

Multicentric Reticulohistiocytosis with S100 Protein Positive Staining: A Case Report

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SUMMARY Multicentric reticulohistiocytosis is a very rare systemic disease that affects skin, mucosa and joints. We reported a case of a woman with multicentric reticulohistiocytosis who presented typical skin syndromes and arthralgia. Immunohistochemical analysis showed positive staining for S100 protein, which was reported negative in the majority of previously presented cases. Other immunohistochemical markers (CD68(+), CD1a(-), langerin (-) and complete histologic and clinical picture were specific enough to make the definitive diagnosis of multicentric reticulohistiocytosis. The patient was administered prednisone just when arthritis appeared and we believe that this therapy protected her from the development of destructive arthritis. No autoimmune disease or internal malignancy was observed during 12-month follow up.

KEY WORDS: histiocytosis, non-Langerhans cell, S100 protein

INTRODUCTION

Multicentric reticulohistiocytosis (MR) is a rare systemic disorder of unknown etiology, classified as a non-Langerhans cell histiocytosis. It mainly affects skin, mucosa and synovia, and usually causes destructive symmetric arthritis. MR often affects internal organs and can also coexist with autoimmune diseases and/or malignancy (1). Goltz and Laymon (2) introduced MR as a new nosologic entity in 1954.

CASE REPORT

A 30-year-old Caucasian woman was admitted to the Wroclaw Department of Dermatology

because of dark-red nodules that appeared on the skin of her hands. The diameters of the lesions were between 2 and 7 mm. The nodules were hard, painless and had a tendency to linear arrangement like Koebner phenomenon (Fig. 1). There were additional small nodules localized along the proximal nail fold, known as a 'coral beads' sign. Moreover, there were numerous small papules symmetrically located on the face, in particular on the dorsal part of the nose. No erosions, ulcers or scales were observed.

Histology of the biopsy specimens obtained from the skin of the nose and hands showed very



Figure 1. Clinical presentation with dark-red nodules on the skin of the hands. Small nodules localized over the proximal nail folds are known as a 'coral beads' sign.

similar patterns characterized by abundant infiltration of histiocytes with homogeneous copious eosinophilic cytoplasm and multinucleated giant cells (large histiocytes) with finely granulated cytoplasm of 'ground glass' appearance (Fig. 2). The dermis was infiltrated throughout its thickness and there were no changes seen in the epidermis covering the lesion. An admixture of scattered chronic inflammatory cells was seen.

Immunohistochemical analysis showed a very strong expression of CD68, positive staining for S100 protein (Fig. 3) and complete absence of

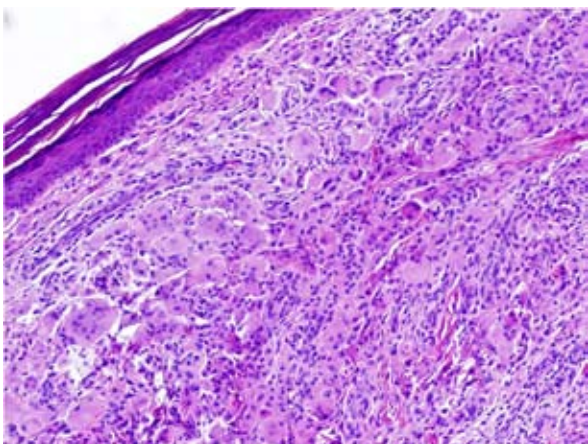


Figure 2. Skin biopsy. Abundant infiltration of histiocytes with homogenous copious eosinophilic cytoplasm and multinucleated giant cells (large histiocytes) with finely granulated cytoplasm of 'ground glass' appearance. The epidermis covering the lesion remained unchanged. Scattered chronic inflammatory cells present in the dermis (hematoxylin-eosin staining) (magnification X100).

CD1a labeling and langerin (antibodies supplied by DAKO: CD68 code N1577, S-100 – N1573, CD1a – N1616; antibody supplied by Nocastra: NCL – langerin; staining procedure: EnVision + System-HRP [DAB]). Electron microscopy did not demonstrate Birbeck granules.

