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AUTOIMMUNE / AUTOINFLAMMATORY SYNDROME INDUCED BY ADJUVANTS (ASIA): MORPHEA CASE REPORT AFTER METALLIC BONE PROSTHESIS

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ABSTRACT

Introduction: The adjuvant-induced autoimmune / autoinflammatory syndrome corresponds to the group of diseases capable of being induced or accelerated by external agents, known as adjuvants that can trigger an immune response in the host. After exposure, several autoimmune diseases can be triggered by such substances, such as rheumatoid arthritis, systemic lupus erythematosus, mixed connective tissue disease and scleroderma. **Case Report:** Here we report a case of a 69-year-old female patient sought dermatology care due to the appearance of a brownish spot on her right leg 3 years ago, which presented a progressive increase in size and alteration in appearance. The patient reported placing a bone prosthesis made of chromium-cobalt and titanium in his right leg for 12 years. The patient underwent an incisional biopsy of the lesion and histopathological examination revealed an epidermis with slight acanthosis and a densely pigmented brown basal layer, in the dermis proliferation of fragmented and hyalinized collagen fibers, compatible with cutaneous scleroderma. **Conclusion:** In the present case, our patient presented adjuvant-induced autoimmune / autoinflammatory syndrome 12 years after the surgical procedure. Thus, such pathology must be taken into account in the differential diagnosis of autoimmune diseases, if the patient has a history of invasive procedures.

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INTRODUCTION

The adjuvant-induced autoimmune / autoinflammatory syndrome (ASIA) corresponds to the group of diseases capable of being induced or accelerated by external agents, known as adjuvants that can trigger an innate or adaptive immune response in the host (Loyo, 2013; Balbi, 2017; Pavlov - Dolijanovic, 2017; Tervaert, 2018). Various substances have been reported to be adjuvant, including environmental agents, drugs (anticancer agents), irradiation, exposure to organic solvents, silica, heavy metals, cocaine, vaccines, silicone prostheses and mineral oil injections (Balbi, 2017; Aounallah, 2018). After exposure, several autoimmune diseases can be triggered by such substances, such as rheumatoid arthritis (RA), Sjogren's syndrome, systemic lupus erythematosus (SLE), mixed connective tissue disease, scleroderma, among others (Balbi, 2017; Pavlov-Dolijanovic, 2017). The clinical presentationis quite variable, being marked by periods of activation and remission (Balbi, 2017). The diagnosis is made based on major and minor criteria created by Shoenfeld and Agmon-Levin, requiring the presence of at least two major criteria or a major and two minor criteria (Loyo, 2013; Watad, 2018; Hawkes, 2015). The treatment of ASIA is not yet well established, but in general there is an improvement of the condition after removal of the trigger and introduction of immunosuppressive therapy directed by the most prominent manifestation (Tervaert, 2018).

Case Report

A 69-year-old female patient sought dermatology care due to the appearance of a brownish spot on her right leg 3 years ago, which presented a progressive increase in size and alteration in appearance. She denied local, systemic symptoms or previous treatments. She also reported placing a bone prosthesis made of chromium-cobalt and titanium in his right leg for 12 years due to osteoporosis. The patient denied smoking, drinking or other comorbidities. Previous radiography showed the presence of a hip joint bone prosthesis on the right side (Figure 1), with preserved joint space and signs of bone demineralization. The dermatological examination revealed a

brown sclerotic plaque, with a lacy margin and areas of atrophy, located in the posterior region of the right thigh (Figure 2).

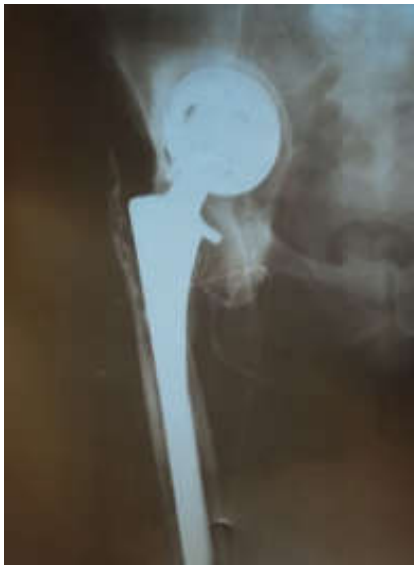

Figure 1. Righacetabular joint radiography showing hip joint prosthesis

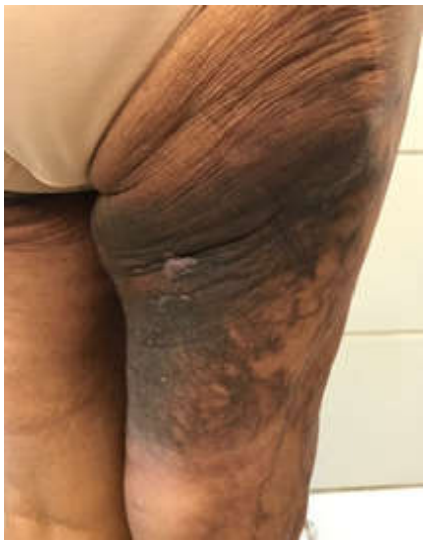

Figure 2. Sclerotic hyperchromic plaque in the posterior region of the right thigh

