A Rare Variant of Schnitzler Syndrome: A Case Study

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Abstract

Schnitzer Syndrome is a rare auto-inflammatory disease characterized by a chronic urticarial neutrophilic dermatosis and an IgM monoclonal gammopathy. We report a rare case of the syndrome consisting of a chronic urticarial neutrophilic dermatosis, an IgG and IgA kappa light chain monoclonal gammopathy, and multiple systemic inflammatory symptoms including fatigue, arthralgias, and bone pain. For a decade, this patient suffered from musculoskeletal pain and a persistent cutaneous urticarial reaction refractory to multiple pharmacologic interventions. This case condition was a history of multiple different biopsy confirmed diagnoses but ultimately was diagnosed as a rare Schnitzer Syndrome variant. Subsequently, this patient is achieving resolution of symptoms on the IL-1 receptor antagonist, Kineret. We report this unusual case of probable Schnitzer Syndrome in hopes to bring attention to the disease, both clinically and dermopathologically, revisit its proposed pathophysiology, and consider the possibility of rare variations of this often overlooked syndrome.

Case Report

A 51 year old Caucasian woman presented with an asymptomatic, chronic red eruption, originally on her abdomen with extension centrifugally to proximal extremites that has remained stable for greater than 12 years. Past medical history includes osteoarthritis, anxiety, microscopic asena, monoclonal gammopathy of undetermined significance and positive lupus anticoagulant. Review of systems positive for fatigue, arthralgia, and bone pain. Medications included Effievir 15mg with no known drug allergies. Examination of her trunk revealed diffuse urticarial plaques (Figure 3a) and extremities revealed pale rose macules with few raised papules and plaques (Figure 3b). Tenderness to palpation was appreciated over the tibia and iliac bones. Axillary lymphadenopathy was also present. Laboratory studies: positive ANA 1:160, homogenate pattern, and negative reflex screen, normal complement C3, C4, and CH50 elevated, p-ANCA 1:40; normal ESR, positive for lupus anticoagulant, low positive for cardioplin antibody, slightly elevated IgG and IgM titers, normal beta-2 microglobulin, elevated PTT; microscopic asena, subtle IgG and IgA kappa monoclonal proteins on serum immunofixation with borderline high kappa/lambda ratio; free kappa monoclonal light chains in urine immunofixation; Quantitative IgG, IgM, and IgA levels within normal limits. Skeletal survey negative for osteolytic lesions. This patient was given the diagnosis of an atypical variant of Schnitzer syndrome and was started on an IL-1 receptor antagonist at a dose of 1.2mg/kg/day. After 1 month of treatment, patient reported significant improvement in her pain and dermatologic eruption (Figure 8). Complications of treatment included injection site reaction, which reportedly occur in 80% of patients with yellowish scaling over resolution to 1-2 weeks. Her injection reactions were controlled with topical clobetorone cream and oral antihistamines.

Dermatopathology

Multiple punch biopsies revealed sparse superficial perivascular lymphocytes infiltrate with mild papillary dermal edema, suggestive of urticaria (Figures 4, 5, 6). The most recent biopsy was taken from the left abdomen indicating an urticarial dermatitis with rare neutrophils and telangiectasia (Figure 7). The findings are subtle and non-specific but could represent a stage in evolution of a neutrophil rich dermatosis, such as Schnitzler syndrome.

Discussion

Schnitzer syndrome is a rare, under diagnosed disorder characterized by chronic urticarial dermatosis, monoclonal gammopathy, and systemic inflammation. A retrospective study at the Mayo Clinic highlighted that this disease is highly under-diagnosed by identifying 46 undiagnosed cases when cross-referencing from their dysproteinemia data base with medical records from all patients with chronic urticaria at the institution22. Nineteen percent of reported patient’s with Schnitzer syndrome developed lymphoproliferative disorders7 which highlights the importance of recognizing the diagnosis and subsequent follow-up in these patients. Liliane Schnitzler was the first to recognize and report the particular combination of chronic urticaria and a monoclonal gammopathy in 1972. Schnitzer syndrome is a diagnosis of exclusion based on established diagnostic criteria originally presented by Lipsker et al in 2001 and later accepted by Konig et al in 2007 (Table 1.1). Our patient suffered from chronic urticarial dermatosis, monoclonal gammopathy, and systemic symptoms including lymphadenopathy, anemia, arthralgia, and bone pain. By definition, this patient was diagnosed with Schniter syndrome and is believed to have an atypical bicalon variant of the classic presentation. Although IgM monoclonal gammopathy is the biological hallmark of the disease, variants have been reported in <10% of cases23-25. A literature search completed by de Koning revealed IgM kappa subtype in 85% of patients18. Variant cases of IgG subtype constituted 7% of the reported cases. A critical variant of the bicalon gammopathy was present in 7 cases18. We present the first case of a bicalon gammopathy including IgM kappa monoclonal protein in addition to IgA kappa monoclonal protein. IL-1 plays the major role in the pathophysiology of Schnitzler Syndrome. The dermatologic manifestation is a mast cell independent urticarial reaction. A local inflammatory response, via IL-1, is thought to induce the skin lesions. It is postulated that mutations of genes in the IL-1 pathway may be responsible for disease21. Currently, the majority of data supports that the monoclonal gammopathy is caused by the systemic inflammation6. Chronic urticaria and monoclonal gammopathy are both considered to be common in the general population, however, Bida et al observed the prevalence of MUGS and chronic urticaria occurring together in the same patient is actually quite low22 which may suggest a single etiology being more likely than multiple etiologies in a single patient. Although Schnitzer syndrome is traditionally considered a neutrophilic urticarial dermatosis (Table 2), a small percentage of specimens does demonstrate superficial perivascular mononuclear infiltrate suggestive of chronic urticaria and lymphocytic inflammation, as was evident in earlier biopsies in this patient. This highlights the notion of neutrophil rich dermatosis being a stage of evolution in Schnitzler syndrome.

Conclusion

We report an atypical case of Schnitzler syndrome consisting of a chronic urticarial neutrophilic dermatosis, an IgG and IgA kappa light chain monoclonal gammopathy, and multiple systemic inflammatory symptoms. In recent years, treatment with IL-1 receptor antagonist leads to complete remission of the dermatologic manifestations and musculoskeletal pain in patients with Schnitzler syndrome18. The malignant potential and available success in treatment, prompted reporting of this unusual case in hopes to expand the differential diagnosis and consider Schnitzer syndrome in any patient whom presents with a chronic urticarial dermatosis and monoclonal gammopathy. This patient is finally achieving resolution of symptoms and overall improvement in quality of life on an IL-1 receptor antagonist.

References


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