A case of treatment-refractory paraneoplastic polymyalgia rheumatica that improved after tumor resection: Paraneoplastic polymyalgia rheumatica and papillary thyroid carcinoma

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ABSTRACT

We present a case of a 53-year-old man whose clinical history, examination, and laboratory markers were deemed consistent with the diagnosis of polymyalgia rheumatica (PMR). His symptoms were initially relieved by oral steroids but unexpectedly returned with repeated attempts to taper the steroid dose slowly over time. Among the extensive evaluations for his symptoms, magnetic resonance imaging (MRI) of the cervical spine was performed and demonstrated an incidental thyroid mass. This was eventually diagnosed as papillary thyroid carcinoma and a total thyroidectomy was performed 6 months after his PMR symptom onset. The patient's refractory PMR symptoms resolved shortly thereafter, and he was successfully weaned from oral steroids. This remission following tumor resection posed an interesting question of a paraneoplastic process, which will be explored here.

Key Words: polymyalgia rheumatica; papillary thyroid carcinoma; paraneoplastic syndrome; proximal weakness; myalgias; case report

Introduction

PMR without giant cell arteritis is an inflammatory rheumatological syndrome most commonly seen in people over the age of 50 with clinical symptoms of pain and stiffness in the neck, bilateral hips, and shoulder girdle. There is no clear diagnostic test for this condition, but severely elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) as well as morning stiffness are proposed diagnostic criteria.[1] Previous reports suggest an association between PMR and malignancies especially in cases with younger age, mild inflammatory marker levels, or partial corticosteroid response.[2,3] Occasionally, the PMR symptoms may be the first clinical expressions of disseminated cancer.[4]

Case Presentation

A 53-year-old male with hyperlipidemia presented with a 2-month history of gradual progressive pain and subjective weakness in his shoulders and hips. The patient's symptoms evolved to include diffuse myalgias and arthralgias. Notably, his upper extremities were more affected than his lower as he ultimately became unable to lift his arms above his head. Intermittent fevers that exacerbated his symptoms were reported by the patient. He had no rashes or dermatological conditions, and denied jaw claudication, temple pain, headaches, or visual changes. There were no family members with known autoimmune or neuromuscular disorders, though there was a first-degree relative with thyroid cancer.

On clinical examination, he had normal muscle tone and bulk without atrophy, but he endorsed tenderness to mild pressure over his deltoid, trapezius, and bicep muscles bilaterally. He exhibited nearly full motor strength on initial resistance but this seemingly gave way to pain in his deltoids, triceps, left wrist extension, finger spread, and hip flexion. Otherwise, his strength was preserved. It was strongly speculated that his strength was impaired by pain, but this was difficult to distinguish with true muscular weakness on multiple examinations with varying clinicians and their interpretations. His sensory exam showed subtle sensory loss to pinprick and temperature in his bilateral lower extremities in a length-dependent fashion. His deep tendon reflexes were normal in the upper and lower extremities.

On initial evaluation, the patient presented with subacute progressive myalgias, arthralgias and pain-confounding motor impairment in the setting of fevers without antecedent infection. Polymyalgia rheumatica was a likely differential, but the subacute progression of severe symptoms prompted a rule-out of mimickers. With motor symptoms far exceeding sensory (and preserved reflexes), a myopathy was in the differential diagnosis, especially an autoimmune, inflammatory or necrotic variant. Certain myopathies can present with asymmetric deficits, such as inclusion-body myositis; however, the timing of his symptom-onset argues against such chronic processes. The patient's upper extremities were far more affected than his lower, so multiple cervical radiculopathies were also considered particularly in the context of worsening chronic neck pain. Other non-neurologic processes can also present with such symptoms including rheumatoid arthritis and fibromyalgia among others.

