatitis B virus (HBV), and hepatitis C virus (HCV) were negative. A peripheral blood smear showed no abnormal cells or malaria parasite. Glycated hemoglobin (HbAlc) level was 7.1%. Serum creatine phosphokinase (CPK) and aldolase, urinalysis, and stoll examination were normal. Blood and urine cultures yielded no organisms. A chest X-ray and an ultrasound of the abdomen and pelvis were performed, followed by echocardiography and computed tomography (CT) scans of the chest, abdomen, and pelvis; all results were within normal parameters. An autoimmune profile was ordered, including antinuclear antibodies (ANA), rheumatoid arthritis (RA) factor, anti-cyclic citrullinated peptide (anti-CCP) antibodies, extractable nuclear antigen (ENA) profile, cytoplasmic anti-neutrophil cytoplasmic antibodies (c-ANCA), and perinuclear anti-neutrophil cytoplasmic antibodies (p-ANCA), but all results were negative.

**Table 1. Patient’s blood work-up.**

<table>
<thead>
<tr>
<th>Investigation</th>
<th>Patient’s Value</th>
<th>Reference Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (G/dl)</td>
<td>13.6</td>
<td>12.0-16.0</td>
</tr>
<tr>
<td>TLC (per mm$^3$)</td>
<td>10.1</td>
<td>4,000-11,000</td>
</tr>
<tr>
<td>Platelets (per mm$^3$)</td>
<td>245</td>
<td>150,000-450,000</td>
</tr>
<tr>
<td>ESR (mm/hour)</td>
<td>68</td>
<td>up to 20</td>
</tr>
<tr>
<td>CRP (mg/dl)</td>
<td>26</td>
<td>up to 5.0</td>
</tr>
<tr>
<td>Procalcitonin (ng/ml)</td>
<td>&lt;0.03</td>
<td>&lt;0.5</td>
</tr>
<tr>
<td>Serum creatinine (mg/dl)</td>
<td>1.0</td>
<td>0.6-1.4</td>
</tr>
<tr>
<td>Albumin (G/dl)</td>
<td>3.8</td>
<td>3.5-5.0</td>
</tr>
<tr>
<td>Globulin (G/dl)</td>
<td>2.9</td>
<td>1.8-3.2</td>
</tr>
<tr>
<td>Serum bilirubin (mg/dl)</td>
<td>0.8</td>
<td>up to 1.0</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>41</td>
<td>less than 35</td>
</tr>
<tr>
<td>ALT (U/L)</td>
<td>38</td>
<td>less than 35</td>
</tr>
<tr>
<td>Alkaline phosphatase (U/L)</td>
<td>106</td>
<td>30-120</td>
</tr>
<tr>
<td>TSH (iU/ml)</td>
<td>0.95</td>
<td>0.35-4.95</td>
</tr>
<tr>
<td>Free T3 (ng/dl)</td>
<td>132</td>
<td>60-180</td>
</tr>
<tr>
<td>Free T4 (ng/dl)</td>
<td>1.4</td>
<td>0.8-1.8</td>
</tr>
<tr>
<td>PSA (ng/ml)</td>
<td>1.65</td>
<td>&lt;4.0</td>
</tr>
</tbody>
</table>

Notes: TLC – total leucocyte count; MCV – mean corpuscular volume; ESR – erythrocyte sedimentation rate; CRP – C-reactive protein; AST – aspartate transferase; ALT – alanine transaminase; TSH – thyroid stimulating hormone; T3 – triiodothyronine; T4 – thyroxine; PSA – prostate-specific antigen.

**Diagnosis**

Given the negative results for infectious and malignant conditions, along with raised inflammatory markers and mild shoulder stiffness, a diagnosis of PMR was made.

**Treatment and Follow-up**

The patient was started on a trial of oral prednisolone at a dose of 20 mg/day, which resulted in the resolution of symptoms. His blood pressure and blood glucose were monitored to prevent any steroid-related adverse effects. He was maintained on prednisolone at a dose of 15 mg/day for the next four weeks, with normalization of ESR and CRP levels followed by gradual medication tapering. The patient is currently asymptomatic and has experienced no adverse effects from the therapy.

