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CASE REPORT

Late-onset Parry–Romberg syndrome in a patient with newly diagnosed HIV-2 infection

Síndrome de Parry-Romberg de início tardio em doente com diagnóstico inaugural de infeção por VIH-2

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Abstract

Sclerodermoid syndromes encompass a wide spectrum of rare diseases, with variable clinical presentation and severity. We present a case of a 31-year-old woman, Fitzpatrick's phototype V, who presented to our dermatology department with a 5-year history of linear atrophy of her right hemiface, which rapidly progressed during the first 2 years and then stabilized. There were no identifiable triggers, namely, drugs, infections, or trauma. Physical examination revealed a linear depression on her right hemiface, alongside a mild right enophthalmos. Laboratory examination revealed a positive human immunodeficiency virus (HIV) type 2 serology, with detectable viral load. The skin biopsy was compatible with late-stage morphea. The diagnosis of Parry–Romberg syndrome and HIV-2 infection was established. This patient illustrates a case of late-onset Parry–Romberg syndrome, in which HIV-2 infection may have been the trigger, due to a possible mechanism of molecular mimicry.

Keywords: Human immunodeficiency virus. Localized scleroderma. Parry–Romberg syndrome. Progressive facial hemiatrophy.

Resumo

Os síndromes esclerodermiformes englobam um vasto espetro clínico de doenças raras, com expressividade e gravidade variáveis. Apresentamos o caso de uma mulher de 31 anos, fototipo V de Fitzpatrick, encaminhada à consulta de Dermatologia por atrofia da hemiface direita com 5 anos de evolução, com evolução rápida nos primeiros 2 anos e posterior estabilização. A doente negava trauma, utilização de novos fármacos ou produtos tópicos. No exame físico, observava-se depressão linear na hemiface direita e enoftalmia ligeira homolateral. Analiticamente, a serologia do Vírus da Imunodeficiência Humana (VIH) 2 foi positiva, com carga viral detetável. A biópsia cutânea foi compatível com morfeia em fase tardia com mínima inflamação. Estabeleceu-se o diagnóstico de Síndrome de Parry-Romberg e infeção por VIH-2 (diagnóstico inaugural). Esta doente ilustra um caso de Síndrome de Parry-Romberg de surgimento tardio associado ao diagnóstico de VIH-2, que pode ter sido o desencadeante para a sua manifestação, por um possível mecanismo de mimetismo molecular.

Palavras-chave: Vírus da imunodeficiência humana. Síndrome de Parry-Romberg. Esclerodermia localizada. Hemiatrofia facial progressiva. Síndrome de Parry-Romberg.

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Introduction

Scleroderma syndromes encompass a wide spectrum of rare diseases that are characterized by skin thickening[1,2], and they include immune-mediated prototypical diseases such as systemic sclerosis and localized scleroderma[1,2], but also other scleroderma-like diseases that may result from abnormal tissue deposits, genetic variations, exogenous substances, and metabolic alterations[1]. The clinical presentation and severity of scleroderma syndrome are extremely variable[1], with divergent patterns of organ involvement, autoantibody profiles, management, and prognostic implications[1,2], and establishing the correct diagnosis is frequently challenging. Morphea, also known as localized scleroderma, is an immune- mediated disease that occurs in many clinical forms[1,2], and its pathogenesis is a combination of genetic predisposition and environmental triggers, such as infections, local trauma, and drugs[2,3].

Case report

A 31-year-old woman, Fitzpatrick's phototype V, with no known comorbidities or chronic medication, presented to our dermatology outpatient department with a 5-year history of linear atrophy of her right hemiface (Fig. 1), which rapidly progressed during the first 2 years and then stabilized. Simultaneously, the patient mentioned paroxysmal hemicranial throbbing headache. She denied any other symptoms, including blurred vision or diplopia. There was no identifiable trigger, such as drugs, symptomatic infections, or local trauma.

Physical examination revealed a linear depression on her right hemiface, including the frontoparietal, malar, and mental regions, with thickening of the adjacent skin, alongside a mild right enophthalmos (Fig. 1). Neurologic exam was normal.

