

Raynaud phenomenon as an isolated manifestation of autoimmune/inflammatory syndrome induced by adjuvants (ASIA)

Sirs,

In genetically predisposed individuals, some adjuvants, such as silicone, may trigger a set of symptoms, described as autoimmune/inflammatory syndrome induced by adjuvants (ASIA), also known as Shoenfeld syndrome (1). The clinical spectrum of ASIA is wide. It may manifest as general (fatigue, fever), neurological (memory loss, visual disturbance, paresthesia), dermatological (rash, alopecia), gastrointestinal or rheumatic and autoimmune-related symptoms such as arthralgia, myalgias, Raynaud's phenomenon (RP) and even digital ischemia. The presence of autoantibodies has also been reported (1-3).

RP describes a symptom related to digital vascular compromise and typically is exacerbated by the vasoconstrictive effects of cold exposure and other sympathomimetic drivers (2). Several studies reported an increased incidence of RP in women with breast implants (BI), in most cases secondary to a systemic rheumatic disease or accompanied by the other symptoms above-mentioned (1-3). In neither of these cases, RP appeared as the only symptom or there was a spontaneous resolution, even after BI removal (2-7).

A 51-year-old female, followed at our Rheumatology outpatient clinic over the last 15 years for spondyloarthritis, presented with a new onset biphasic RP on both hands and feet, manifested by exposure to cold and not associated with digital ulcers, for the previous six months. One and a half years before, she received silicone BI for aesthetic reasons. She had a background medical history of smoking, chronic gastritis and periarticular shoulder pathology. She was taking sulfasalazine, acemetacin, and esomeprazole. Symptomatic therapy for RP was not initiated considering its benign course.

Laboratory tests revealed a normal blood cell count and renal function; non-increased inflammatory parameters (C-reactive protein: 0.05 mg/dl and erythrocyte sedimentation rate: 15 mm/h) and no complement consumption or hypergammaglobulinaemia. Antinuclear and extractable nuclear antigen antibodies were negative. On systemic sclerosis (SSc) immunoblot panel, anti-RNA-polymerase II was transiently weak positive, and ten months later anti-Th/To also tested weak positive. Capillaroscopy was normal. High-resolution chest computed tomography revealed retro-mammary prostheses with bilateral pleating, possibly corresponding to intraprosthetic rupture (Figure 1). Between appointments, she consulted her plastic surgeon and had both her BI removed. Two weeks later she reported a spontaneous resolution of RP, that has not relapsed over the last year.

Although silicone in BI has mixtures of various sized polymer compounds, many of them are smaller than the pores of the shell. Leakage can occur with or without the shell

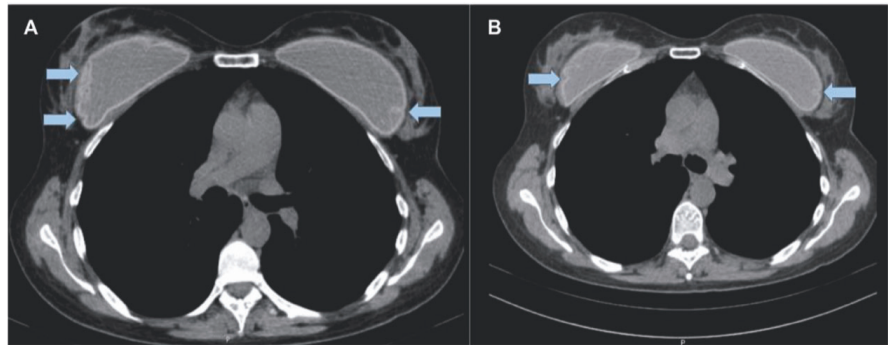


Fig. 1A: High-resolution chest computed tomography revealing the presence of retro-mammary prostheses with bilateral pleating with greater expression on the right, possibly corresponding to intraprosthetic rupture (arrow).

rupture and this phenomenon can trigger an immune response (8) and subsequent ASIA. The vast majority of the literature describes RP cases that are considered secondary to systemic rheumatic diseases, diagnosed after silicone BI implantation, usually SSc or systemic lupus erythematosus (1-6). After the removal of silicone BI, the disease frequently persists, although cases of improvement have been also reported. In most instances, regardless of whether BI are removed or not, clinical benefit was only noted after therapy initiation (1,7). Goren *et al.* defined four groups of women at risk of developing ASIA after BI implantation. Our patient presents characteristics of two groups: autoimmune disorder previously diagnosed (spondyloarthritis) and she is prone to develop autoimmunity with relevant environmental triggers (tobacco smoke) (9). The case we describe is unique because RP appeared as an isolated symptom and totally resolved after the removal of BI meeting ASIA syndrome 2 major criteria (10).

To the best of our knowledge, this is the first description of RP as an isolated manifestation of ASIA syndrome that totally reverted after the removal of silicone BI. We hope our report contributes to raising awareness of similar manifestations of Schoenfeld syndrome that may benefit, when feasible, from the removal of the inciting agent.

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References

- PAVLOV-DOLJANOVIC S, VUJASINOVIC STUPAR 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): 1405-11. <https://doi.org/10.1007/s00296-017-3731-4>
- SUH LJ, KHAN I, KELLEY-PATTESON C, MOHAN G, HASSANEIN AH, SINHA M: Breast implant-associated immunological disorders. *J Immunol Res* 2022; 2022: 8536149. <https://doi.org/10.1155/2022/8536149>
- BURJA B, HOČEVAR A, ŠEKORANJA D *et al.*: PR3-ANCA vasculitis as manifestation of ASIA syndrome following aesthetic breast augmentation: a new kid on the block? *Clin Exp Rheumatol* 2022; 40(4): 865-66. <https://doi.org/10.55563/clinexp/rheumatol/64ff7j>
- COHEN TERVAERT JW, MARTINEZ-LAVIN M, JARA LJ *et al.*: Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) in 2023. *Autoimmun Rev* 2023; 22(5): 103287. <https://doi.org/10.1016/j.autrev.2023.103287>
- WATAD A, BRAGAZZI NL, MCGONAGLE D *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. <https://doi.org/10.1016/j.clim.2019.03.007>
- COLARIS MJL, DE BOER M, VAN DER HULST RR, COHEN TERVAERT JW: Two hundreds cases of ASIA syndrome following silicone implants: a comparative study of 30 years and a review of current literature. *Immunol Res* 2017; 65(1): 120-28. <https://doi.org/10.1007/s12026-016-8821-y>
- VASEY FB, HAVICE DL, BOCANEGRA TS *et al.*: Clinical findings in symptomatic women with silicone breast implants. *Semin Arthritis Rheum* 1994; 24(1 Suppl 1): 22-8. [https://doi.org/10.1016/0049-0172\(94\)90106-6](https://doi.org/10.1016/0049-0172(94)90106-6)
- MUSTAFÁ JCR, FLEURY EFC, DIJKMAN HBPM: Case report: Evidence of migratory silicone particles arising from cohesive silicone breast implants. *Front Glob Womens Health* 2022; 3: 730276. <https://doi.org/10.3389/fgwh.2022.730276>
- GOREN I, SEGAL G, SHOENFELD Y: Autoimmune/inflammatory syndrome induced by adjuvant (ASIA) evolution after silicone implants. Who is at risk? *Clin Rheumatol* 2015 34(10): 1661-6. <https://doi.org/10.1007/s10067-015-2931-0>
- SHOENFELD Y, AGMON-LEVIN N: 'ASIA' - autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun* 2011; 36(1): 4-8. <https://doi.org/10.1016/j.jaut.2010.07.003>