

Received: 2018.11.16 Accepted: 2019.01.07 Published: 2019.04.07

A Case of Polymyalgia Rheumatica Following Robotic-Assisted Radical Prostatectomy for High-Grade Prostate Cancer

ABEF Madeleine S. Deming

Internal Medicine Consult Service, Clinical Center, National Institutes of Health (NIH), Bethesda, MD, U.S.A.

Authors' Contribution: Study Design A Data Collection B Statistical Analysis C Data Interpretation D Manuscript Preparation E Literature Search F Funds Collection G

Corresponding Author: Madeleine S. Deming, e-mail: madeleine.deming@nih.gov Conflict of interest: None declared

Patient: Male, 61 Final Diagnosis: Polymyalgia rheumatica Symptoms: Shoulder and hip pain Medication: — Clinical Procedure: — Specialty: General and Internal Medicine

Objective: Rare co-existence of disease or pathology Background: Polymyalgia rheumatica (PMR) is a common rheumatic disease in patients over the age of 50 years. Underlying triggers for PMR are not well understood, but there have been reports of cases presenting prior to the diagnosis of prostate cancer, with one case of PMR presenting following prostatectomy. This report is of a case of PMR that presented following robotic-assisted radical prostatectomy for high-grade prostate cancer and includes a discussion of the possible associations.

Case Report: A 61-year-old man underwent a robotic-assisted radical prostatectomy for high-grade prostate adenocarcinoma, Gleason grade 4+4=8. The surgical procedure and the patient's postoperative recovery were uneventful, and he was discharged from hospital on the day after surgery. Approximately two weeks later, he developed bilateral symptoms of pain in the groin, thigh, and shoulder girdle. His erythrocyte sedimentation rate (ESR) (30 mm/h) and C-reactive protein (CRP) (16.2 mg/L) levels were raised. A diagnosis of PMR was made and treatment with tapered dosing of methylprednisolone resulted in a 90% improvement in symptoms after four weeks.

Conclusions: A case of PMR following robotic-assisted prostatectomy for high-grade prostate carcinoma is presented. To the author's knowledge, this is only the second report of PMR following prostatectomy and the only reported case following robotic-assisted radical prostatectomy.

MeSH Keywords: Polymyalgia Rheumatica • Prostatectomy • Prostatic Neoplasms • Robotics

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/914152

1505 — — 11



Background

Polymyalgia rheumatica (PMR) is a common rheumatic disease in patients over the age of 50 years. A recently published large-scale population-based study estimated the incidence of PMR to be 95.9 per 100,000 individuals over the age of 40 (95% CI, 94.9–96.8) [1]. PMR is now considered to be a component of a spectrum of chronic inflammatory diseases that also includes giant cell arteritis (GCA), which is the most common type of vasculitis found in this age group. While GCA is a diagnosis made through arterial biopsy, PMR is a clinical diagnosis characterized by severe pain and stiffness of the hip and shoulder girdles which is worse in the morning, and is associated increased serum markers of inflammation including erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) [2].

There have been several previously reported cases of prostate cancer presenting with PMR, which has been considered to represent a component of a paraneoplastic syndrome triggered by malignancy [3,4]. In these previous reports, symptoms consistent with PMR were identified prior to the diagnosis of prostate cancer and resolved following treatment. To the author's knowledge, there has only been one other case reported in the literature of PMR presenting after following robotic-assisted prostatectomy [5].

This report is of a case of PMR that presented following robotic-assisted radical prostatectomy for high-grade prostate cancer and includes a discussion of the possible associations.

Case Report

A 61-year-old man was diagnosed with high-grade prostate adenocarcinoma, Gleason grade 4+4=8, and was referred to the urology service for robotic-assisted radical prostatectomy. He underwent staging that included a bone scan that was negative for metastatic disease. His past medical history was significant for hyperlipidemia for which he was prescribed simvastatin, 10 mg daily. He had a ten-year history of chronic osteoarthritis of the right shoulder and a 20-year history of chronic osteoarthritis of the left knee, and had undergone surgery of the right shoulder and left knee arthroscopy. However, despite his history of osteoarthritis, before undergoing prostatectomy, he was able to play basketball for several hours a week and to jog on an inclined treadmill. His father had been diagnosed with rheumatoid arthritis at an unknown age.

