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Case Report

Lower limb arterial thrombosis due to biopolymer injection: A case report

Milly J. Vecino-Moreno^a, Álvaro J. Vivas^b, Gabriel J. Tobón^c, David Aguirre-Valencia^{d,e,*}

^a Department of Clinical Sciences, Rheumatology Unit, Faculty of Health Sciences, Universidad Icesi, Cali, Colombia

^b Department of Research and Innovation, Clinical Research Center, Fundación Valle del Lili, Cali, Colombia

^c Department of Medical Microbiology, Immunology and Cell Biology, Southern Illinois University, Springfield, IL, USA

^d Department of Clinical Sciences, Center for Research in Rheumatology, Autoimmunity and Translational Medicine, Universidad Icesi, Cali, Colombia

^e Department of Internal Medicine, Rheumatology Unit, Fundación Valle del Lili, Cali, Colombia

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ABSTRACT

Introduction: Demand of biopolymer injections has steadily increased in the last decade. Complications associated with this procedure can be innocuous or even life-threatening, presenting from immediately to years later, locally or systemically, with mechanical, inflammatory, or autoimmune characteristics.

Objectives: To present a rare manifestation of an increasing health problem, clinicians must be attentive to this kind of complication.

Materials and methods: Clinical and laboratory data were searched from the clinical history; informed consent was obtained, and the Ethics Committee of Fundación Valle del Lili reviewed and approved this study. We report a patient who presented long-standing symptoms but only consulted after the onset of an acute lower limb arterial thrombosis that could have been fatal without rapid intervention. Ischemia was secondary to arterial obstruction related to biopolymer migration.

Results: A femoral and popliteal embolectomy was performed in which severe soft tissue fibrosis and encapsulated bodies were observed. The patient received thromboprophylaxis and low-dose oral glucocorticoid presenting a favorable evolution.

Conclusions: This substance probably acted as a foreign body and triggered an inflammatory reaction with a subsequent state of hypercoagulability, fibrosis, and nodule formation.

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* Corresponding author.

E-mail address: david.aguirre@fvl.org.co (D. Aguirre-Valencia).

Trombosis arterial de miembros inferiores por inyección de biopolímeros: reporte de caso

R E S U M E N

Palabras clave:

Trombosis arterial
Biopolímeros
Enfermedades autoinmunes
Síndrome
autoinmune/inflamatorio
inducido por adyuvantes
Material extraño

Introducción: La demanda de inyecciones de biopolímeros ha aumentado constantemente en la última década. Las complicaciones asociadas con este procedimiento pueden ser inocuas o incluso potencialmente mortales; se presentan desde inmediatamente hasta años después, local o sistémicamente, con características mecánicas, inflamatorias o autoinmunes.

Objetivos: Presentar una rara manifestación de un problema de salud creciente; los médicos deben estar atentos a este tipo de complicación.

Materiales y métodos: Los datos clínicos y de laboratorio se buscaron en la historia clínica; se obtuvo el consentimiento informado y el Comité de Ética de la Fundación Valle del Lili revisó y aprobó este estudio. Reportamos un paciente que presentaba síntomas de larga evolución, pero que solo consultó tras el inicio de una trombosis arterial aguda de miembros inferiores que podría haber sido mortal de no ser por una intervención rápida. La isquemia fue secundaria a obstrucción arterial relacionada con la migración de biopolímeros.

Resultados: Se realizó embolectomía femoral y poplítea en la que se observó fibrosis severa de partes blandas y cuerpos encapsulados. El paciente recibió trombopprofilaxis y glucocorticoides orales a dosis bajas, y presentó evolución favorable.

Conclusiones: Esta sustancia probablemente actuó como un cuerpo extraño y desencadenó una reacción inflamatoria con un posterior estado de hipercoagulabilidad, fibrosis y formación de nódulos.