**Discussion**

An inflammatory joint disease, PMR, is usually seen in patients over 50 years of age and presents as pain and prolonged morning stiffness involving the neck, shoulders, and hip girdles. The diagnosis of PMR is challenging due to a lack of specific clinical examination findings, laboratory tests, or imaging studies to diagnose the condition [11]. The diagnostic, therapeutic, and prognostic aspects of imaging studies in PMR are poorly documented and require further clarification [11]. Delays in diagnosing PMR and other systemic vasculitides can be detrimental, as these diseases have the potential to progress, causing significant morbidity or mortality and increasing the socio-economic burden [12]. Various steps that may be taken to address...
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this issue include increasing awareness by educating both the public and healthcare professionals, particularly GPs, regarding the clinical features of these conditions, facilitating timely referrals of suspected patients to rheumatologists, expanding the rheumatology workforce, and implementing readily available tests for prompt diagnosis to streamline patient care [12]. These steps can potentially improve disease outcomes by maintaining remission and minimizing damage accrual, thereby improving life quality for these patients [12].

Chuang et al. and Healey et al. have described diagnostic criteria for PMR, with the latter including rapid response to < 20 mg/day of prednisolone as one of the criteria; however, they are not widely used in routine clinical practice [11, 12]. In 2012, new classification criteria for PMR were proposed by the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR); however, they are applicable only to patients meeting preliminary criteria of age > 50 years, bilateral shoulder pain, and raised ESR or CRP levels [14, 15]. These classification criteria help reduce the heterogeneity of positive cases based on a subset of typical manifestations, thereby lowering the probability of false positive diagnosis. However, they may not be fulfilled in atypical PMR cases [13]. The drawbacks of most PMR diagnostic criteria are their unsatisfactory sensitivity and specificity, as well as the fact that they were developed for populations with a high prevalence of PMR. Therefore, a thorough clinical assessment and the exclusion of other causes remain essential in the diagnosis of PMR [7, 8]. Our patient presented with nocturnal pyrexia of unknown origin (PUO) persisting for a duration of two months, accompanied by mild shoulder stiffness and tenderness. His ESR and CRP levels were elevated, but other investigations for infections, malignancies, and autoimmune disorders were negative. These findings collectively guided towards a diagnosis of PMR, which was further supported by the rapid response and resolution of the patient’s symptoms after initiation of corticosteroids. This presentation is similar to a case reported by Mahdy et al., detailing PMR in a 61-year-old South Asian woman presenting with nocturnal pyrexia [15].

Treatment of PMR is largely based on corticosteroid use. A dose of 12.5 mg to 25 mg of oral prednisolone daily, or its equivalent, is recommended [16, 17]. While intramuscular methylprednisolone is an alternative, oral prednisolone is associated with rapid symptom resolution and better outcomes compared to the intramuscular route. At present, there is no consensus regarding the definition of remission in PMR, but most of them include the resolution of clinical symptoms and reductions in ESR to below 40 mm/h and CRP levels to < 1 mg/dL [18]. In our case, after initiating 15 mg/day of oral prednisolone, there was complete resolution of symptoms and normalization of ESR and CRP levels by the 4-week follow-up. For patients with refractory PMR who do not respond to steroids or experience relapse, treatment with methotrexate is recommended [19, 20]. Tocilizumab has recently been recommended for the treatment of PMR as a steroid-sparing agent with good efficacy and a low adverse effect profile [21, 22]. Numerous ongoing studies are investigating the role of baricitinib, sarilumab, and rituximab in the treatment of PMR, with preliminary results showing promise [23].

Conclusions
Nocturnal pyrexia is an atypical and rare presentation of PMR. The present case report underscores the importance of thoroughly investigating all differential diagnoses of PUO, irrespective of the patient’s ethnic origin, to facilitate timely diagnosis. Prompt initiation of treatment with corticosteroids can effectively reduce the morbidity and disability associated with PMR and improve quality of life for affected patients.

Ethical Statement
The case report was conducted in compliance with the World Medical Association Declaration of Helsinki “Ethical Principles for Conducting Medical Research Involving Human Subjects”.

Informed Consent
Detailed informed consent was taken from the patient and his son prior to data collection and manuscript submission.

Data Availability
The data are available on reasonable request.

Conflict of Interest
The authors declare that they have no conflicts of interest.

Financial Disclosure
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References


