

HYPERCALCEMIA FROM SARCOIDOSIS SUCCESSFULLY TREATED WITH INFLIXIMAB

J.G. Huffstutter¹, J.E. Huffstutter²

¹University of Tennessee Chattanooga; ²Clinical Assistant Professor of Medicine, University of Tennessee Health Science Center

ABSTRACT. Sarcoidosis is a systematic inflammatory condition with a variable clinical course. While many patients have a benign, indolent illness, some patients have more severe manifestations. Therapy is determined by an individual patient's disease manifestations and the response to treatment. We report a case of sarcoidosis beginning with lymphadenopathy, initially controlled with steroids and immunosuppressive therapy. Our patient tolerated treatments poorly and developed severe hypercalcemia with progressive renal insufficiency. Intravenous infliximab was given with prompt resolution of hypercalcemia and very gradual improvement in renal function. Discontinuation of therapy resulted in immediate elevation of serum calcium. This patient has now responded for four years to infliximab treatment with no serious adverse events and continued improvement in renal function. Prompt infliximab therapy should be considered for patients with severe hypercalcemia from sarcoidosis unresponsive to steroids or other more conventional treatments. (*Sarcoidosis Vasc Diffuse Lung Dis* 2012; 29: 51-52)

KEY WORDS: sarcoidosis, infliximab, hypercalcemia

INTRODUCTION

Sarcoidosis is a systemic inflammatory condition of unknown cause with varied clinical manifestations (1). Granulomas may be seen in a variety of organs and are commonly seen in the lung, lymph nodes, upper respiratory tract, eyes, and heart. Less commonly, inflammatory lesions are seen in the brain and kidney (2). We report the case of a patient with known sarcoidosis manifested as lymphadenopathy, parotid enlargement and constitutional features of fatigue and fever. After years of control with steroids and methotrexate, she developed sudden hypercalcemia associated with renal insufficiency. In-

tolerance to corticosteroids and ineffectiveness of traditional immunosuppressive therapies forced the use of biologic therapy. She had a prompt improvement of hypercalcemia with infliximab and a gradual but sustained response regarding kidney function.

CASE REPORT

The patient is a 45-year-old white female who presented in July of 1998 with cervical lymphadenopathy. A biopsy showed noncaseating granulomas, consistent with sarcoidosis. She was treated with 60 mg of prednisone with improvement in lymph node size and pain, but she continued to have constitutional features of fever and fatigue. After multiple attempts to taper steroids, methotrexate at doses up to 20 mg weekly and hydroxychloroquine at 200 mg twice daily were added with some improvement, although prednisone at 20 mg daily was still

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Correspondence: Jessica G Huffstutter B.S.

University of Tennessee Chattanooga

Tel. (423) 432-8423

E-mail: Jessicahgrace@gmail.com

Table 1.

Date	October 2004	March 2005	July 2005	October 2005	November 2005	December 2005	January 2006
Calcium	9.30	9.30	11.5	12.5	13.0	10.5	9.40
Creatinine	1.5	1.4	2.4	2.5	3.1	2.5	1.8
ACE level	76	99	112	123		116	65

required for constitutional complaints. Refractory stomatitis developed and azathioprine at a dose of 50mg three times daily was substituted for methotrexate. Leukopenia limited azathioprine dosing. She developed increased serum calcium and creatinine in October of 2005 (Tab. 1). A renal biopsy revealed a low grade IgA nephropathy with foci of intratubular calcium phosphate. No evidence of renal granulomas or tubular interstitial nephritis was noted. High doses of steroids had no effect on the rising levels of calcium and creatinine, and she tolerated the prednisone very poorly. Numerous renal stones developed. Infliximab was given intravenously at a dose of 5 mg/kg with a loading dose at 0, 2, and 4 weeks. Infliximab was then administered every eight weeks. There was a prompt decrease in serum calcium levels and a stabilization of serum creatinine. Nephrolithiasis was treated with lithotripsy and cystoscopy with eventual removal of all stones. Steroids were discontinued and the patient has been maintained on infliximab 5 mg/kg given every 8 to 9 weeks.

DISCUSSION

Disease manifestations of sarcoidosis are related to extensive granuloma formation resulting from elevated levels of tumor necrosis factor. Medications that bind tumor necrosis factor, such as infliximab, remove these excess levels, resulting in granuloma dissolution. In a recent review of renal manifestations of sarcoidosis, hypercalcemia was identified in 32% of patients (3). Hypercalcemia in sarcoidosis is the result of elevated levels of 1-25 hydroxyvitamin D that comes from the conversion of 25 hydroxyvitamin D by these granulomas (4). Renal biopsies revealed renal granulomatous interstitial nephritis in 79% with interstitial nephritis without granulomas in the remaining 21%. Our patient's biopsy revealed a low grade IgA nephropathy with foci of intratubular calcium phosphate and no evidence of interstitial nephritis. The etiology of the renal insufficiency in our patient was severe hypercalcemia causing exten-

sive renal calcifications. A previous case of renal sarcoidosis successfully treated with infliximab has been reported (5). This case differed from ours in that their patient had documented granulomatous infiltration of the kidney, while our case is the first to describe renal failure due to hypercalcemia successfully treated with infliximab. Serum calcium normalized within two weeks of her first infliximab infusion and remained normal until a lapse in therapy resulted in a transient rise. The serum creatinine peaked shortly before the first infliximab infusion and has gradually improved over the last four years of therapy. It is now 1.6 mg/dl with an estimated creatine clearance of 37 ml/min. The prompt use of infliximab when the patient's serum calcium and creatinine levels were elevated prevented further damage. Clinicians need to be aware of this particular complication of sarcoidosis and the need for aggressive management.

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