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SILICONE DISEASE (ASIA) - A CASE REPORT

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RESUMO

A introdução do silicone nos procedimentos estéticos suscitou preocupações quanto aos possíveis impactos do silicone no corpo. As próteses mamárias continuam a ser uma das cirurgias plásticas mais frequentemente realizadas no Brasil e no mundo, apesar de estarem ligadas a numerosas complicações. Além disso, o uso do silicone tem sido correlacionado com a síndrome autoimune induzida pelo adjuvante (ASIA), pelo que ocorre uma resposta inflamatória devido à presença de uma substância capaz de aumentar a imunogenicidade de um antígeno. Este estudo aborda um desses casos de ASIA, também conhecido como doença do silicone, a fim de avaliar o seu impacto na vida cotidiana das pacientes que foram submetidas a um procedimento protético mamário. Foram analisados catorze artigos relacionados com o relato do caso da paciente, recolhidos em várias plataformas, tais como PUBMED, Scientific Electronic Library Online, Science Direct, e Google Academic. A paciente tinha sido submetida à mamoplastia de aumento em 2000. Dois anos mais tarde, começou a sentir sintomas de mialgia, artralgia, e depressão, implicando fibromialgia. Após a remoção da prótese, o material foi biopsiado, e concluiu-se que tinha ocorrido uma reacção imunológica devido ao implante. Uma vez que pouco se sabe sobre a ASIA, este estudo visa aumentar a compreensão da síndrome e ajudar a diagnósticos futuros.

Palavras-chave: Doenças auto-imunes, Implante de mama, Cirurgia Plástica, Silicones.

ABSTRACT

The introduction of silicone in aesthetic procedures has raised concerns regarding the possible impacts of silicone on the body. Breast prostheses are still one of the most commonly performed plastic surgeries in Brazil and worldwide despite being linked to numerous complications. Additionally, the use of silicone has been correlated with autoimmune syndrome induced by adjuvant (ASIA), whereby an inflammatory response occurs due to the presence of a substance capable of increasing the immunogenicity of an antigen. This study addresses one such case of ASIA, also known as silicon disease, in order to assess its impact on the daily lives of patients who have undergone a breast prosthetic procedure. Fourteen articles relating to the patient's case report were analyzed, collected from various platforms, including PUBMED, Scientific Electronic Library Online , Science Direct, and Google Academic. The patient had undergone breast augmentation in 2000. Two years later, she began experiencing symptoms of myalgia, arthralgia, and depression, implicating fibromyalgia. After removal of the prosthesis, the material was biopsied, and it was concluded that an immunological reaction had occurred due to the implant. Since little is known about ASIA, this study aims to increase the understanding of the syndrome and to assist future diagnostics.

Keywords: Autoimmune Diseases, Breast Implantation, Plastic Surgery, Silicones;

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INTRODUÇÃO

The use of silicone in surgical procedures began in 1960, but it was not used in breast prostheses till then. However, due to concerns linking this prosthetic material with increasing incidences of cancer, and autoimmune and connective tissue diseases, the Food and Drug administration (FDA), the largest federal agency of the United States Department of Health and Human Services, prohibited its applicability 30 years later. However, soon after, the National Institute of Health (NIH) regulated and re-approved the use of silicones in aesthetic procedures due to a lack of evidence regarding their harmful effects. Recently, the discussion over the use of silicone in aesthetic procedures has re-emerged largely due to new problematic evidence (García and Lena, 2021).

In a recent survey, it was found that the number of cosmetic surgical procedures conducted worldwide had increased by 7.1% in 2019. Breast augmentation is still the most common aesthetic procedure, representing 15.8% of the total, with a prevalence in young people aged 19–34 years (53.9%), followed by liposuction and eyelid surgery. The United States and Brazil rank first and second, respectively, in the number of aesthetic surgeries performed annually, collectively accounting for the highest number of plastic surgeons in the world (25%) (ISAPS, 2021).

Since the introduction of silicone in aesthetic procedures, studies have investigated its impact on the body, including infections, ruptures, capsular formations, and various other diseases arising from surgery. Although research has suggested that breast prostheses can cause several complications, including autoimmune diseases, it is still one of the most commonly performed plastic surgeries (Matias, 2021).

