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REVIEW BREAST SURGERY

A Review of the Literature on the Management of Silicone Implant Incompatibility Syndrome

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Abstract

Background Silicone implant breast augmentation has been routinely performed since the 1960s. Emerging literature suggests the existence of a clinical syndrome, silicone implant incompatibility syndrome (SIIS) resulting from silicone implants. Autoimmune reactivity develops, with subsequent symptoms including myalgias, arthralgias, chronic fatigue, sleep disturbance and cognitive impairment. While the existence of a clinical entity is currently being established in the literature, there are currently no guidelines on management.

Method Literature review was conducted using Medline and PubMed databases with key terms searched for, prior to hand-searching and bibliographical review until February 2019. The relevant literature was reviewed to determine whether consensus exists on the most appropriate management strategy.

Results Forty-nine articles relevant to SIIS were identified with twenty-one of these specifically outlining treatment. Of these, only five provided data on larger cohorts, three provided conclusions from literature reviews, and the remainder were small case series or isolated case reports. Improvement in symptoms was obtained by medical management of their immune response, by explantation and by simply counselling on the condition itself.

Conclusions A new clinical condition is being described that appears to suggest a link between silicone implant use and various symptoms in a cohort of patients. The subsequent treatment of SIIS is yet to be agreed upon. Further research is required to establish guidelines for diagnosis and ensure evidence-based treatment, and that patients and clinicians have a more refined understanding of the potential risks of silicone breast implant use.

Level of Evidence III This journal requires that authors assign a level of evidence to each article. For a full description of these Evidence-Based Medicine ratings, please refer to the Table of Contents or the online Instructions to Authors www.springer.com/00266.

Keywords SIIS · ASIA · Breast · Silicone · Autoimmune

Introduction

Silicone implant breast augmentation has been routinely performed since the 1960s [1]. While the theory that silicone implants cause immunological disorders has not been proven [2–7], emerging literature suggests the existence of a clinical syndrome, silicone implant incompatibility syndrome (SIIS). SIIS is theorised to result from silicone implants, and sequelae of this include autoimmune reactivity, with subsequent symptoms including myalgias, arthralgias, chronic fatigue, sleep disturbance and cognitive impairment. This condition is a subtype of autoimmune syndrome induced by adjuvants (ASIA), first described in 2011 by Schoenfeld [8]. This condition represents a triggering of the immune system to foreign material in a genetically predisposed individual. While the existence of a clinical entity is currently being established in the

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literature, there are currently no guidelines on the approach to management.

Method

A literature review was conducted using Medline, CINAHL and PubMed databases with key terms searched for. Included terms included silicone implant incompatibility syndrome, SIIS, Schoenfeld's syndrome, autoimmune inflammatory syndrome induced by adjuvants and breast implant illness. Subsequently, additional papers were located by bibliography review and through manual searching until the review period ended in February 2019. Papers were included if they specifically discussed SIIS, ASIA in the setting of silicone breast implants or breast implant illness and how it can be managed. Only articles written in English in the adult population were included. The relevant literature was then analysed to determine whether a consensus exists on the most appropriate treatment plan.

Results

Forty-nine articles relevant to SIIS were identified with twenty-one of these studies specifically outlining ways in which the condition can be treated, or approaches to selection of an appropriate treatment plan for an individual patient. Of the relevant papers, only five provided data on larger cohorts, three provided conclusions from review of the literature, and the remainder were small case series or isolated case reports.

Variable treatment plans and results were noted throughout these papers. Of the larger studies, Colaris et al. [9] compared a historical cohort of 100 women from 1985 to 1992 with adjuvant breast disease to a cohort of 100 women with SIIS diagnosed in 2014. They found that the symptom profile in these two groups was comparable and that improvement in symptoms was often noted post-explantation in around 50% of women. The similarities in the two cohorts suggest that the disease entity has not evolved significantly over the last 30 years of silicone implant use. A cohort of 80 patients were described by Maijers et al. [10] which showed 52 women in the cohort electing to undergo explantation. Of these women, 27 had partially improved symptoms and nine complete symptom resolution. A cohort study of 32 women by Cohen Tervaert and Kappel [11] showed concurrent autoimmune disease in 17 women and a trend towards symptom development after a long lead time, postulating that implant ageing and rupture may be an important factor. Those women with concurrent autoimmune disease showed improvement in symptoms with medical management. Explantation and often re-implantation with saline-filled implants were the treatment of choice for Thomas et al. [12] in a series of 25 women who achieved subjective symptom improvement at the expense of a 20% morbidity rate from the explantation surgery. Rohrich et al. [13] prospectively studied explantation patients in 38 women with matched controls and found that postoperatively there was a statistically significant improvement in the subjective health of these patients, perhaps suggesting that explantation is of benefit despite no clear objective evidence.

