

## CASE REPORT

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# A Case of Transient ACTH Deficiency Associated with Polymyalgia Rheumatica

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**Abstract:** We report a case of 79-year-old man, who was diagnosed to have transient ACTH deficiency associated with polymyalgia rheumatica (PMR). The patient presented with sudden onset bilateral shoulder pain, which was gradually aggravated. Plasma ACTH was undetectable, and both serum cortisol and urinary 17-OHCS were very low. Other pituitary hormones were normal, suggesting that hypothalamo-pituitary-adrenal (HPA) axis is selectively damaged. However, within several weeks, plasma ACTH returned to normal, and showed a normal increase response to corticotropin-releasing hormone stimulation test. These results indicated that ACTH deficiency was only transient. After hydrocortisone (10 mg/day) was administered, his symptoms became suddenly improved. Based on those results and clinical course, ie, elevated erythrocyte sedimentation rate, negative rheumatoid factor and the typical symptoms, which showed improvement to glucocorticoid therapy, the final diagnosis was PMR, which was associated with transient ACTH deficiency.

This is the first report of a case of PMR, in which the HPA axis was examined in its very acute phase. It was demonstrated that the case was associated with the transient adrenocortical hypofunction, which was recovered during a short time. It is therefore possible that PMR may show a different responsiveness of HPA axis depending on its phases.

**Keywords:** polymyalgia rheumatica (PMR), ACTH deficiency

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## Introduction

Polymyalgia rheumatica (PMR) is a common disorder in the elderly, characterized by aching and morning stiffness in the neck, shoulders, and pelvic girdle, along with constitutional symptoms (malaise, weight loss, fever).<sup>1</sup> Cutolo and colleagues have proposed a hypothesis that PMR may share some clinical features with the steroid-withdrawal syndrome or adrenal insufficiency, such as dramatic and rapid disappearance of the symptoms after glucocorticoid treatment.<sup>1-4</sup>

Here we present a case of PMR, which was indicated to have transient ACTH deficiency. The pathogenetic significance of association of the two disorders is discussed.

## Case Report

A 79-year-old man was admitted to department of neurology because of severe bilateral shoulder pain and proximal muscle weakness of lower extremities, which began one month ago. He had neither pelvic girdle pain nor flexion contracture. Neurological examinations indicated no abnormality. The neurologist suspected a possibility of muscle weakness caused by some endocrinopathy, and performed endocrinological examinations, which revealed low serum cortisol (1.8 µg/day) and undetectable plasma ACTH (<5 pg/ml) level. Other laboratory findings such as blood electrolytes and glucose levels were normal. Since these results indicated a possibility of ACTH deficiency, the patient was transferred to department of diabetes and endocrinology. However, urinary 17-OHCS level was low (1.4 mg/day). Other pituitary hormone and thyroid hormone levels were normal, including their responses to provocative tests, such as thyrotropin-releasing hormone, luteinizing hormone-releasing hormone, and growth hormone-releasing hormone. Nonsteroidal anti-inflammatory drug, (etodalac 600 mg/day, po) was given, which caused some, but not complete, improvement of his symptoms. Serum CRP was positive (11.64 mg/dl), and erythrocyte sedimentation rate was increased (66 mm/hr). Rheumatoid factor was negative. Imaging studies showed no evidence for the presence of any malignancy. Corticotropin-releasing hormone (CRH) and ACTH stimulation tests were performed. ACTH showed slightly blunted response to CRH from slightly high basal level (238 to 266 pg/ml).

Rapid ACTH stimulation proved a slightly blunted increase in cortisol from slightly high basal level (20.0 to 25.7 µg/dl).

Hydrocortisone (10 mg/day) was started with a rapid and complete improvement of his symptoms, such as shoulder pains, after 2 days. Both CRP and erythrocyte sedimentation rate became normalized. Both serum ACTH and Urinary 17-OHCS levels were also became normal range after three weeks (13.9 pg/ml and 6.0 mg/day, respectively).

Based on those results and clinical course, ie, elevated erythrocyte sedimentation rate, negative rheumatoid factor and the typical symptoms, which showed improvement to glucocorticoid therapy, the final diagnosis was PMR, which was associated with transient ACTH deficiency.

## Discussion

This patient was found to have PMR and transient ACTH deficiency, although he did not show flexion contracture sometimes associated with adrenocortical insufficiency.<sup>5</sup>

Cutolo and his colleagues suggested that PMR shares clinical features with the steroid-withdrawal syndrome or adrenal insufficiency, such as the abrupt onset, the clinical response to glucocorticoid therapy.<sup>1-3</sup> They found that reduced production of adrenal hormone (cortisol, dehydroepiandrosterone sulfate) at baseline in patients with active and untreated PMR.<sup>1</sup> ACTH induced a significantly higher peak of 17-hydroxyprogesterone (17-OHP) in patients with PMR than in controls, although CRH stimulation or ACTH stimulation evoked a normal ACTH and cortisol response, respectively, suggesting that the defect seems mainly related to CYP21A2 21-hydroxylase deficiency.<sup>1,3</sup>

In our patients, the treatment with hydrocortisone, 10 mg per day, resulted in an improvement of his symptoms. This dose is generally not enough for management of PMR, which requires generally prednisone, 10 to 20 mg per day equivalent, which is in the range of 40 to 80 or so mg of hydrocortisone. This dose of 10 mg of hydrocortisone likely is a good dose for adrenal insufficiency, especially if transient, but generally not for PMR.

These results suggest that hypothalamo-pituitary adrenal (HPA) axis may play a role in pathogenesis of PMR, justifying use of glucocorticoid in its



treatment. It was also indicated that PMR patients without corticosteroid treatment had higher serum cortisol in relation to IL-6 compared to PMR patients without long-standing disease and with corticosteroid treatment.<sup>3</sup> However, the cortisol level in PMR patients was lower than expected under inflammatory conditions.<sup>3</sup> They have proposed a hypothesis that PMR is associated with a decrease in HPA axis responsiveness to inflammatory stimuli, such as IL-6, which may be linked to aging process.<sup>3</sup>

In contrast, Pacheco et al recently reported that the responses of cortisol and dehydroepiandrosterone to low-dose ACTH challenge were not significantly lower in patients with PMR than in healthy subjects.<sup>4</sup> They also found that the acute phase reactants did not show a clear relationship with adrenal hormones, indicating that the abnormalities of HPA found in PMR were the consequences of chronic illness rather than a crucial factor contributing to the pathogenesis of PMR.<sup>4</sup>

This is the first report of a case of PMR, in which the HPA axis was examined in its very acute phase. It was indicated that the case was associated with the transient adrenocortical hypofunction, which was recovered during a short time. It is therefore possible that PMR may show a different responsiveness of HPA axis depending on its phases, and that the discrepancies between the reports<sup>1,6</sup> might be attributable to the different phase of PMR examined.

## Disclosure

This manuscript has been read and approved by all authors. This paper is unique and is not under consideration by any other publication and has not been published elsewhere. The authors and peer reviewers of this paper report no conflicts of interest. The authors confirm that they have permission to reproduce any copyrighted material. Written consent was obtained from the patient or relative for publication of this study.

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