Laboratory examination revealed a positive human immunodeficiency virus (HIV) type 2 serology, with a viral load of 1,832 copies/mL and a CD4+ lymphocyte count of 452 cells/μL. Other sexually transmitted infections were excluded, namely, hepatitis B and C, syphilis, as well as cervicitis agents including gonorrhea and chlamydia (through urine polymerase chain reaction). Autoantibodies, namely, antinuclear antibodies, were negative, and the remaining infectious serologies were negative. The laboratory workup was otherwise unremarkable. Histopathologic examination of a 4-mm punch skin biopsy was compatible with late-stage morphea (Fig. 2). The patient had ophthalmology and neurology appointments and had a brain magnetic resonance imaging (Fig. 3) examination that revealed soft tissue atrophy on the right frontoparietal, malar and mental regions, and right enophthalmos. Given the unilateral atrophy involving an entire side of the face, with ill-defined margins and minimal inflammation, the diagnosis of Parry–Romberg syndrome with neurologic involvement in the form of migraines was established, alongside a new diagnosis of stage-2 HIV-2 infection. In this clinical setting, HIV-2 infection may have been the infectious trigger for the manifestation of progressive facial hemiatrophy. Other alternative diagnosis and possible triggers, such as other infections, autoimmune diseases, metabolic alterations, and drugs, were excluded on clinical, histopathologic, and laboratory grounds.

Figure 1. Clinical image. **A and B:** a linear depression on the patient's right hemiface, affecting the frontoparietal, malar, and mental regions, with thickening of the adjacent skin, alongside a mild right enophthalmos.

A multidisciplinary discussion of the different management approaches for this case was conducted, including dermatology, rheumatology, infectious diseases, ophthalmology, neurology, and plastic and reconstructive surgery. Treatment options were also discussed with the patient. We took into consideration that the patient had a long-standing disease with a 5-year duration, which stopped progressing and remained stable for over 3 years, and that she had a new diagnosis of stage-2 HIV-2 infection. Therefore, we decided to initiate antiretroviral therapy (dolutegravir, abacavir, and lamivudine) and not to prescribe immunosuppression, maintaining clinical and radiological surveillance. Given the disease stability after 1 year of follow-up, the patient was also referred to an evaluation for reconstructive procedures and aesthetic improvement of the atrophic areas.

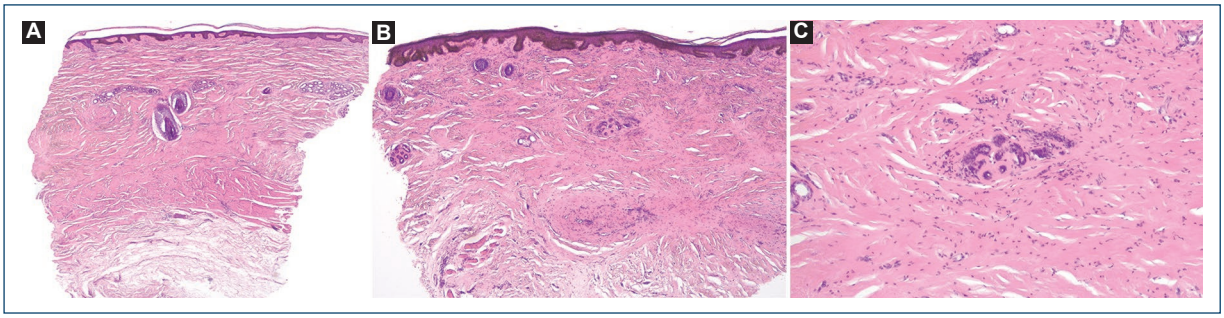

Figure 2. Histopathologic examination. **A:** (hematoxylin-eosin, original magnification ×25) square-shaped skin biopsy with epidermal atrophy, and highly packed eosinophilic thickened collagen bundles in the reticular and papillary dermis; **B:** (hematoxylin-eosin, original magnification ×40) thickened collagen bundles and sclerosis of the reticular dermis, entrapped and atrophic adnexal structures, with loss of surrounding adipose tissue, and minimal inflammation; **C:** (hematoxylin-eosin, original magnification ×100) hyalinization of collagen fibers with entrapment of an eccrine sweat gland without its surrounding adipose tissue. These histopathologic findings are consistent with late-stage stabilized morphea.