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Introduction

Biopolymer injections for esthetic purposes is a public health problem; although its usage dates back from more than a century, its demand has steadily increased in the last decade.¹ A wide variety of complications are associated with this procedure, which can be innocuous or even life-threatening; presenting from immediately to years later, locally or systemically, with mechanical, inflammatory or autoimmune characteristics.² In our country there are a lot of oil preparations with and without biopolymers or silicone used for esthetic purposes in different body areas, such as face, hands, breasts, gluteus and thighs. Unfortunately, these procedures are in many times performed by non-health care professionals.³ The pharmacological effects of these substances are largely unknown, although it has been reported that these can migrate to other organs as emboli, causing a secondary inflammatory or ischemic process.⁴ We report a case of a patient who presented long-standing symptoms, but only consulted after the onset of an acute lower limb arterial thrombosis that could have been fatal without a rapid intervention.

Case report

A 63-year-old mestizo woman, with a history of biopolymer injection in hands and thighs and augmentation mammaplasty fifteen years ago was admitted to the emergency department because of thigh pain. The patient reported

chronic fatigue and myalgia predominantly in the lower limbs in recent years. One month before admission, she reportedly had a progressive bilateral medial thigh pain associated with tumefaction, erythema and changes in skin color; she also presented paresthesia, dysesthesia and bilateral weakness of lower extremities. Then, four days before consulting, her pain became unbearable, with reddish and purplish skin color in the distal third of her right leg that limited its mobility. She reported absence of fever, thoracic pain or dyspnea; she reported being an active smoker and taking no medications. Her medical history was unremarkable.

On examination, the patient was alert and fully oriented. She was pale and appeared ill. The temperature was 36°C, the blood pressure 125/72 mmHg, the pulse 64 beats per minute, the respiratory rate 17 breaths per minute, and the oxygen saturation 98% while she was breathing ambient air, and the weight 46 kg. The heart and lung sounds were normal. Medial surface of her right thigh was warm, with tenderness, mild induration and associated erythema (Fig. 1A), while distal portion of the same extremity was cold and had associated erythema and diminished sensitivity; her popliteal and dorsalis pedis pulses of the same limb were absent and capillary refill time was 4–5 s. Her left leg was cold; both soles of her feet had violaceous discoloration, which was more pronounced in the right foot (Fig. 1B). The remainder of the examination was normal.

A critical limb ischemia was suspected, a CT angiography was performed; it showed thrombosis of the right femoral artery since its origin, thrombosis of the right popliteal artery and of the distal segment of the posterior tibial artery. Anterior



Fig. 1 – Lesions of the lower limbs. Panel A. Medial surface of the right thigh: warm, tenderness, mild induration and associated erythema. Panel B. Left leg: her left leg was cold; both soles of her feet had violaceous discoloration, which was more pronounced in the right foot.

tibial and distal peroneal artery of the same limb had adequate blood flow provided by collateral circulation. Additionally, deep and superficial venous thrombosis with extension into the ipsilateral iliac vessels was observed, as well as partial thrombosis of the left popliteus artery with extension into the tibioperoneal trunk. Laboratory tests revealed a normal hemogram, ESR 10 mm/h (reference range 0–30 mm/h), C-reactive protein 3.64 (reference range 0–1 mg/dL), prothrombin time 11.8s, partial thromboplastin time 51.6s, international normalized ratio 1.02. Likewise, IgM and IgG anticardiolipin antibodies (aCL) were negative, as were IgM and Ig Anti-Beta-2-Glycoprotein I antibodies, antinuclear antibodies (ANAs), extractable nuclear antigen antibodies (ENAs), and anti-neutrophil cytoplasmic antibodies (ANCA). Complement levels were normal (C3 levels 122.13 mg/dL, C4 levels 42 mg/dL). No other laboratory parameters were obtained.

A femoral and popliteal embolectomy was performed, in which severe soft tissue fibrosis and encapsulated bodies were observed. She received enoxaparin 50 mg bid and low dose oral glucocorticoid (prednisone 5 mg QD) by considering biopolymers as possible triggers of this inflammatory/autoimmune phenomenon. The patient had favorable evolution. A timeline

of the clinical findings and evolution is shown in Fig. 2. Unfortunately, the patient did not attend the respective follow-up in subsequent controls. Thus, its clinical and laboratory evolution is unknown.