A negative drug history ruled out drug-induced myalgia and the patient's creatine kinase, complete blood count, and comprehensive metabolic panel were normal. The ESR and CRP were elevated at 42 mm/hr (normal range: 0-15) and 1.59 mg/dL (normal range: <0.50), respectively, initiating the consideration of inflammatory processes. A serum autoimmune screening panel

consisting of rheumatoid factor, cyclic citrulline peptide IgG/IgA, antinucleotide antibody, ribonucleoprotein extractable nuclear antibody, anti-Smith extractable nuclear antibody, SCL-70 extractable nuclear antibody, and Sjogren's syndrome antibody titers was unremarkable. A nerve conduction study and needle electromyogram were performed with consequent normal results. A MRI C-spine was obtained prior to neurologic evaluation due to earlier concerns of a symptomatic radiculopathy. The results were unremarkable, except for an incidental discovery of a complex nodule of the right thyroid lobe.

The patient's ESR and CRP values were only modestly elevated relative to what is often seen in PMR patients. However, given his symptoms and exclusion of other diagnoses, a presumptive diagnosis of PMR was made.

The patient was treated with a 5-day course of daily 40 mg tablets of oral prednisone with plans to taper to 20 mg over four weeks. His repeat ESR and CRP had normalized within the week of starting his steroid therapy at 13 mm/hr and 0.150 mg/dL, respectively. His symptoms and proximal pains with motor impairment were significantly relieved. In the months that followed, attempts to taper the oral steroids below the 20 mg dosage were met with a return of symptoms, ensuing the patient continue to take 20 mg daily for several months.

During this time, the patient was also being evaluated for the incidental thyroid mass seen on the MRI C-spine. Pathology determined the mass to be papillary thyroid cancer. The patient opted for a complete thyroidectomy due to his family history of thyroid cancer. Follow-up ultrasound was negative for residual thyroid tissue, and no pathologic lymph nodes, masses, or nodules were visualized.

Following his thyroidectomy, the patient's arthralgias and myalgias resolved within weeks. Thereafter, his prednisone was decreased to 10 mg and later 5 mg without the return of symptoms. He remained active and reported being able to routinely lift heavier weights while exercising. Since that time, the patient stopped taking prednisone and has not returned to the neurology clinic.

Discussion

Cancer risk and autoimmune rheumatic diseases may have a bidirectional relationship as chronic inflammation could initiate tumorigenesis or anti-tumor immune responses could result in autoimmunity.[5] Although there is only scant evidence that PMR is a true paraneoplastic disease, there are several reports supporting this relationship with malignancies. Additional studies have shown that PMR symptoms subside following tumor excision and cancer remission.[6-8] PMR and the coincidental finding of papillary thyroid carcinoma has been reported once previously. The case considers a patient with thyroid cancer and accompanying PMR whose symptoms resolved following a thyroidectomy with continual taper of steroid therapy.[8]

In our clinical case, the patient presented with clinical features and laboratory findings consistent with PMR. The patient was greater than 50 years of age and presented with bilateral shoulder and pelvic girdle pain limiting movement for >1 month in the setting of elevated inflammatory markers with a robust steroid response. According to the recommended EULAR/ACR classification, this patient's presentation meets the core inclusion criteria accruing a maximum score of 6.[1] There were no findings on history or workup to suggest another systemic inflammatory or neurologic disorder. His initial workup for PMR had led to an incidental discovery and subsequent identification of papillary thyroid carcinoma of his right lobe. When his refractory PMR symptoms finally resolved after the resection of this tumor, it prompted the inquiry of a potential causal association between his rheumatologic disorder and thyroid cancer.

Prior investigations have suggested that such a causal relationship could exist, indicating that PMR may present as a paraneoplastic process related to neoplasms of the colon, breast, and lung with some limited evidence for lymphoma, prostate and hematologic malignancy.[2,3,7,9] Prior studies have shown there may be an association between PMR and immunologic markers to help classify patients with PMR. HLA-DR genotyping and evaluating the subclassifications of T cells and cytokines may be useful indicators.[10,11] Theoretically, excessive T-cell response and downstream effects may arise from the release of tumor-associated antigens underlying a paraneoplastic mechanism not yet proven. This case report accentuates the careful consideration of a possible paraneoplastic form of PMR in patients such as ours, who present with symptoms consistent with PMR but are relatively younger, have only modest elevations of inflammatory markers and cannot be successfully weaned from steroids.

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