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IgA Myeloma and Still's Disease in a patient with bilateral silicone breast implants

Case Report

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Abstract: We report a case of a woman with bilateral silicone breast implants who presented with recurrent high grade fever, joint and muscle aches. An extensive workup failed to indicate an infectious source of her illness, so based on her symptoms a clinical diagnosis of Adult Onset Still's disease was made. However, subsequent investigations revealed raised IgA paraprotein levels in her serum which led to a bone marrow examination. Bone marrow examination was consistent with IgA Myeloma. Chemotherapy was commenced which led to a decrease in the paraprotein level. In addition, she was treated with non steroidal anti-inflammatory drugs and intra-articular steroid injections which provided marked symptomatic relief. The case indicates a possible association of Myeloma and Adult Onset Still's Disease in a patient with bilateral silicone breast implant.

Keywords: *Silicone • Breast implants • Myeloma • Adult Onset Still's Disease • Antigenic stimulation*

Abbreviations

Ig - immunoglobulin,
NSAIDs - non steroidal anti-inflammatory drugs,
CRP - C reactive protein,
USS - ultrasound scan,
MRI - magnetic resonance imaging,
AOSD - adult onset still's disease,
MGUS - monoclonal gammopathy of unknown significance,
IL6 - interleukin 6,
TNF - tumour necrosis factor.

1. Case Report

A 38 year old woman presented with flu-like symptoms, high-grade fever with rigors, macular rash, joint pain and muscle aches. Past medical history was significant for hysterectomy and insertion of bilateral silicone breast implants performed 3 years prior to presentation. She had no recent travel history and was in a stable relationship with her partner. Physical examination was unremarkable except for the presence of pain in large joints and the macular rash. Blood investigations revealed mildly raised CRP; blood, urine and stool culture were all negative for infectious agents. Atypical viral serology was negative. Screening for hepatitis and HIV infection as well as connective tissue disorders was negative. On further questioning the patient stated that she had tenderness of the left breast. The possibility of infected breast implants led to urgent breast ultrasound scan (USS). Breast USS showed undulation of the right breast implant in the upper quadrant and an extremely irregular outline of the left implant in the lower quadrant, an appearance highly suspicious of rupture at that site. She was then referred to breast surgeons, who were skeptical of a breast implant infection but requested MRI of the breast. Breast MRI was interpreted as grade II complicated implants, *i.e.* multiple folding of the implant walls with few small cysts in both glands, more conspicuous on the left. Once a breast implant infection

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was ruled out, our rheumatology colleagues gave a clinical diagnosis of Adult Onset Still's Disease (AOSD). However, subsequent blood examination showed markedly raised IgA paraprotien levels. An urgent bone marrow aspiration and examination performed by the hematologists revealed malignant-appearing plasma cells comprising 8% of the marrow.

In view of her symptoms and atypical bone marrow presentation she was given a trial of high dose steroids with thalidomide. Later bone marrow trephine biopsy result revealed an even higher plasma cell infiltrate to 20%. Chemotherapy comprising cyclophosphamide, dexamethasone and thalidomide was then commenced. After 6 cycles of chemotherapy, the paraprotien levels in her serum returned to normal but she still continued to have muscle and joint pains. She was referred back to the rhematologists and treated with NSAIDs and intraarticular steroid injections which provided her with significant symptomatic relief.

2. Discussion

This case report indicates a possible association of silicone breast implants with Myeloma and Adult Onset Still's Disease.

Several clinical entities for silicone-induced disease have been proposed, namely siliconosis, silicone-related disease, silicon reactive disorder, silicon disease syndrome, and silicon implant disease. It has been postulated that the leakage of silicone from a breast implant could stimulate cells to form granulomas, which might be capable of disrupting the immune system. In this hypothesis, silicone plays the role of an adjuvant which provides constant non-specific stimulation of immune system [1].

The exact mechanism for formation of the disease processes of multiple Myeloma and Adult Onset Still's Disease is unclear, but the mechanism could be related to chronic antigenic stimulation. A retrospective study conducted in 1996 in patients with monoclonal gammopathy of unknown significance (MGUS) looked into the possible association between socioeconomic status, residence, alcohol and tobacco habits, occupational exposure to toxic substances, chronic antigenic stimulation and the risk of developing MGUS. The study revealed that occupational exposure to asbestos, fertilizers, and mineral oil was associated with increased risk of MGUS. Chronic immune stimulating conditions when considered as a group presented a significant association with the risk of developing MGUS [2].

A similar study conducted in 1992 looked into the ability of silicone to elicit an antibody response and to potentially be responsible for adjuvant disease in humans. Several immunological functions including lymphocyte subset analysis and natural killer cytotoxic activity among others were studied in patients with a history of silicone implants. Results of lymphocyte subpopulation analysis showed a significant (60%) increase in the T helper/suppressor ratio in subjects with silicone implants. When natural killer activity was assessed significant inhibition of the ability of lymphocytes to kill tumor target cells was observed in patients with silicone implants [3]. Concerns about the immune effects of silicone were further heightened when Potter *et al*. provided experimental evidence of development of plasmacytomas in 80% of genetically susceptible mice by injecting silicone gel from breast implants [4].

The exact pathophysiology of Adult Onset Still's Disease is still unknown. It has been suggested by researchers that Adult Onset Still's Disease is a cytokine-driven disorder in view of the presenting signs and symptoms. Pro-inflammatory cytokines such as IL6, TNF alpha and interferon. have been implicated in the pathogenesis of Adult Onset Still's Disease [5].

In addition to possibly producing abnormalities of the immune system, silicone is also postulated to produce a pro-inflammatory state. Macrophage activation is responsible for degrading silicone elastomers by release of reactive oxygen molecules. As a result, migration of silicone may occur either through transportation in macrophages or following implant rupture, both of which might potentiate a systemic inflammatory response [6]. A study conducted in California suggested that oxidants produced from degradation of silicone products preferentially inactivate CD8+ suppressor T cells. Bcl-2, a proto-oncogene, acts by preventing apoptosis. Studies on Bcl-2 gene products suggest that they have anti-oxidant activity, implying that apoptosis may involve reactive oxygen species. Related studies with Bcl-2 deficient mice demonstrated that animals expressed lower levels of thymic CD8+ T lymphocytes. These observations support the hypothesis that CD8+ T cells are more susceptible to oxidant-induced inactivation than other T-cell subsets. This preferential inactivation of CD8 T cells by the pro-oxidant shift may in turn result in the loss of immunological tolerance [6].

The uniqueness of this case rests on the fact that this patient presented with a clinical syndrome of IgA Myeloma and Adult Onset Still's Disease which possibly is associated with bilateral silicone breast implants. It still remains to be seen if removal of the breast implant would lead to a regression of the disease activity in this patient.

In conclusions, this patient with silicone breast implants developed IgA Myeloma and Adult Onset Still's Disease. Silicone is considered to be a potentially inert substance but little is known about its long term effects. The international agency for research on cancer has concluded that silicone implants are not carcinogenic in breast tissue [7] but more research needs to be conducted on whether individuals with silicone implants are at increased risk of developing diseases such as Myeloma and Adult Onset Still's Disease.

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