Discussion

In 2011 Shoenfeld proposed that siliconosis, macrophagic myofasciitis syndrome (MMF), gulf war syndrome (GWS) and post-vaccination phenomena that share clinical and pathogenic resemblances were included under a common syndrome entitled the “Autoimmune (Auto-inflammatory) Syndrome Induced by Adjuvants” (ASIA).² Autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome) groups non-specific disorders characterized by dysregulations in the immune system following exposure to an adjuvant. Amongst systemic clinical manifestations of ASIA syndrome, the most common are arthralgia, chronic fatigue, fever and lymphadenopathy; the median time described between exposure to adjuvants and the onset of clinical symptoms ranges from 1 week to 5 years.⁵

Shoenfeld et al. created several major and minor criteria in the diagnosis of the ASIA syndrome. Some of the major criteria were defined as exposure to an external stimuli (infection, vaccine, silicone, adjuvant) prior to clinical manifestations; typical clinical manifestations like myalgia, arthralgia or arthritis; chronic fatigue; neurological manifestations; cognitive impairment; improvement by removal of inciting agent and biopsy of involved organs. Minor criteria range from the presence of autoantibodies or antibodies against the suspected adjuvant to involvement of an autoimmune disease.² In a Colombian cohort of 190 patients with ASIA syndrome, the most frequent symptoms were: myalgia (92.1%), arthralgia (77.9%), asthenia and adynamia (77.9%) and neurological findings (55.8%).⁶

Our patient fulfilled three of the major criteria proposed by Shoenfeld²: exposure to an external stimulus (silicone, adjuvant) prior to clinical manifestations, myalgia, and chronic fatigue.

Adjuvants are substances that enhance antigen-specific immune responses, such as aluminum hydroxide, mineral

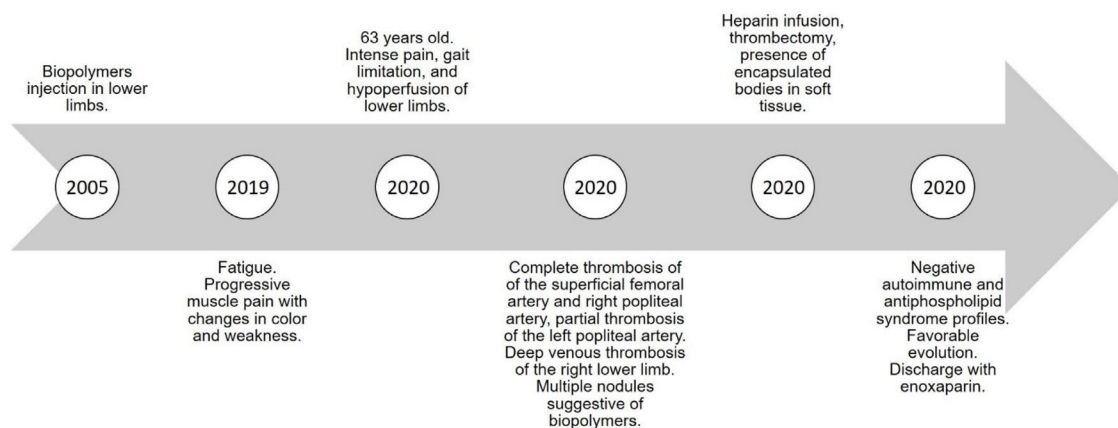


Fig. 2 – Timeline of the clinical findings and evolution.

oils, and silicone gel⁵; patients are usually exposed to adjuvants in the scenario of implanted foreign bodies for esthetic purposes, activating antigen presenting cells and promoting antibody production. Pachón et al. reported the frequency of adjuvants related to ASIA syndrome in their study group; they found that polydimethylsiloxane was the most prevalent (90%), followed by polymethylmethacrylate (6.8%) and paraffin (2.1%).⁶ T lymphocytes recognize these substances and orchestrate an inflammatory reaction at the injection site, with the consequent development of granulomas. Mobilization of adjuvants into other tissues produce other local or systemic manifestations, including edema, erythema, fistulas and organ failure. However, to our knowledge, there are no reports of arterial thrombosis related to biopolymer injection.