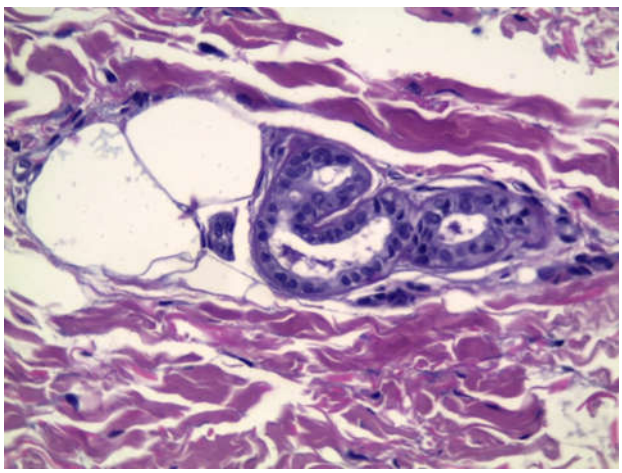

Figure 3. Anatomopathology study (Hematoxilin-Eosin): Thickened collagen surrounding the adipose tissue and the acinar glands

The patient underwent an incisional biopsy of the lesion and histopathological examination revealed an epidermis with slight acanthosis and a densely pigmented brown basal layer, in the dermis proliferation of fragmented and hyalinized collagen fibers, which extended from the superficial dermis to the deep limit of the biopsy, crossing the acini of the sweat glands and the adipose tissue, compatible with cutaneous scleroderma (Figure 3). The stains for Congo red and Alcian blue were negative, discarding, respectively, the hypotheses of cutaneous amyloidosis and mucinoses with a pattern similar to scleroderma. Protein electrophoresis, Anti-nuclear factor, anti-SCL70, anticentromere, anti-double helix DNA, rheumatoid factor and laboratory tests for blood count, urea, creatinine, TGO, TGP, FA, GGT, PCR, blood glucose, glycated hemoglobin, serological tests for hepatitis B, C, HIV and HTLV were normal. The final diagnosis was morphea and we opted for topical corticosteroid treatments, so far without clinical improvement. The patient remains in serial outpatient follow-up.

DISCUSSION

The term adjuvant-induced autoimmune / autoinflammatory syndrome or Shoenfeldsyndrome, was recently created to represent the group of diseases induced or accelerated by external agents, known as adjuvants (Loyo, 2013; Balbi, 2017; Pavlov-Dolijanovic, 2017, Shoenfeld, 2011). Initially, it was described for silicone, squalene and post vaccination, but later extended to other substances capable of inducing similar responses (Balbi, 2017). After the exposure, those agents are able to trigger an exacerbated immune response in predisposed individuals and cause the induction of autoantibodies (Watad, 2018; Frances, 2014). Adjuvants act by mimicking pathogen-associated molecule patterns (PAMPs) leading to activation of the immune system by increasing the activity of dendritic cells and macrophages, as well as promoting activation of B and T lymphocytes leading to a more robust immune response (Tervaert, 2018). Many agents have been described as adjuvants, including environmental agents, drugs (anticancer agents), irradiation, exposure to organic solvents, silica, heavy metals, cocaine, subcutaneous injections of mineral oils, vaccination (HPV, influenza and HBV) and prostheses for silicone (Balbi 2017; Aounallah, 2018; Kivity, 2012). Adjuvants can trigger non-specific autoimmune manifestations or manifestations that meet the classification criteria for autoimmune diseases such as rheumatoid arthritis (RA), Sjogren's syndrome, Systemic lupus erythematosus (SLE), mixed connective tissue disease, systemic sclerosis, as well as other connective tissue disorders (Balbi, 2017; Pavlov-Dolijanovic, 2017).

The clinical presentation of ASIA is quite varied and is marked by episodes of activation and remission. The time between exposure to the external agent and the manifestation of the overlying disease is variable, with descriptions from 1 month to 39 years after exposure to silicone (Balbi, 2017; Pavlov-Dolijanovic, 2017). The diagnosis suggested by Shoenfeld and Agmon-Levin was based on four major criteria: exposure to external stimuli, appearance of characteristic clinical manifestations, histopathological changes and improvement of the condition after the removal of the adjuvant and other minor criteria such as the development of autoantibodies, detection of Specific HLA, evolution of an autoimmune disease in addition to other clinical manifestations, requiring at least two major or one major and two minor criteria for the diagnosis of ASIA