Pavlov-Dolijanovic and Vujasinovic Stupar [1] published a case series of three patients: a patient with SIIS showing no improvement from explantation and two other cases who elected not to have their implants removed. A series of three sisters demonstrated resolution of the hallmark symptoms on replacement of the silicone implants with hydrogel implants, demonstrating the role that genetics may play in development [14]. Eleven single-case reports also document isolated experience with this condition [15–25]. In some cases, improvement was seen with medical management without the need for explantation through the use of various agents including hydroxychloroquine, steroids, methotrexate, plasmapheresis and light therapy [15, 17, 18, 24]. On the contrary, explantation resolved symptoms in others [19–22]. Kivity et al. [16] present a case report in which removal of implants did not relieve symptoms; however, subsequent steroid therapy aided in recovery. In two separate case reports, explantation was performed; however, both patients required ongoing medical therapy [23, 25]. The scenario of trialling medical management with some initial improvement and subsequent relapse in symptoms was also described [15]. From these studies, improvement in symptoms was obtained by medical management of their immune response, by explantation of their implants and by counselling on the condition itself and retention of implants. The variable treatment pathways have not gone unnoticed by those reviewing the topic, with both review articles by Hirmand et al. and Shons and Schubert [6, 7] advocating for management plans to be decided on a case-by-case basis and in consultation with an autoimmune specialist. The decision to proceed to explantation appears to be worth considering based on the review figure of 60–80% of patients improving post the procedure [26].

Discussion

A broad spectrum of concurrent autoimmune conditions is described in the literature which manifests both prior to implant insertion and subsequently. This supports the thoughts of Watad et al. [27] who summarises the likely

pathogenesis of SIIS as an endogenous or exogenous autoimmune trigger in a genetically predisposed individual. A paper by Zazgornik et al. [28] compared 36 women with silicone implants to matched controls and found that autoantibodies were significantly higher in the silicone implant cohort despite the women being symptom free, further highlighting this theorised silicone autoimmune triggering. It is also worth noting that the time interval varies greatly in those cases published between implant insertion and symptom development [1]. Importantly, the potential for this syndrome to cause harm in certain patients must be considered and avoidance of silicone breast implantation should be encouraged when predisposing factors are found [29]. These include previous adjuvant-induced autoimmune disease, a prior diagnosis of an autoimmune disease and those who are genetically predisposed to autoimmune disease [1]. A web-based registry exists for ASIA syndrome, with multicentre international patient recruitment. Descriptive analyses of this large cohort of 300 patients, published by Watad et al., documented an eighty-nine per cent rate of diagnosis with another rheumatological condition [30]. This information again highlights the importance of patient selection and consent when undergoing silicone breast augmentation. A study has been done into the potential relationship between vitamin D deficiency and the development of SIIS. It was noted that the risk of developing autoantibodies was significantly higher in those with vitamin D deficiency [31]. It has not been documented, however, whether supplementation could prove to be another treatment avenue for this condition. It is also important for clinicians to note that on rupture of silicone implants patients may be at risk of SIIS development, as highlighted in a case series of four patients with rupture all meeting diagnostic criteria for SIIS [32]. Debate still is evident in the benefits of explantation versus medical management. While in many cases of SIIS, explantation is advocated, Thomas et al. [12] remind clinicians that explantation itself is not without risk, and discuss the importance of informed consent at both preimplantation and prior to explantation.

Importantly, silicone gel implant use has been extensively reviewed in regard to long-term safety following their removal from the American market in 1992 and subsequent reintroduction in 2006. A large systematic review in 2016 found no conclusive evidence for any detrimental long-term health outcome in patients with implants [33], building on the review literature previously documented [34–36]. A study of 749 women with silicone breast implants and 1498 matched controls found no association between breast implants and connective tissue disease, with only morning stiffness occurring at a significantly increased rate in silicone-exposed women [4]. A case series of 156 referred for rheumatic complaints in the setting of breast implants was found mostly to have non-specific symptoms and normal investigations, with only a small subset suggesting the possibility of a cause and effect relationship [37]. In both of these larger cohort studies, no suggested management was proposed or evaluated. A study done comparing 100 patients presenting for explantation during the silicone moratorium and 100 matched patients without breast implant exposure also found no significant difference in biochemical markers of connective tissue disease including rheumatoid factor, ESR and ANA [38]. The important thing to consider from these large epidemiological studies is that while a large increased risk of connective tissue disease related to implants has been excluded [39], sample sizes were too small to exclude an increase in extremely rare connective tissue diseases. These studies were also not designed to identify a clinical entity that was yet to be described, namely SIIS. It is also important to consider that despite the long-term outcomes in breast implant patients being studied on a large scale, and no causal relationship being found, the concern regarding this condition is real, and often shared on social media. This concept was explored by Tang et al. [40] and reminds us that with an autonomous cohort of patients with the ability to keep abreast of new research we must remain positioned to provide them with information to make informed decisions regarding their care based on the most up-to-date evidence.