These compounds lead to tissue alterations and injuries. A study that analyze 500 cases from the ASIA syndrome international registry found that 13.8% of patients already had another prior autoimmune disorder before the exposure to foreign materials; additionally, autoimmune susceptibility given by a family history of autoimmune condition was documented in 34.5% of cases.⁵ Despite our patient had no prior personal or family history of autoimmune disorders it is fundamental to highlight the importance of addressing these questions during the patient's evaluation.

In general terms, acute ischemia of a limb can be caused by arterial trauma or acute arterial obstruction⁴; the latter as consequence of embolism or arterial thrombosis. In our patient, acute ischemia was secondary to arterial obstruction related to biopolymer migration; this substance probably acted as a foreign body and triggered an inflammatory reaction with a subsequent state of hypercoagulability (as evidenced with concomitant deep vein thrombosis), fibrosis and nodule formation.

Clot removal allowed perfusion of the affected extremity. Nevertheless, considering the presence of subcutaneous nodules and systemic manifestations (such as chronic fatigue and myalgias), and anticoagulation with low-molecular-weight heparin; we administered low-dose oral glucocorticoids and hydroxychloroquine for immunomodulation.⁵ Some researchers have proposed that patients with ASIA syndrome should be treated with a multidisciplinary management that involves pain control, evaluation by rheumatology, physiotherapy, psychiatry, and palliative care if necessary to guarantee an adequate follow-up to prevent functional and psychological sequelae.⁷

The use of biopolymers for cosmetic purposes is increasing, with a diverse range of associated complications, many of which can be life-threatening. Patients should be asked about minor procedures and history of autoimmune or autoinflammatory disease if ASIA syndrome is suspected.

Ethical approval

The patient authorized the publication of this case and signed an informed consent for this purpose. The institutional ethics committee approved this work (#502).

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Conflict of interest

The authors declare that they have no conflict of interest.

REFERENCES

1. Data M. Cosmetic Surgery National Data Bank Statistics. *Aesthet Surg J*. 2017;37 Suppl. 2:1–29, <http://dx.doi.org/10.1093/asj/sjx076>.
2. Shoenfeld Y, Agmon-Levin N. 'ASIA' – autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun*. 2011;36:4–8, <http://dx.doi.org/10.1016/j.jaut.2010.07.003>.
3. Cala-Urbe L, Navarro-Escobar A, León JC, Buitrago-García D, Teherán A. Características de individuos sometidos a infiltración de materiales extraños con fines estéticos sobre los que se realizó investigación judicial en Colombia. *Cir Plást Ibero-latinoam* [Internet]. 2017;43:137–42. Available from: <https://www.redalyc.org/articulo.oa?id=365551819006> [accessed 28.02.23].
4. Schmid A, Tzur A, Leshko L, Krieger BP. Silicone embolism syndrome: a case report, review of the literature, and comparison with fat embolism syndrome. *Chest*. 2005;127:2276–81, <http://dx.doi.org/10.1378/chest.127.6.2276>.
5. Watad A, Bragazzi NL, McGonagle D, Adawi M, Bridgewood C, Damiani G, et al. Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) demonstrates distinct autoimmune and autoinflammatory disease associations according to the adjuvant subtype: insights from an analysis of 500 cases. *Clin Immunol*. 2019;203:1–8, <http://dx.doi.org/10.1016/j.clim.2019.03.007>.
6. Pachón JE, Salazar MC, Pores AM, Rizo VZ. Clinical and immunological characteristics of patients with biopolymers and autoimmune inflammatory syndrome induced by adjuvants. *Plast Reconstr Surg Glob Open*. 2021;9:e3796, <http://dx.doi.org/10.1097/GOX.0000000000003796>.
7. Pachón JE, Salazar MC, Rizo VZ. Classification for staging and managing patients with biopolymer-induced human adjuvant disease. *Plast Reconstr Surg Glob Open*. 2022;10:e4137, <http://dx.doi.org/10.1097/GOX.0000000000004137>.