Here, we discussed about autoimmune syndrome induced by adjuvant (ASIA), because of its link to breast augmentation or repair procedures. Due to over-exposure of the body to an antigen, the immune response is constantly stimulated in individuals who are already genetically predisposed to an exacerbated autoimmune response, thereby impairing their quality of life and contributing to the prevalence of various symptoms, such as myalgia, arthralgia and headache (Tervaert, 2018). In this study, a case report on ASIA, also known as silicone disease, was addressed to highlight the negative impacts of breast implantation on the body. This study aims to contribute to research, assist health professionals with diagnostics, and raise societal awareness about the potential complications of aesthetic procedures. For brief discussion, a comprehensive search was conducted on the case report using 14 articles, written in either Portuguese, English or Spanish, and collected from scientific databases, including PUBMED, Scientific Electronic Library Online, Science Direct and Google Academic, using the keywords "Autoimmune Diseases", "Breast Implant", "Plastic Surgery", and "Silicones."

45-year-old female patient, underwent breast augmentation for the first time in November 2000. In August 2002, the patient developed various symptoms, including arthralgia, myalgia, fatigue, severe pain in the left scapula region, and depression. Upon seeking medical assistance, the patient was diagnosed with lower back pain and was prescribed to undergo treatment with physiotherapy and anti-inflammatory drugs, which failed to alleviate symptoms. By 2008, the patient was still experiencing several symptoms, and after several clinical investigations and examinations, a possible diagnosis of fibromyalgia was proposed. The patient denied having any risk factors or a family history of autoimmune diseases. Subsequent physical examinations were performed by probing the tender points, with these areas giving a positive diagnosis for fibromyalgia.

The patient began treatment with antidepressants that were changed over the years, which included Amitriptyline, Fluoxetine, Escitalopram, Citalopram, Paroxetine, Bupropion, Duloxetine, Venlafaxine, Desvenlafaxine, and Diazepam. Venlafaxine (antidepressant) and cyclobenzaprine (muscle relaxant) provided the most relief. During this period, the patient gained weight (10 kg) over a short period, worsening her depressive state.

In 2009, due to the time elapsed with the implant (about 10 years) and the feeling that the prosthesis had stiffened, it was decided after consultation with the plastic surgeon that the prosthesis should be replaced. Even after surgery, the symptoms persisted with even greater intensity than before, drastically affecting the patient's quality of life. Other symptoms were also reported, including photophobia, hemeralopia, episodes of amnesia, dyspnea, vertigo, and intolerance to several foods.

In 2017, the patient underwent a routine mammogram, which was inconclusive of any positive mammographic findings in the right breast (BI-RADS category 1). Although findings in the left breast mammographic were deemed most likely benign (BI-RADS category 3) without other significant clinical abnormalities, malignancy was not definitively ruled out. In 2018, upon consultation with a gynecologist, drug treatment with cannabis was prescribed, commencing with orange oil, a chemotype rich in cannabidiol (CBD), followed by blue oil, a chemotype with balanced doses of CBD and Tetrahydrocannabinol (THC), and then progressing to green oil, a compound rich in THC. Although these compounds

initially resulted in an increase in pain tolerance, the therapy was discontinued after 6 months as the patient became unresponsive to treatment.

A new mammogram was performed, resulting in inconclusive mammographic findings (BI-RADS category 0). A complementary ultrasound of the breast was conducted, which diagnosed an echographic aspect suggestive of nodules in the right breast (BI-RADS category 3). In 2018, the patient underwent repeated laboratory testing, ultrasound, magnetic resonance imaging, in addition to antinuclear factor testing, the results of which showed no changes, corroborating the possible diagnosis of fibromyalgia.