The patient's pre-operative laboratory investigations were within the normal range, including serum calcium, phosphorus, and alkaline phosphatase (ALP) levels. He underwent robotic-assisted radical prostatectomy, which involved a standard protocol and was uncomplicated. The surgical procedure

included placing the patient in the Trendelenburg position, followed by abdominal insufflation and laparoscopy. The surgery lasted for six hours and forty minutes, with no hypoxic or hypotensive episodes. The estimated blood loss during surgery was 400 ml, which was within the expected range for the procedure. He was stable postoperatively and was discharged home on the day following surgery.

Approximately two weeks after discharge from the hospital, he developed an acute onset of bilateral groin pain and over the next few days he experienced a shooting pain down the back of his thighs and legs. He also noticed some mild pain in his shoulder. Twenty-eight days after his surgery, he attended the local emergency room for worsening pain and was treated with a course of ciprofloxacin for possible urinary tract infection. He was then treated with a seven-day course of methylprednisolone (Medrol Dosepak) using a tapered dose. His symptoms initially improved, but on the sixth day of steroid treatment, he developed increased pain that prompted him to return to the emergency room, where he was given a second course of methylprednisolone, which again resulted in clinical improvement. He was also prescribed oxycodone 10 mg six hourly, but with no effect. One month after surgery, he referred himself to a community orthopedic surgeon who administered hyaluronic injections in both knees. Two months after his surgery, he was seen at our facility for evaluation of his symptoms of persistent and severe pain.

Two months following robotic-assisted radical prostatectomy, the patient's symptoms included pain and stiffness involving his hips and shoulders, which were worse at night and on waking in the morning. The pain was severe, which he rated as >10/10, which led him to sleep in a recliner. He also reported a single episode of blurred vision several weeks previously. On examination, his temperature was 36.8°C, his blood pressure was 131/88 mmHg, his heart rate was 94 beats per minute, and his respiratory rate was 18 breaths per minute, and his digital pulse oximeter reading was 96% on room air. He was alert, oriented, and in moderate distress due to pain. The range of motion of his upper extremities was limited due to pain and stiffness, and there was tenderness on palpation at the mid-scapular area of his back, extending over his shoulders to the sub-clavicular area in a cape-like distribution. There was no joint tenderness, warmth, erythema, or swelling of the shoulders, elbows, wrists, or hands, and muscle wasting was present. His proximal and distal pulses were normal, and his grip strength was normal. On examination of his lower extremities, there was tenderness in the groin area and along the medial aspect of both thighs, with pain and stiffness that limited the range of motion of both hips on external and internal rotation. Palpation of the temporal arteries showed mild tenderness but there was no nodularity.

On the latest hospital admission, the patient's erythrocyte sedimentation rate (ESR) (30 mm/h) and C-reactive protein (CRP) (16.2 mg/L) levels were raised. Laboratory tests for infection were unremarkable and repeat imaging remained negative for bone metastasis. A temporal artery biopsy was negative for giant cell arteritis. A diagnosis of PMR was made and treatment with tapered dosing of methylprednisolone, 20 mg daily, resulted in a 90% improvement in symptoms after four weeks. Gradual tapering of steroid therapy was planned over six months to one year. At one-month follow-up, his ESR and CRP had decreased to 6 mm/h and 1 mg/L, respectively and he reported a 90% improvement in his symptoms.

Discussion

In a previously reported case of an acute presentation of polymyalgia rheumatica (PMR) following robotic-assisted radical prostatectomy, the authors proposed that either the cytokine release from tissue injury associated with surgery or sympathetic neural activation from surgical stress might have been an underlying trigger [5]. There have been no studies on the possible mechanisms leading to PMR following surgery, but as with other types of malignancy, the progression of prostate cancer is associated with inflammation [6]. In prostate cancer, the inflammatory cytokine, interleukin-6 (IL-6), has been shown to be involved in the progression to the more aggressive phenotype, which is castration-resistant [7]. Studies in mouse models have shown that orchiectomy resulted in increased levels of IL-6 in the bone marrow [8], indicating that androgen depletion might play a role in the stimulation of IL-6.