Dagan et al. [15] elegantly conclude their case report with a discussion regarding the decision to explant. They describe a stepwise progression of initially trialling medical management prior to considering surgery. We would support this as a good framework for treatment and, however, would expand upon it suggesting an algorithm that begins with a clear informed consent process and identification of risk factors for SIIS development prior to implantation. Subsequently, if SIIS does develop, we would advocate for early multidisciplinary input. The first-line treatment strategy should be centred around patient education and acknowledgement of their symptoms. If this fails to alleviate the condition, medical management should be trialled under the guidance of an autoimmune specialist. In the cohort of patients who have ongoing issues despite this, we would then advocate for explantation to be considered. Again, it should include a very clear informed consent process given explantation is not without risk. This treatment algorithm can be seen in Fig. 1.

Conclusion

Silicone implant use is potentially linked to symptoms in a cohort of patients. The subsequent treatment of the SIIS cohort is yet to be agreed upon. While prior review articles

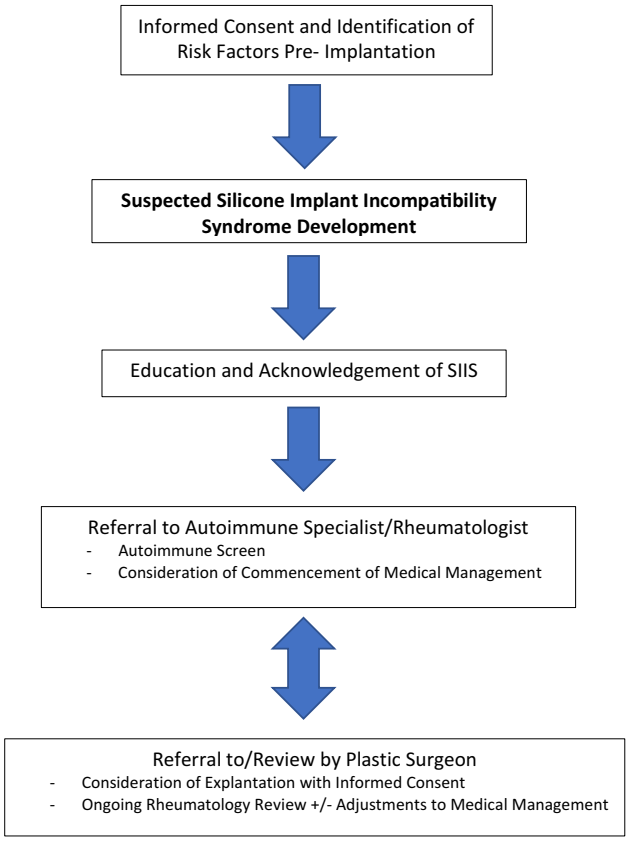

Fig. 1 A proposed algorithm for treatment of silicone implant incompatibility syndrome

have been published, their emphasis has not been entirely focused on the treatment of this condition. Often focus has been centred around diagnosis and potential pathogenesis, which is something that we do not have the scope to address in this paper. This paper serves as a summary of the current information on management, with a subsequent proposed treatment algorithm. Further research is required to determine causality, establish guidelines for diagnosis and ensure that this condition can be treated in an evidence-based way. Currently, these patients have been managed by explantation, medical therapy with immunosuppression and education. It is important that patients and clinicians have a more refined understanding of the potential risks of silicone breast implant use and the evolving evidence surrounding this new clinical entity. At this stage, patient management should be approached in a case-by-case fashion with informed consent to allow for optimal outcomes for each individual. We recommend a simple algorithm to assist clinicians in managing this condition in a systematic way beginning with the simplest interventions.

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Ethical Compliance Statement

Conflicts of interest The authors declare that they have no conflicts of interest to disclose.

Ethical Standards This article does not contain any studies with human participants or animals performed by any of the authors.

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