CASE REPORT

Case Report: Late onset of generalized isomorphic morphea in a postmenopausal woman [version 1; peer review: awaiting peer review]

Marie Angelique Lazo-Betetta¹, Renzo Perez-Vasquez², Arantxa Sanchez-Boluarte³, Fiorella Inga-Berrospi⁴, J. Antonio Grandez-Urbina⁵

¹School of Medicine, Universidad San Martin de Porres, Lima, Peru
²Universidad Nacional Mayor de San Marcos, Lima, Peru
³School of Medicine, Universidad Peruana Cayetano Heredia, Lima, Peru
⁴Research Center, Universidad Privada Norbert Wiener, Lima, Peru
⁵Universidad Continental, Lima, Peru

Abstract

Morphea is an inflammatory, sclerosing skin condition of unknown cause that generally does not present systemic manifestations. A 66-year-old Caucasian Peruvian female patient, who was previously a nurse, presented with a prior history of 4 years of indurated dermal plaque lesions with constant progression. Diagnosis of morphea was made by clinical examination and skin biopsy. The patient started topical treatment with methoxsalen and phototherapy. When no improvement was seen, it was switched to methotrexate. However, due to changes in liver profile, phototherapy was restarted with progressive clinical improvement. It is essential to differentiate all morphea subtypes for proper management.

Keywords

Isomorphic generalized morphea; indurated plaque; postmenopausal woman
Background
Morphea is a rare, sclerosing inflammatory condition of the skin that can involve underlying soft tissues and cause a severe cosmetic and functional defect of unknown etiology. Associated factors, such as genetic predisposition, immune dysregulation, and environmental factors, have been reported\cite{1,2}. The current classification includes five subtypes: circumscribed, generalized, linear, pan-sclerotic, and mixed (Table 1)\cite{3,4}. Generalized morphea has two patterns of cutaneous distribution, symmetric distribution and isomorphic distribution, which occurs almost exclusively in postmenopausal patients\cite{5,6}. The annual incidence ranges between 3.4 and 27 cases per 1,000,000 people, and is more frequent in women than men. This disease has a peak of bimodal incidence, with the age of presentation being between 7 and 11 years in children and 44 and 47 years in adults\cite{7,8}.

Case presentation
Information of the patient
A 66-year-old postmenopausal Caucasian Peruvian female patient, who was previously a nurse of Swedish ancestry, with prior history of Type 2 Diabetes Mellitus and insignificant family history presented at an outpatient facility of an allergy and immunological center in Lima, Peru. She had a prior history of pathology biopsy report of morphea, she was treated with topical methoxsalen previously (with good outcome) in Sweden.

Clinical findings
The clinical episode began four years ago, starting with indurated, painless skin lesions without erythema in the breast folds, which progressively increased locally. These lesions appeared in other regions, such as the hip and upper and lower extremities, presenting plaques with indurated hiccups and hyperpigmentation (Figure 1–Figure 3). The patient was diagnosed with morphea following clinical examination and a prior pathological biopsy, which reported morphea, in Sweden. A timeline of care is available in Figure 4.

Treatment
Initially, pharmacological treatment was initiated, we use topical treatment with methoxsalen (0.1% lotion applied 30 minutes before phototherapy) and phototherapy (light therapy using artificial ultraviolet A light) the wavelength was 315–400 nm with 3.10–3.94 eV photon energy in lesions five times a week for six months. The patient had good adherence to the treatment. However, no improvement was seen, so the treatment was changed to methotrexate administrated orally (7.5 mg twice a week). Measuring the tolerance of the pharmacological treatment with liver profile (aspartate and alanine transaminases and total, indirect and direct bilirubin were measured). After six weeks, the patient exhibited alterations in liver profile, this being an expected adverse event. Therefore, the medication was discontinued, after which phototherapy was restarted twice a week, without topical treatment. Visible improvement of the lesions was achieved, the upper limbs being the location that was initially remitted. Subsequently, the frequency of phototherapy went from twice a week to once a week, for two years (Figure 1).
Follow-up
Currently, the patient has inactive lesions with the presence of dystrophies and atrophic skin, with annual follow-up controls to assess for disease remission and a good prognosis. The patient has a follow-up period of two years after last course of treatment and is seen every year.

Discussion
Morphea is a rare disease, with an estimated incidence of 27 cases per million people. It is suggested that it has an autoimmune origin. In relation to pathophysiology, little is known until now. However, some risk factors have been proposed, the most reported being: trauma, radiation, *Borrelia burgdorferi* infection, and certain medications. The age of presentation of this disease in childhood and adulthood, is the age range of 4–62 years, with a mean age of presentation of 35–37 years; in addition, it is more frequent in women than in men, with a ratio of 3:1. The presentation is characterized by erythematous or violaceous skin lesions, with the progression of the disease sclerotic plaques develop in the center of these lesions. In some patients,
one of the predominant characteristics is the development of hyperpigmentation, and sclerosis may be limited or absent\textsuperscript{11}. Generalized morphea is characterized by superficial, long, and coalescing plaques in multiple parts of the body. This type of morphea is more common in adults than in children, and sclerosis usually occurs in the trunk, upper and lower limbs, with preservation of the face, hands, and feet\textsuperscript{11,12}.