syndrome (Loyo, 2013; Watad, 2018; Hawkes, 2015; Shoenfeld, 2011). Both scleroderma and scleroderma-like syndromes can be triggered by external agents, so a differential diagnosis must be made with the disorders that also present fibrosis and skin thickening (Niklas, 2016). Among these, there are scleromyxedema, scleredema, nephrogenic systemic fibrosis, eosinophilic fasciitis, chronic graft versus host disease, porphyria cutaneatarda and other minor forms (Ferreli, 2017). Morphea, a localized form of scleroderma, which affects only the skin and adipose tissue, presents to the histopathological examination broad and sclerotic collagen bundles that surround and replace the subcutaneous tissue, with deep perivascular lymphoplasmacytic infiltrate (Niklas, 2016; Ferreli, 2017). The treatment of ASIA is not well established due to low evidence, but it is recommended to remove the causative agent when possible and to introduce immunosuppressive therapy directed by the most prominent clinical manifestation (Balbi, 2017). In patients with localized cutaneous scleroderma, when left untreated, the morphea plaques tends to soften spontaneously over a period of 2 to 5 years (Ferreli, 2017). In the study by Loyo et al. the manifestation of Still's disease was described in a young adult after placement of a metallic chin prosthesis consisting of nickel and titanium, with significant improvement in the clinical condition after surgical removal of the prosthesis (Loyo, 2013). In the report by Frances et al. there was an improvement in the profile of morphea induced by silicone after the introduction of prednisone in an immunosuppressive dose, even without the surgical removal of the prostheses (Frances, 2014). In the present case, considering the patient's age, the presence of osteoporosis and the absence of local or systemic symptoms, we opted not to introduce systemic corticotherapy, but only topical, without a significant response so far.

Conclusion

In the present case, it was possible to observe the development of the autoimmune / autoinflammatory syndrome induced by adjuvants after placing a bone prosthesis made up of chromium-cobalt and titanium in the right leg 12 years ago due to osteoporosis. The clinical presentation observed was morphea, the localized form of scleroderma, demonstrating that even in the long term, exposure to external factors can lead to the development of Shoenfeld syndrome. Thus, such pathology must be taken into account in the differential diagnosis of autoimmune diseases, if the patient has a history of invasive procedures.

REFERENCES

Aounallah A, Lahouel I, Mokni S, Ksiaa M, Hayouni M, Belajouza C, et al. Atypical generalized morphea-like scleroderma occurring in a patient exposed to organic solvents and having chronic hepatitis C virus infection. *Indian J Dermatol Venereol Leprol.* 2018; 84(2):221-224.

Balbi GGM, Montes RA, Vilela VS, Andrade MAB, Nóbrega MM, Azulay-Abulafia L, et al. Rapidly progressive diffuse systemic sclerosis after local vitamins A, D and E complex injections: literature review and report of two cases. *Immunol Res.* 2017;65(1):285-292

Cohen Tervaert JW. Autoinflammatory/autoimmunity syndrome induced by adjuvants (ASIA; Shoenfeld's syndrome): A new flame. Autoimmun Rev 2018; 17(12):1259–64. Doi: https://doi.org/10.1016/ j.autrev.2018.07.003.

Ferreli C, Gasparini G, Parodi A, Cozzani E, Rongioletti F, Atzori L.Cutaneous Manifestations of Scleroderma and Scleroderma-Like Disorders: a Comprehensive Review. *Clin Rev Allergy Immunol.* 2017; 53(3):306-336.

Frances L, Leiva-Salinas M, Angelica MB, Marin I, Silvestre JF. Morphea as a sign of autoimmune syndrome induced by adjuvants (ASIA). *Eur J Dermatol.* 2014; 24(3):377-8

Hawkes D, Benhamu J, Sidwell T, Miles R, Dunlop RA. Revisiting adverse reactions to vaccines: A critical appraisal of Autoimmune Syndrome Induced by Adjuvants (ASIA). *J Autoimmun.* 2015; 59:77-84.

Kivity S, Katz M, Langevitz P, Eshed I, Olchovski D, Barzilai A. Autoimmune Syndrome Induced by Adjuvants (ASIA) in the Middle East: morphea following silicone implantation. Lupus. 2012; 21(2):136-9.

Loyo E, Jara LJ, López PD, Puig AC. Autoimmunity in connection with a metal implant: a case of autoimmune/autoinflammatory syndrome induced by adjuvants. Autoimmun Highlights. 2013;4:33-38

Niklas K, Niklas AA, Majewski D, Puszczewicz M. Rheumatic diseases induced by drugs and environmental factors: the state-of-the-art – part one. Reumatologia. 2016; 54(3):122-7.

Pavlov-Dolijanovic S, VujasinovicStupar N. Women with silicone breast implants and autoimmune inflammatory syndrome induced by adjuvants: description of three patients and a critical review of the literature. *Rheumatol Int.* 2017; 37(8):1405-1411

Shoenfeld Y, Agmon-Levin N. "ASIA" - Autoimmune/ inflammatory syndrome induced by adjuvants. *J Autoimmun* [Internet]. 2011;36(1):4–8. Available from: http://dx.doi.org/10.1016/ j.jaut.2010.07.003

Watad A, Quaresma M, Bragazzi NL, Cervera R, Tervaert JWC, Amital H, et al. The autoimmune/inflammatory syndrome induced by adjuvants (ASIA)/Shoenfeld's syndrome: descriptive analysis of 300 patients from the international ASIA syndrome registry. *Clin Rheumatol.* 2018;37(2):483–93.

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