Persistent extranodal marginalzone lymphoma in thecapsule of a re-explanted siliconeprosthesis following breastimplant-associated anaplasticlarge cell lymphoma

To the Editor:

We recently reported on a case in which the capsule around a silicone prosthesis, which had been removed from the left breast due to breast implant-associated anaplastic large cell lymphoma (BIA-ALCL), demonstrated the co-existence of extranodal marginal zone lymphoma (MZL) on the abluminal aspect of the capsule while on the luminal aspect of the capsule BIA-ALCL was diagnosed [1]. At surgery, a complete capsulectomy was performed and a new silicone implant was inserted.

After the surgery, the patient was followed every 3 months for a period of 20 months with no clinical, imaging, or laboratory signs of recurrence.

However, due to recent US Food and Drug Administration (FDA) announcements, 2019 National Comprehensive Cancer Network (NCCN) consensus guidelines [2], and other professional international recommendations and publications [3-6] regarding the influence of silicone breast implants on autoimmunity and BIA-ALCL, we encouraged the patient to remove her silicone implants. This procedure was performed 20 months after the BIA-ALCL diagnosis and included the removal of the silicone implants and a complete re-capsulectomy on the left breast.

The histopathological examination of the re-excised capsule has revealed the persistence of the extranodal marginal zone lymphoma on the abluminal aspect of capsule while on the luminal aspect giant cell granulomatous response was found with no malignancy [Figure 1A].

Immunohistochemistry staining demonstrated positive staining for CD20+, Ki67+ with an overall proliferation index of 3% [Figures 1B, 1C] and CD 5+. The stains for CD1a and CD 23 were negative.

These follow-up findings after 20 months may suggest that B-cell lymphoma is associated with the presence of silicone breast implants. A possible explanation can be attributed to the continuous and long-standing systemic immune stimulation response secondary to leakage or sweating of the silicone even though the implant had been removed, which caused B-cell proliferation resulting in neoplastic transformation.

Reinforcement of this assumption is found in the commentary by Bacon and O'Donoghue [7], in which the authors described subgroups of B-cell lymphomas that may directly arise within, and as a result of, silicone implant periprosthetic microenvironment. This condition may proliferate to a systemic disease.

In addition, this case demonstrates that the complete surgical ablation of the capsule and the removal of the silicone implant is the most current efficacious treatment available to eradicate the indolent BIA-ALCL in the breast [2] with no recurrence. Thus, by removing the local chronic antigen stimulation and/or inflammatory cytokins the neoplastic transformation of T-cells was terminated.

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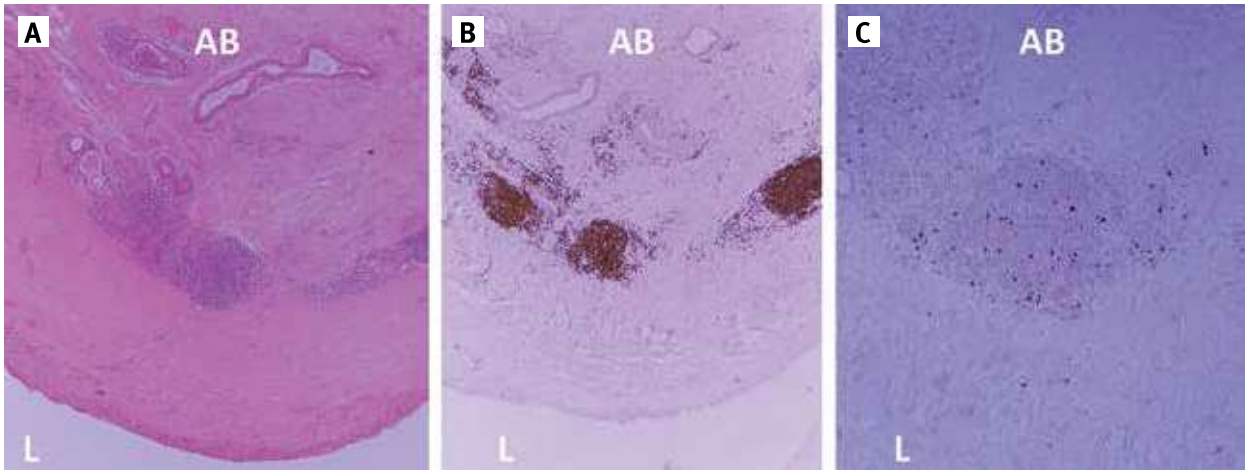
Figure 1. [A] Histological section of the re-excised capsule demonstrating the persistence of the extranodal marginal zone lymphoma on the abluminal aspect of capsule (AB) while on the luminal aspect (L) giant cell granulomatous response was found with no malignancy (hematoxylin and eosin stain, ×40), **[B]** Histological section of the excised capsule demonstrating the positive CD20+ staining of the extranodal marginal zone lymphoma on the abluminal aspect of capsule (×40), **[C]** Histological section of the excised capsule demonstrating the positive Ki67+ staining of the extranodal marginal zone lymphoma on the abluminal aspect of capsule with an overall proliferation index of 3% (×100)