In 2019, after reading an article on silicone disease and identifying several related symptoms, the patient sought care from another plastic surgeon, who requested new ultrasound examinations, indicating the presence of benign echographic growths (BI-RADS category 2) in both breasts. The patient decided to undergo surgery to examine the prostheses without advice from the surgeon, since there was no conclusive diagnosis for silicone disease. During the surgery, it was noticed that the left prosthesis had been displaced, in addition to the presence of nodules on the right side of the implant. The breast nodule and capsules of both prostheses were taken for biopsy, concluding intense fibrosis associated with chronic inflammation and a refringent foreign body in the right breast nodule (Figure 1). Additionally, capsules associated with fibrosis were noticed in the right and left breasts, which were indicative of chronic inflammation and the presence of giant cells of the foreign body type. The patient was diagnosed with an autoimmune reaction caused by a foreign body, better known as ASIA. During the first week post-surgery, the symptoms progressively disappeared, and the patient lost weight within 2 months. The patient was gradually taken off all medication, except for antidepressants used to treat other diagnoses. In addition, she underwent another clinical evaluation for fibromyalgia, but this diagnosis was ruled out.

II - DISCUSSION

The quest for the ideal female body and improved self-esteem based on social concepts, whether by adding volume to the breasts or restoring breast volume after weight loss or pregnancy, makes breast augmentation the most commonly performed female aesthetic surgical procedure in the world. This type of aesthetic surgery makes use of various types of implants, such as cohesive silicone gels, liquid silicone gels, or saline implants, to increase breast size (Fernández-palma, 2018).

When implanted in the human body, breast silicones generate cellular inflammatory responses, which are important for agglomerating cells at the surgery site and promoting the healing process. Such responses cause the body to create thin connective tissue around the prosthesis to protect the body from the foreign material. However, when the inflammatory reaction is exacerbated, this conjunctive capsule can lose elasticity, leading to capsular contracture, which can deteriorate the implant and even rupture it over time. Control of the physiological inflammatory response occurs through the interaction of the body with the texture of the implants, and different prosthesis technologies have attracted attention. One of these is nanomedicine, a subdivision of nanotechnology, whereby the texture and shape are modified at the nanoscale to increase not only the contact of the implant with the body but also the surface roughness. Studies have shown favorable results in rougher textures, such as Siltex and Biocell surface texturing, even though a consensus has not been reached (Mendonça Munhoz et al., 2017).

Figure 1 - Right breast prosthesis with evident nodule (black arrow).

Despite being an authorized aesthetic procedure, breast prostheses can have serious consequences for the body, including autoimmune diseases, silicosis, implant incompatibility syndrome, arthralgias, myalgias, severe neurological manifestations, irritable bowel syndrome, respiratory tract infections, recurrent cystitis, and allergies. However, the period for the onset of symptomatologic manifestations is long due to the need for the intracapsular substance to migrate out of the breasts and reach the

bloodstream and other organs. For this to occur, the prosthesis must age and/or rupture (Pavlov-dolijanovic and Stupar, 2017)

Among these complications, ASIA is an autoimmune disease caused by an inflammatory response of the body induced by adjuvant factors, including hormones, vaccines, aluminum, and silicone implants, which are responsible for the symptoms of the patient in the reported case (Matias, 2021). An adjuvant factor refers to any substance that can increase the immunogenicity of an antigen without activating an immune response (Sparice-pulido et al., 2018). They can influence both adaptive and innate immunity by activating receptors, especially Toll, NOD type, and lectin type C receptors, generating the recruitment and activation of proteins and the formation of cytokines. This leads to the chemotaxis of dendritic cells and activation of antigen-presenting cells, thereby increasing antigen transfer to areas with excess B and T cells (Carrillo and Aguilar, 2022).

The material used in prostheses is polydimethylsiloxane (PMSD), and over time, the capsule can deteriorate and break, allowing the intracapsular medium to reach the bloodstream and causing various systemic effects with symptoms of a nonspecific autoimmune disease, such as in the case of the patient with symptoms resembling fibromyalgia. This occurs due to the phagocytosis of silicone particles by macrophages, leading to the production of cytokines and neutrophils (Caravantes-cortes et al., 2020). In addition, breasts naturally have their own microbiota, which form biofilms when in contact with the surface of the breast prosthesis. This can cause an inflammatory response in patients undergoing breast enhancement procedures that activates interleukins-6 (IL-6) and inhibits regulatory T cells. In the capsule formed around the implants, the predominant inflammatory cells produce pro-fibrotic cytokines owing to the inactivation of regulatory T cells, manifesting a chronic inflammatory immune response. The group most susceptible to developing ASIA from silicone implantation has not yet been defined, but it is known that pre-existing allergies and predisposition to autoimmune diseases are risk factors, despite the denial of these aspects in this study. It has been reported that most women who undergo breast augmentation have pre-existing allergies, suggesting intolerance to silicone or other substances present in implants, thereby causing symptoms (MAIJERS et al., 2013). In addition, studies have shown a correlation between vitamin D deficiency and the syndrome, since this vitamin is essential for immunity, and its loss is associated with an increased risk of autoimmune diseases due to the hyperactivity of B lymphocytes, which may lead to the development of autoantibodies in patients with ASIA (Colaris et al., 2017). Shoenfeld and Agmon-Levin (2011), developed a list of criteria for the diagnosis of ASIA, requiring the presence of two major criteria or one major and two minor criteria for diagnostic confirmation (Sparice-pulido et al., 2018).