Regarding the complications of this disease, the injuries caused to the skin can generate functional deterioration and limitation of the motility range of the affected area. The disease can also produce arthralgia, edema, and contractures in the extremities. Initially, sclerotic plaques are formed, which after months and years become hypopigmented or hyperpigmented atrophic plaques that manifest as depressions in the skin\textsuperscript{11,13}. In patients with compromised dermis, subcutaneous tissue and muscle, squamous cell carcinoma may be formed due to the present of chronic inflammation\textsuperscript{16,17}.

In many patients, the diagnosis can only be achieved using clinical findings. However, some imaging studies such as ultrasound, 2-D shear wave elastography and magnetic resonance imaging would be useful in assessing and quantifying morphea extension. In other and histopathological changes, such as compromised dermis, subcutaneous tissue and muscle, may be useful to confirm the diagnosis and evaluate the extent of the disease. Skin biopsy can provide additional information in those patients where the physical examination is inconclusive, also allows us to have information on the depth of the condition and the activity of the disease. Walker \textit{et al.} assessed a cohort of 83 adults and children with morphea, where they sought to systematize morphological changes and determine the association between histopathological and clinical findings\textsuperscript{18}. In total, 91 biopsies were performed in 83 patients, and they found three patterns of dermis involvement: superficial, deep, and total sclerosis, which can occur in the different morphea subtypes. For example, in the generalized symmetric morphea, a pattern of deep affection of the dermis predominates; in the generalized isomorphic morphea, a pattern of superficial affection is often presented; on the other hand, lichen sclerosis morphea involves a pattern of linear and superficial affection. In this case, after having carried out a detailed study, skin biopsy was performed, which confirmed the diagnosis of morphea\textsuperscript{18}.

Dharmasi \textit{et al.}\textsuperscript{19} conducted a cohort study of 181 patients vs controls with the objective of determining the prevalence of antinuclear antibodies, anti-histone antibodies and anti-single-strand DNA antibodies finding that the prevalence of morphea is 34% antinuclear antibodies, 12% anti-histone antibodies and 8% anti-single-strand DNA antibodies. Concerning the patient discussed in this case study, we did not have the results of autoantibodies, so it is not possible to stratify it in any of the groups mentioned above.

The differential diagnosis for morphea is usually systemic sclerosis, this being a systemic disease characterized by progressive dermal sclerosis with the involvement of internal organs. The typical cutaneous manifestations are evidenced symmetrically at the proximal level, presenting as sclerodactyly, Raynaud’s syndrome, facial, trunk and/or limb sclerosis with significant functional limitation, sometimes accompanied by pulmonary and cardiac involvement. Regarding the patient, the condition was exclusively cutaneous without systemic manifestations and without compromising the proximal part of the hands, as happens in systemic sclerosis, also taking into account that the condition is currently in remission without treatment\textsuperscript{20}.

It should be taken into account that the patient was previously diagnosed and had received treatment in Sweden. The patient therefore had access to an advanced health system and did not encounter present economic limitations; it was possible to have timely diagnosis and treatment, which positively affected prognosis. However, within the limitations of the study, it was not possible to have access to the patient’s complete medical history; only the information provided adequately by the patient was used. At present, there are various treatment options for active lesions in generalized morphea, whether superficial or deep\textsuperscript{21}. Concerning superficial lesions, it is possible to initially use phototherapy as the first line of treatment throughout the body\textsuperscript{22}. If phototherapy is ineffective, a systemic treatment that includes methotrexate or mycophenolate, alongside systemic glucocorticoids, should be used\textsuperscript{23}. If the lesions are deep, immediate use of systemic treatment is recommended and phototherapy should be avoided due to poor penetration of ultraviolet light in the deep tissues\textsuperscript{24}. There is also topical therapy in which corticosteroids, vitamin D, and tacrolimus are used. However, it has not proven to be useful in cases of generalized morphea\textsuperscript{25}.

**Conclusions**

1. Early diagnosis is essential to prevent disease progression, complications, and improve the patient’s quality of life.

2. Likewise, it is of high relevance to determine the form of presentation of the disease to achieve optimal response to treatment and a favorable prognosis. Similarly, the possibility of atypical cases whose age of presentation is not expected should be taken into account.

3. Because there are currently no specific guidelines for the management of Morphea, we recommend that physicians should customize the treatment according to the clinical characteristics of each patient.

**Data availability**

All data underlying the results are available as part of the article and no additional source data are required.

**Consent**

Written informed consent for publication of their clinical details and clinical images were obtained from the patient.
References


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