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Case-based Review

Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) with postural orthostatic tachycardia syndrome after silicone breast implantation: Case report

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Abstract

This study illustrates two patients who developed autoimmune/inflammatory syndrome induced by adjuvants (ASIA) with postural orthostatic tachycardia syndrome (POTS) after silicone breast implant (SBI) and improved after SBI extraction.

Keywords: ASIA, postural orthostatic tachycardia syndrome, silicone breast implantation

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Introduction

Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) is a recently described autoimmune disorder, characterized by the presence of autoimmune manifestations or disease development after adjuvants contact.[1] An extensive description of 500 subjects about ASIA was recently published and showed a female predominance, and most cases were well-defined as immune diseases and were linked to exposure to hepatitis B and influenza vaccination.[2]

There are several autoimmunity cases after silicone breast implants (SBIs) represented as Sjögren syndrome, systemic lupus erythematosus, Still's disease, undifferentiated connective disease, and others. In the detailed description mentioned earlier, 12.5% of the cases were associated with SBI.[2]

This article aims to report the case of a patient who developed ASIA with postural orthostatic tachycardia syndrome (POTS) after SBI.

Case Presentation

Case 1

A 49-year-old female patient submitted to an SBI in 2003, initiated diffuse pain, severe fatigue, myalgias, arthritis, and episodes of sudden tachycardia compatible with POTS. She received prednisone 20 mg day^{-1}, hydroxychloroquine, methotrexate 15 mg $week^{-1}$, and methylprednisolone pulse therapy at last three times, with partial improvement. In 2019, she came to our private clinic, and her physical examination demonstrated telangiectasias on her face, microcheilia, reabsorption of her finger pads, and sclerodactyly. A diagnosis of limited systemic sclerosis (SSc) was determined.[3] Laboratory tests revealed positive antinuclear antibodies with a titer of 1:640. Anti-Ro/SS-A, anti-La/SS-B, anti-U1RNP, antineutrophil cytoplasmic antibody (ANCA), rheumatoid factor, anti-CCP, antibeta2 glycoprotein, anticardiolipin, anti-Scl-70, and anticentromere were undetected.[3] Laboratory tests also revealed the following: erythrocyte sedimentation rate of 9 mm/1st hours, C-reactive protein of 0.11 mg L^{-1} (nr: <0.5 mg L^{-1}), vitamin D 27 ng mL^{-1} (nr: >30 ng mL^{-1}), hypergammaglobulinemia at serum electrophoresis of 1.42 g dL^{-1} (nr: <0.66-1.32 g dL^{-1}), and serum kappa levels of 408 mg dL^{-1} (nr: 170-370 mg dL^{-1}). She was positive for HLA-DRB1, DQA1, and DQB1. A diagnosis of ASIA was determined (Table 1). Electrocardiography and 24-hour Holter showed sinusal tachycardia. Echocardiography was normal. The SBI was removed, and the microscopic analysis showed capsulitis with mild inflammatory cell involving the capsule. After 4 months, she felt better, with marked reduction of POTS episodes, although the SSc skin alterations continued; vitamin D, gammaglobulinemia, and kappa levels normalized.

Table 1. Shoenfeld's Criteria for ASIA Present in Our Cases

Major Criteria	Case 1	Case 2
1. Exposure to an external stimuli (infection, vaccine, silicone, and adjuvant) prior to clinical manifestations	+	+
2. Appearance of one of the clinical manifestations listed below:		
• Myalgia, myositis, or muscular weakness		–
• Arthralgia and/or arthritis	+	–
• Chronic fatigue, nonrestful sleep, or sleep disturbances	+	+
• Neurological manifestations (especially those associated with demyelization)	+	–
• Cognitive alterations and loss of memory	+	–
• Fever and dry mouth	+	+
3. Removal of the initiating agent induces improvement	+	–
4. Typical biopsy of the involved organs	–	
Minor Criteria		
1. Appearance of autoantibodies directed against the suspected adjuvant	–	–
2. Other clinical manifestations (e.g., irritable bowl syndrome)	–	+
3. Specific HLA (e.g., HLA-DRB1 and HLA-DQB1)	+	N/A
4. Initiation of an autoimmune illness (e.g., multiple sclerosis and systemic sclerosis)	SSc	Possible APS

For the diagnosis of ASIA, there must be the presence of at least two major or one major and two minor criteria.
APS, antiphospholipid syndrome; N/A, not assessed; SSc, systemic sclerosis.