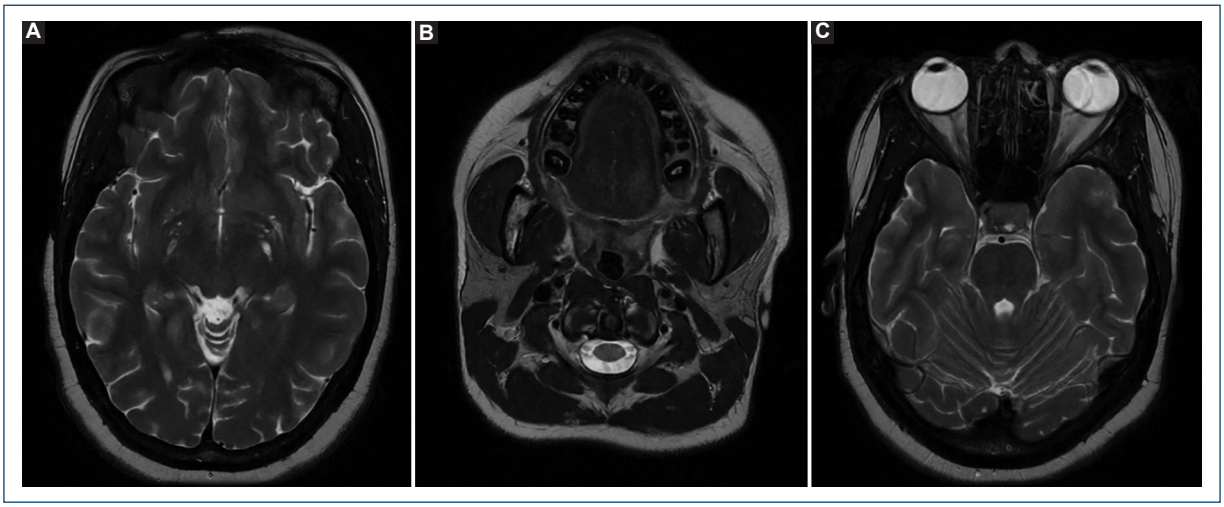

Figure 3. Head magnetic resonance imaging. Atrophy of the skin and underlying soft tissue with fat paucity on the right frontoparietal **(A)**, and mental regions **(B)**, and mild right enophthalmos **(C)**.

Discussion

Parry–Romberg syndrome (progressive facial hemiatrophy) is an acquired, infrequent disease that is considered a unique form of linear morphea, characterized by unilateral facial skin and subcutaneous tissue atrophy after an initial phase of thickening[4,5]. It predominantly affects female patients, and its onset is more frequent during the first and second decades of life[4-6]. This disease usually progresses in the first 2-3 years and then stabilizes, with remaining skin thickening and atrophy but without inflammation[4,5]. The diagnosis is clinical, and histopathologic studies can help corroborate the clinical suspicion. There is a risk for systemic involvement, mainly neurological and ophthalmological, which may be severe and disabling, and should therefore be excluded. It is recommended that the patients are evaluated in ophthalmology and neurology appointments and that adequate diagnostic investigations are carried out, namely, neurologic imaging[4]. Differentiating Parry-Romberg syndrome form *en coup de sabre* linear scleroderma is very challenging and there is significant overlap. Both diseases have a similar age of onset (mean age of 11 years), predominantly affect women, and present as lesions that progress over time until they reach stability few years later. There are no definite criteria generally agreed upon to differentiate these two

clinical entities but a lesser degree of inflammation, a more severe atrophy, and the unilateral involvement of an entire side of the face favor Parry-Romberg syndrome[4].

The pathogenesis of Parry-Romberg syndrome is complex and not completely understood. It is considered an immune-mediated disease, and its manifestation is multifactorial, resulting from a combination of genetic predisposition and environmental triggers, namely, infections and drugs[1,4-6]. The atypical late-onset of the disease in this patient, as well as a previously unknown diagnosis of HIV-2, lead us to believe that this infection may have played a role as a trigger for the clinical manifestation of progressive facial hemiatrophy. The association between HIV and scleroderma, although rare, has been previously reported in the literature[7,8]. It is believed that patients living with HIV infection can develop, paradoxically, autoimmune disorders such as scleroderma due to sequential homologies between viral proteins and autoimmune antigens, molecular mimicry[7-9]. In fact, HIV may directly induce tissue damage in skin, endothelial and synovial cells, causing an increased expression of self-antigens. These self-antigens are later recognized by a dysregulated immune system (immunodeficiency combined with loss of immune self-tolerance) because of their similarities to the virus itself, inducing an autoimmune response[7-9].

Treatment of this disease is challenging and no standardized treatment algorithm currently exists. Immunosuppression only has a role during the inflammatory phase with disease progression. Once the disease stabilizes, the goal of treatment is esthetic and functional enhancement[4-6].

This is a remarkable clinical case of Parry-Romberg syndrome with atypical features, such as its late onset in association with HIV-2 infection. This case draws attention to a rare and frequently overlooked immune-mediated disease that dermatologists should be acquainted with. No treatment guidelines are available; however, previous reports have stated that classical immunosuppressant drugs could be useful in the active phase of the disease to stop progression but are not indicated in late-stage and stable disease,[4] as in our case, and especially in the setting of newly diagnosed HIV infection. Given the rarity and heterogeneity of this disorder, therapeutic decisions should always be made on a case-by-case basis.

Conclusion

This patient illustrates a case of late-onset Parry-Romberg syndrome, in which HIV-2 infection may have been the trigger. The association between HIV and scleroderma, although rare, has been reported, and may be due to the structural homology of virus proteins and self-antigens. The coexistence of immune dysfunction and various autoimmune phenomena in patients with HIV is intriguing and further studies are needed to better understand the role of HIV as an infectious trigger for scleroderma.

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Conflicts of Interest

None.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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