The findings from a clinical study of 100 men with localized prostate cancer who underwent radical prostatectomy reported a transient reduction in serum testosterone levels following surgery with a nadir at one month and return to the baseline at three months following surgery [9]. The authors proposed that factors during surgery, including ligation of the Santorini venous plexus and the use of the Trendelenburg position, could cause transient ischemic changes to the testes resulting in a reduction in testosterone [9]. Also, levels of IL-6 have been shown to be increased in patients with PMR with levels of IL-6 showing a significant correlation with disease

activity and with an increased risk of relapse [10]. Treatment with the anti-IL-6 receptor monoclonal antibody, tocilizumab, has been shown to result in some improvement in the symptoms of PMR in limited case studies [10]. IL-6 may have exert its effects on patients with PMR by regulating the balance between pro-inflammatory T-helper 17 (Th17) cells, and regulatory T-cells (Tregs) that suppress the immune response [11].

In the case presented in this report, although IL-6 levels were not measured, it is likely that high-grade prostate cancer was associated with inflammation and that the surgical procedure resulted in a transient decrease in postoperative serum levels of testosterone. An increase in the levels of circulating pro-inflammatory cytokines, including IL-6, might have tipped T-cell regulation to a pro-inflammatory state and acted as a trigger for the onset of PMR. This patient had a family history of rheumatoid arthritis, and it is possible that he was primed for the development of PMR following the triggering event of prostatectomy.

Conclusions

To the author's knowledge, this is the second case report of a diagnosis of polymyalgia rheumatica (PMR) following robotic-assisted radical prostatectomy. While PMR has been described elsewhere as part of a paraneoplastic syndrome associated with prostate cancer, the timing and presentation of PMR, in this case, suggested that the procedure of prostatectomy might have acted as a trigger for the onset of PMR. Prospective studies to measure the serum levels of testosterone and inflammatory cytokines, including IL-6, in patients with high-grade prostate cancer before and after prostatectomy might identify the mechanisms of the inflammatory response that may have resulted in PMR.

Acknowledgments

The author thanks Cindy Clark, National Institutes of Health (NIH) Library Writing Center, for manuscript editing assistance.

Conflict of interest

None.

References:

1. Partington RJ, Muller S, Helliwell T et al: Incidence, prevalence and treatment burden of polymyalgia rheumatica in the UK over two decades: A population-based study. *Ann Rheum Dis*, 2018; 77:1750-56
2. Neshar G, Breuer GS: Giant cell arteritis and polymyalgia rheumatica: 2016 update. *Rambam Maimonides Med J*, 2016; 7(4)
3. Kane I, Menon S: Carcinoma of the prostate presenting as polymyalgia rheumatica. *Rheumatology (Oxford)*, 2003; 42: 385-87
4. Emamifar A, Hess S, Gildberg-Mortenson R, Hansen IM: Association of remitting seronegative symmetrical synovitis with pitting edema, polymyalgia rheumatica, and adenocarcinoma of the prostate. *Am J Case Rep*, 2016; 17: 60-64
5. Suntharasivam T, Gnanapragasam VJ: Polymyalgia rheumatica following robotic radical prostatectomy. *Int J Surg Case Rep*, 2012; 3: 354-55
6. Sfanos KS, De Marzo AM: Prostate cancer and inflammation: The evidence. *Histopathology*, 2012; 60: 199-215

7. Nguyen DP, Li J, Tewart AK: Inflammation and prostate cancer: The role of interleukin 6 (IL-6). *BJU Int*, 2014; 113: 986–92
8. Zhang J, Pugh TD, Stebler B et al: Orchiectomy increases bone marrow interleukin-6 levels in mice. *Calcif Tissue Int*, 1998; 62: 219–26
9. Gacci M, Tosi N, Vittori G et al: Changes in sex hormone levels after radical prostatectomy: Results of a longitudinal cohort study. *Oncol Lett*, 2013; 6: 529–33
10. Macchioni P, Boiardi L, Catanoso M et al: Tocilizumab for polymyalgia rheumatica: Report of two cases and review of the literature. *Semin Arthritis Rheum*, 2013; 43: 113–18
11. Samson M, Audia S, Fraszczak J et al: Th1 and Th17 lymphocytes expressing CD161 are implicated in giant cell arteritis and polymyalgia rheumatica pathogenesis. *Arthritis Rheum*, 2012; 64: 3788–98