Case 2

A 28-year-old female undergone to an SBI 9 years ago. Five years later, she initiated rosacea, daily episodes of sudden tachycardia compatible with POTS, insomnia, memory and concentration reduction, casein intolerance, and anxiety with several panic attacks and had two spontaneous fetal losses with 6 and 8 weeks. She had a positive anticardiolipin (68 and 51 MPL after 3 months) and lupus anticoagulant (twice). She denied thrombosis or thrombocytopenia. Her Beck Anxiety Inventory (BAI) was 30 (normal: <10). Laboratory tests showed antinuclear antibodies with a titer of 1:640 with a dotted fine speckled pattern and positive anti-DFS70. Other autoantibodies were negative. 25-OH-vitamin D was 27 ng mL^{-1}. Thrombophilia screening was normal. Serology for infectious diseases was absent. Electrocardiography and 24-hour Holter showed several episodes of sinusal tachycardia, with echocardiography normal. She received an ASIA diagnosis (Table 1). She was treated with vitamin D3 20,000 IU day^{-1}, and it was suggested to extract the SBI (Figure 1). After 6 months, she returned much better, with good energy, memory and concentration normalized, BAI reduced to 12, skin lesions disappeared, intestinal symptoms improved, only three episodes of tachycardia in 6 months, titer reduction of ANA (1:320), and anticardiolipin to 20 MPL.

Main Points

- Autoimmune/inflammatory syndrome induced by adjuvants (ASIA) is characterized by the presence of autoimmune manifestations or disease onset after adjuvants contact.
- There are several cases of ASIA after silicone breast implant (SBI). This article reports a patient who developed postural orthostatic tachycardia syndrome (POTS) after SBI.

Discussion

Genetic and environmental factors, such as vitamin D deficiency, silica, solvents exposure, and hormonal dysbalances, were the most critical factors involved with SSc. There is an increased risk of developing SSc 13-fold higher in the patients' first-degree relatives.[4] Silica and solvents are the most associated factors with SSc.[4] Low levels of vitamin D are described in these patients when compared to healthy controls.[5] Our patients had vitamin D insufficiency and SBI as risk factors identified.

Regarding APS related to ASIA. Some case reports describe APS's rare association following vaccinations.[6,7] More interestingly, an interesting case APS is described after SBIs.

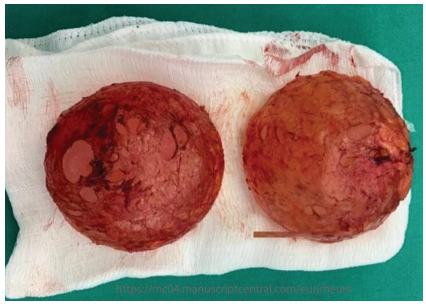

Figure 1. The two silicone breast implants "en bloc" extraction and capsulectomy immediately after surgical procedure (from patient case 2 here described).

Alusík et al.[8] observed in a 37-year-old woman who developed 17 years after SBI. Our patient fulfilled the international criteria for APS.[9]

In a large study, Watad et al.[2] confirmed the association of SBI and autoimmune diseases. The authors evaluated 24 651 SBI recipients and 98 604 matched SBI-free women and found in a multivariable Cox regression model analysis, a hazard *ratio* of 1.45 risk for at least one autoimmune/rheumatic disorder in women with SBI compared with those without implants.[2]

POTS is an autonomic nervous system disorder in which a change from the supine position to an upright position causes an abnormally large increase in heart rate or tachycardia (30 bpm within 10 minutes of standing or head up tilt) with stable levels of blood pressure. This variability on heart rate is followed by a reduction in brain blood flow and may started several symptoms linked to cerebral hypoperfusion.[10] POTS affects commonly women and has genetic and environmental factors linked to its pathophysiology. Drugs such as antihypertensive and also drugs that act on central nervous system are common causes for POTS. In some autoimmune conditions, POTS was described and includes systemic lupus erythematosus, Sjögren's syndrome, multiple sclerosis, Raynaud's phenomenon, and ASIA syndrome.[11–15] In our description, both patients had a clinical picture compatible with POTS, confirming this previous association of POTS and ASIA.