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Reference

1. Har-Shai L, Har-Shai Y, Metanes I, Schindler Y, Sabo E, Preis M. Composite breast implant-associated anaplastic large cell lymphoma (BIA-ALCL) and extra-nodal marginal zone lymphoma (MZL) in the capsule of a silicone breast implant. *Autoimmun Rev* 2019; 18 (5): 556-7.
2. Clemens MW, Jacobsen ED, Horwitz SM. NCCN consensus guidelines on the diagnosis and treatment of breast implant-associated anaplastic large cell lymphoma (BIA-ALCL). *Aesthetic Surg J* 2019; 39 (Suppl 1): S3-13.
3. Haik J, Winder G. The influence of time on a first generation silicone gel-filled implant in a human breast. *IMAJ* 2019; 21 (9): 636.
4. Zolotykh VG, Kim AY, Shoenfeld Y, Churilov LP. Galactorrhea following silicone breast implant placement *IMAJ* 2019; 21 (8): 523.
5. Watad A, Bragazzi NL, Amital H, Shoenfeld Y. Hyperstimulation of adaptive immunity as the common pathway for silicone breast implants, autoimmunity, and lymphoma of the breast. *IMAJ* 2019; 21 (8): 517-19.
6. Fenoglio R, Cecchi I, Roccatello D. ASIA syndrome following breast implant placement. *IMAJ* 2018, 20 (11): 714-16.
7. Bacon CM, O'Donoghue JM. Commentary on: breast implant-associated bilateral B-cell lymphoma. *Aesthet Surg J* 2019; pii: sjz304.

There are many more cons for probiotics

To the Editor:

Suez and his Israeli research group [1] should be congratulated for their perspective on pros, cons, and unknowns of probiotics. They comprehensively highlighted the key topics, biased limitations, and lack of long-term safety of probiotics.

Per definition, probiotics should have beneficial effects on human health, but it appears that they have some potential detrimental effects [2]. In this regard, some additional aspects of their dark side should be enumerated. Their horizontal gene transfer to the microbiome of hostile genes, such as antibiotic resistant genes [3,4] have not been examined. In addition, their corresponding bacteriophage effects and synergistic incorporations of virulent genes [5] and their induction of D-lactate, metabolic acidosis, intestinal bacterial overgrowth, gas, bloating, and brain fogginess [6] are still under investigation.. The gastrointestinal, allergic, genetic, immunogenic, and toxic adverse effects have not been highlighted.

Probiotics are widely used in the processed food industries. A large number of them have been granted the status of generally regarded as safe (GRAS) from the U.S. Food and Drug Administration. Nevertheless, many carry antibiotic resistant genes and other hostile mobile factors like microbial transglutaminase, which was recently suggested to affect autoimmunity [7]. More intriguing is the fact that at least 6 systemic reviews and 16 meta-analysis have recently criticized the probiotic publications as being poorly designed, not standardized, and biased [2]. In addition, the studies were noted as having too high levels of variance and withdrawal rates incompletely reported, as well as under reporting safety concerns, lacking adequate transparency, and being extensively sponsored by manufacturers [2]. Since the probiotics market is booming and many medical and functional indications for their consumption are debatable, yet not substantiated [2], the certainty of their safety is a matter of concern [8].

For a more balanced view, it should be stressed that probiotics were suggested as a parallel or additional therapeutic strategy in autoimmune diseases treatment, but the jury is still out [9-11]. A better understanding of the human intestinal microbiome, before loading the gut with problematic and unclear beneficial probiotic cargo, is highly recommended.

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References

1. Suez J, Zmora N, Eran Segal E, Elinav E. The pros, cons, and many unknowns of probiotics. *Nat Med* 2019; 25, 716-29.
2. Lerner A, Shoenfeld Y, Matthias T. Probiotics: if it does not help it does not do any harm. Really? *Microorganisms* 2019; 7: 104-24.
3. Lerner A, Aminov R, Matthias T. Potential effects of horizontal gene exchange in the human gut. *Front Immunol* 2017; 8: 1630.
4. Zheng M, Zhang R, Tian X, Zhou X, Pan X, Wong A. Assessing the risk of probiotic dietary supplements in the context of antibiotic resistance. *Front Microbiol* 2017; 8: 908.
5. Lerner A, Ramesh A, Matthias T. David and Goliath war revival in the enteric viruses and microbiota struggle. Potential implication for celiac disease. *Microorganisms* 2019; 7: 173.
6. Rao SSC, Rehman A, Yu S, Andino NM. Brain fogginess, gas and bloating: a link between SIBO, probiotics and metabolic acidosis. *Clin Transl Gastroenterol* 2018; 9: 162.
7. Lerner A, Matthias T. Microbial transglutaminase is beneficial to food industries but a caveat to public health. *World J Clin Cases* 2019; 7 (22): 3912-14.
8. Sotoudegan F, Daniali M, Hassani S, Nikfar S, Abdollahi M. Reappraisal of probiotics' safety in human. *Food Chem Toxicol* 2019; 129: 22-9.
9. Zoledziewska M. The gut microbiota perspective for interventions in MS. *Autoimmun Rev* 2019 18: 814-24.
10. Meng X, Zhou HY, Shen HH, et al. Microbe-metabolite-host axis, two-way action in the pathogenesis and treatment of human autoimmunity. *Autoimmun Rev* 2019; 18: 455-75.
11. Shamriz O. Probiotics and autoimmunity: current evidence. *Autoimmun Rev* 2018; 17: 1150-1.

"Nobody can be exactly like me. Sometimes even I have trouble doing it"

Tallulah Bankhead (1902–1968), American actress of the stage and screen known for her husky voice, outrageous personality, and devastating wit

"We confess our little faults to persuade people that we have no large ones"

Francois de La Rochefoucauld (1613–1680), French author