Table 1 - Criteria suggested by Shoenfeld and Agmon-Levin (2011) for the diagnosis of autoimmune syndrome induced by adjuvant (ASIA)

Major criteria:
• Exposure to an external stimulus before clinical manifestations: infection, vaccine, silicone;
• Appearance of one of these clinical manifestations: - Myalgia, myositis, or muscle weakness; - Arthralgia and/or arthritis; - Chronic fatigue, non-restful sleep, or sleep disorders; - Neurological manifestations; - Cognitive impairment, memory loss; - Fever, dry mouth;
• Removal of the initiating agent induces improvement;
• Typical biopsy of involved organs;
Minor criteria:
• Appearance of autoantibodies directed against the suspected adjuvant; • Other clinical manifestations (e.g. irritable bowel syndrome); • Specific HLA (major human histocompatibility complex);
• Emergence of an autoimmune disease (e.g. multiple sclerosis, systemic sclerosis).
For the diagnosis of ASIA, the presence of at least two major criteria or one major and two minor criteria is required.

The most common symptoms related to ASIA are myalgia, arthralgia, chronic fatigue, xerophthalmia, xerostomia, and asthenia, with the latter of these being the most frequently reported in patients (Sparice-pulido et al., 2018). ASIA can only be diagnosed clinically, and there are no specific laboratory tests that can help determine the presence of this comorbidity (Miranda, 2020).

The course of the disease hardly improves with medication alone, however, breast explantation does not

guarantee that the symptoms disappear. Studies have shown that some patients showed improvement and were even cured of ASIA after prosthesis removal, as was the case with the aforementioned patient. However, another group of patients continued to exhibit complications. The reason why the explantation may cause symptoms to recede or disappear entirely is justified by the decrease in the inflammatory response due to the absence of a triggering stimulus. The explanation for the persistence of symptoms even after removal of the prosthesis is due to the presence of silicone materials in lymph nodes and other organs of the body as a result of attempts by cells to remove this substance through phagocytosis. Thus, reports have suggested that the longer a breast prosthesis is retained after the onset of symptoms, the lower the chance of complete recovery after the removal surgery. Since little is known about the ASIA, more studies are needed to investigate the correlation between breast explantation, improvement in quality of life, and the decrease in symptom severity (Miranda, 2020).

CONCLUSION

The negative impacts of the use of breast implants have been demonstrated in the aforementioned case report. Alongside the importance of health professionals showing good comprehension for the clinical history of the patient, it is also important to perform the necessary examinations and highlight the potential risks of breast augmentation during pre-surgical consultations.

Despite the serious consequences that breast augmentation procedures can cause, they are still the most performed aesthetic procedures in Brazil and worldwide. The PMSD used in the prostheses may deteriorate, and the biofilms formed by the breast microbiota can also potentially cause inflammatory responses of an immune or chronic nature.

It is possible to conclude that, although the course of the disease hardly improves with medications alone, breast explantation, despite being the best alternative and resolving most cases, does not always guarantee the best prognosis (Miranda, 2020). In the present study, after being diagnosed with ASIA and undergoing explantation, the patient recovered satisfactorily and the symptoms disappeared. Finally, owing to its rarity and/or underreporting, further studies are needed to investigate the correlation between breast explantation and improvement in the quality of life of patients. Therefore, this study aims to contribute to future research on this syndrome, to help health professionals with the diagnosis by using the criteria suggested by Shoenfeld and Agmon-Levin (2011), and to raise awareness about the consequences of this aesthetic procedure.

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