features regardless of the syndrome. The typical histopathological finding is a dermal neutrophilic infiltrate that tends to be perivascular and also may be perieccrine. Vasodilation and dermal edema also may be seen. These histopathological findings contrast with the typical lymphocytic and eosinophilic infiltrate seen in classic urticaria. Similar histopathologic findings have been seen in other neutrophilic urticarial dermatoses such as Schnitzler syndrome.[4,6]

Differential—The differential diagnoses for CAPSs include Schnitzler syndrome, cold urticaria, systemic-onset juvenile idiopathic arthritis/adult-onset Still disease, and deficiency in IL-1ra. It is important to consider these differential diagnoses for management and treatment options.

Management—The discovery of the *NLRP3* gene mutation as well as an understanding of IL-1 biology has led to targeted therapy for these syndromes. Cryopyrin-associated periodic syndromes are mediated by IL-1β with an in vivo rate 5 times higher than in healthy patients.[4] The blockade of IL-1β results in complete resolution of symptoms.

In the last several years, anakinra, rilonacept, and canakinumab have shown efficacy in targeting IL-1β as receptor antagonists. Anakinra is a short-acting recombinant IL-1ra with a half-life of 4 to 6 hours. This short half-life requires daily injections and the most common adverse events included injection-site reaction and upper respiratory tract infection.[2,4] Rilonacept is a dimeric fusion protein that contains binding regions for the type 1 receptor and the IL-1 receptor accessory protein and is fused to the fragment, crystallizable (Fc) portion of human IgG1. Rilonacept is long acting with a circulating half-life of 8.6 days and offers patients ease of dosing with weekly subcutaneous injections. Rilonacept generally is well tolerated, with the most frequent adverse effects being injection-site reaction, upper respiratory tract infection, headache, arthralgia, and diarrhea.[2,7]

The newest of the treatments for patients with CAPS is canakinumab. It is a fully human IL-1β monoclonal antibody that is specific for IL-1β and not other members of the IL-1 family. It has a mean half-life of 26 days and is dosed subcutaneously once every 8 weeks. The most common adverse effects include nasopharyngitis, rhinitis, nausea, diarrhea, and vertigo.[4] In one study, most patients did not report injection-site reactions.[7] Studies also are underway on VX-765, a caspace-1 targeted therapy that acts upstream in the IL-1β pathway. Treatment with anakinra, rilonacept, and canakinumab generally offers rapid and sustained remission in the majority of MWS patients and helps prevent the development of systemic amyloidosis and lessens the potential for end organ damage.[2,7]

MWS and BCNS—Our patient had an unusual presentation of MWS complicated by BCNS, another rare autosomal-dominant inherited genodermatosis. In an extensive review of PubMed articles indexed for MEDLINE using the search terms *Muckle-Wells syndrome* and *basal cell nevus syndrome*, no association was identified between MWS and BCNS. Basal cell nevus syndrome is linked to *PTCH1* (patched 1) gene mutation with an incidence of 1:150,000 in the United States and Europe and is characterized by a broad range of anomalies including skeletal abnormalities, ectopic calcification, odontogenic keratocysts, facial dysmorphism with macrocephaly, palmoplantar pits, and numerous tumors. Most notable is the early and strong predisposition to develop several to hundreds of BCCs.[9]

Conclusion

Muckle-Wells syndrome may go undiagnosed for many years or may be misdiagnosed as refractory urticaria, as in our patient. It is important to include periodic fever syndromes in the differential diagnosis of refractory urticaria with episodic fever to diagnose these cases of MWS earlier.

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