In conclusion, this article describes two additional cases of ASIA following SBI. Interestingly, both patients had POTS associated with improvement after silicone extraction.

Therefore, in patients with clinical findings after SBI, the physician should think in ASIA and check autoimmunity.

Informed Consent: Written informed consent was obtained from all patients who participated in this study.

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References

1. Shoenfeld Y, Agmon-Levin N. ASIA—autoimmune/inflammatory syndrome induced by adjuvants. *J Autoimmun*. 2011;36(1):4-8. [CrossRef]
2. 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. [CrossRef]
3. Van den Hoogen F, Khanna D, Fransen J, et al. 2013 classification criteria for systemic sclerosis: An American College of Rheumatology/European league against rheumatism collaborative initiative. *Arthritis Rheum*. 2013;65(11):2737-2747. [CrossRef]
4. Ingegnoli F, Ughi N, Mihai C. Update on the epidemiology, risk factors, and disease outcomes of systemic sclerosis. *Best Pract Res Clin Rheumatol*. 2018;32(2):223-240. [CrossRef]
5. An L, Sun MH, Chen F, Li JR. Vitamin D levels in systemic sclerosis patients: A meta-analysis. *Drug Des Devel Ther*. 2017;11:3119-3125. [CrossRef]
6. Diphtheria-tetanus vaccine: First report of antiphospholipid syndrome: Case report. *Reactions Weekly*. 2011;20:0114-9954.
7. Blank M, Israeli E, Shoenfeld Y. When APS (Hughes syndrome) met the autoimmune/inflammatory syndrome induced by adjuvants (ASIA). *Lupus*. 2012;21(7):711-714. [CrossRef]
8. Alusík S, Jandová R, Gebauerová M, Tesárek B, Fabián J. Antikardiolipinový syndrom po plastické operaci prsů [The anticardiolipin syndrome after breast reconstruction]. *Rozhl Chir*. 1990;69(5):298-301.
9. Miyakis S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). *J Thromb Haemost*. 2006;4(2):295-306. [CrossRef]
10. Grubb BP, Kanjwal Y, Kosinski DJ. The postural tachycardia syndrome: A concise guide to diagnosis and management. *J Cardiovasc Electrophysiol*. 2006;17:108-112. [CrossRef]
11. Kanjwal K, Karabin B, Kanjwal Y, Grubb BP. Autonomic dysfunction presenting as postural orthostatic tachycardia syndrome in patients with multiple sclerosis. *Int J Med Sci*. 2010;7:62-67. [CrossRef]
12. Calabrese LH, Davis ME, Wilke WS. Chronic fatigue syndrome and a disorder resembling Sjorgen's syndrome: Preliminary report. *Clin Infect Dis*. 1994;18(Suppl. 1):S28-S31. [CrossRef]
13. Tang S, Calkins H, Petri M. Neurally mediated hypotension in systemic lupus erythematosus patients with fibromyalgia. *Rheumatology (Oxford)*. 2004;43:609-614. [CrossRef]
14. Mallipeddi R, Mathias CJ. Raynaud's phenomenon after sympathetic denervation in patients with primary autonomic failure: Questionnaire survey. *BMJ*. 1998;316:438-439. [CrossRef]
15. Tomljenovic L, Colafrancesco S, Perricone C, Shoenfeld Y. Postural orthostatic tachycardia with chronic fatigue after HPV vaccination as part of the "autoimmune/auto-inflammatory syndrome induced by adjuvants": Case report and literature review. *J Investig Med High Impact Case Rep*. 2014;2(1):232470961452781. [CrossRef]