The clinical features, histologic and immunohistologic pictures indicated a definitive diagnosis of multicentric reticulohistiocytosis.

Radiologic, biochemical and serologic tests revealed no involvement of internal organs including joints and bones, autoimmune disease or malignancy. Rheumatoid factor and antinuclear antibodies were negative. Erythrocyte sedimentation rate and cholesterol concentration were within the normal range.

About half a year after the first skin lesions, the patient presented again for arthralgia. She felt strong pain in the shoulders, elbows, knees and hands joints. Medium doses of prednisone (40 mg/d) were used and complete remission of the joint symptoms was achieved in about two weeks. Skin lesions showed gradual but moderate improvement. Selected skin lesions were also treated with hypodermic injections of steroids, however, without clinical response. The patient has been continuously followed up.

DISCUSSION

We describe this case because of the very low incidence of multicentric reticulohistiocytosis in Polish population. The authors found no report from Poland in the English literature. The world-

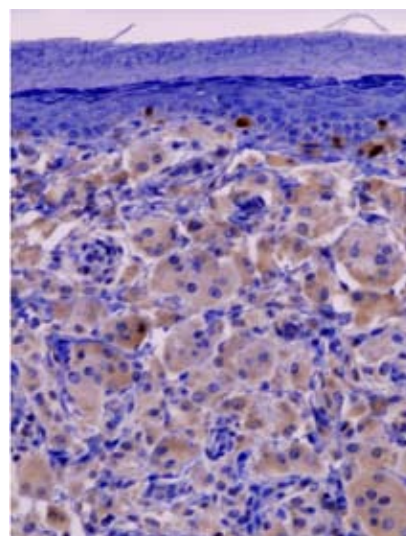


Figure 3. Skin biopsy. Positive staining of histiocytes for S-100 protein (antibodies from DAKO: S-100 – N1573) (magnification X200).

wide incidence of the disease is also very low. Barrow and Holubar (5) found only 33 patients described in medical literature worldwide in the 1954-1969 period, whereas Luz *et al.* (1) found 96 case reports published during the 1977-2001 period.

We consider it worthy of emphasizing the very gentle course of the disease during 12 months and positive staining for S100 protein in our patient. The morphology and localization of skin lesions were typical. Arthritis in MR is symmetric and destructive (3). Hand joints, knees, wrists and hips are usually affected, but all joints can be involved (1). In 40%-60% of cases, joint pain occurs before skin lesions; however, skin manifestations may sometimes precede arthralgia for years. In our patient, joint symptoms occurred about 6 months after skin lesions and short therapy with steroids led to complete remission of joint pain. We assume that, thanks to early treatment, destructive arthritis may never get chance to develop.

In patients suffering from MR many autoimmune diseases have been observed. According to previous reports, comorbidity of MR and rheumatoid arthritis, dermatomyositis, Sjögren's syndrome, scleroderma, primary biliary cirrhosis (4), diabetes mellitus, hypothyroidism (5), vasculitis, celiac disease, and systemic lupus erythematosus (6) has been reported. The association of MR and internal malignancy (about 20%-30%) is also widely known. The role of MR as a paraneoplastic syndrome is discussed because of the very wide spectrum of malignancy types it can be connected with. The oncologic process can occur prior to or simultaneously with MR. In several cases, the treatment of malignancy resulted in complete remission of MR (7).

Because of the rare incidence of MR and its unclear etiopathogenesis, there are no specific therapeutic guidelines. The use of prednisone, hydroxychloroquine, cyclophosphamide, chlorambucil, methotrexate and azathioprine has been mentioned in the literature (1). Recent reports on treatment using anti-TNF agents like etanercept and infliximab in combination with traditional immunosuppressants seem to be promising (8,9). In our patient, we used only prednisone because the course of the disease was mild and the initial remission of the joint symptoms showed some promise.

In most reports, staining for S100 protein was negative (1). Only Miettinen and Fetsch (10)

observed focal expression in a few cases in a series of 44 biopsies and Weber *et al.* (11) revealed S100 protein in one case. It is hard to assess whether positive staining for this marker can be considered decisive for definitive diagnosis. In our patient, definitive diagnosis was based on other pronounced features of MR.

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