

Are Breast Implants Linked to a Rare Form of Lymphoma?

Concerns have recently been raised over reports of a rare type of lymphoma occurring in a small number of women with breast implants. To investigate the potential link, as well as issues related to diagnosis and treatment, the RAND Corporation reviewed all published cases of this lymphoma in women with breast implants and convened a panel of medical experts to help them assess their findings.

A Rare Form of Lymphoma

In 1996, a group of doctors published an article describing a woman with breast implants who developed a rare type of lymphoma next to one of her implants. Lymphoma is a family of many different blood cancers that involve lymphocytes, or white blood cells that help make up the immune system, and is divided into two main types: Hodgkin’s lymphomas and the more prevalent non-Hodgkin’s lymphomas (NHLs). Unlike leukemia, which begins in the bone marrow, lymphomas are tumors that arise in lymph nodes or as a collection of cancer cells in various tissues in the body. The type of lymphoma that has been identified in this and other cases involving women who have received implants is a subtype of NHL, termed anaplastic large cell lymphoma (ALCL).

Since the original article, further attempts to corroborate the link between ALCL and breast implants, including additional case studies and an epidemiologic study from the Netherlands,

Key findings:

- Breast implants appear to be associated with a rare form of lymphoma, anaplastic large cell lymphoma (ALCL), but the evidence to date is insufficient to show that the lymphoma is caused by the implants, to identify risk factors, or to suggest an underlying mechanism of how ALCL develops.
- Experts agree that the accumulation of fluid in the space surrounding a breast implant (called a *seroma*) six or more months after surgery should lead to a thorough diagnostic evaluation for ALCL.
- Experts also agree that a diagnosis of localized ALCL should be managed with removal of the affected implant and surrounding fibrous tissue, but, in the absence of evidence for spread of the disease beyond the breast, radiation treatment and chemotherapy following removal are not required.
- Future research efforts—such as the collaboration between the American Society of Plastic Surgeons and the Food and Drug Administration to develop a breast implant registry—will be required to increase understanding of this disease.

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Corporate Headquarters
 1776 Main Street
 P.O. Box 2138
 Santa Monica, California
 90407-2138
 TEL 310.393.0411
 FAX 310.393.4818

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This research highlight summarizes RAND Health research reported in the following publications:

Kim B, Roth C, Chung KC, Young VL, van Busum K, Schnyer C, and Mattke S, “Anaplastic Large Cell Lymphoma and Breast Implants: A Systematic Review,” *Plastic and Reconstructive Surgery* [Epub February 25, 2011; doi: 10.1097/PRS.0b013e3182172418].

Kim B, Roth C, Young VL, Chung KC, van Busum K, Schnyer C, and Mattke S, “Anaplastic Large Cell Lymphoma and Breast Implants: Results from a Structured Expert Consultation Process,” *Plastic and Reconstructive Surgery* [Epub April 15, 2011; doi: 10.1097/PRS.0b013e31821f9f23].

have been inconclusive. Because of the rarity of this condition, the fact that case studies and large population studies are not designed to identify causative factors, and that the kinds of studies that may provide definitive answers will likely take years, the Plastic Surgery Education Foundation and the Aesthetic Surgery Educational Research Foundation commissioned the RAND Corporation to conduct an exhaustive search of the medical literature and convene an expert panel to evaluate the evidence for a link and its potential implications.

ALCL in the Medical Literature

The exhaustive literature search conducted by RAND identified a total of 36 cases of NHL among women with breast implants, 29 of which were ALCL. Although the women's medical histories were not always reported, 12 of the 29 women had a prior history of a different type of cancer, including eight who had undergone mastectomy for breast cancer and two who had a previous history of ALCL. No conclusions could be drawn about the type of implant most likely to be associated with ALCL or the length of time required between breast implantation and tumor development. While some patients received chemotherapy and/or radiation, the treatment consisted in most instances of surgically removing the affected implant and surrounding tissue, which appeared to successfully control the disease. No deaths were reported among any of the 16 women for whom follow-up information was available.

An Expert Panel Weighs In

The evidence so far cannot answer the questions of whether breast implants increase a woman's risk for ALCL, whether all women with implants should undergo special tests, or how the condition should be treated. Years of research will be required to answer those difficult questions. To provide immediate guidance to women who have or are considering having breast implants and their surgeons, RAND researchers provided the information obtained from the literature review to a panel of experts representing multiple disciplines, including cancer epidemiology, oncology, immunology, pathology, and material science.

The panel members were asked to read the review and provide responses to a spectrum of questions related to the causes, diagnosis, and management of ALCL associated with breast implants, based on their reading of the review and their own knowledge. Expert panels such as this one have proven to be a scientifically sound way to gather information on how experts make decisions about the diagnosis and treatment of a variety of conditions. In the absence of data from clinical trials, such information can be the basis of medical guidelines.

Association or Causation?

The experts agreed that the evidence suggests a link between breast implants and ALCL—that is, the women would not have developed the condition had they not received an implant—but they expressed uncertainty about whether implants actually cause the disease. They emphasized further that the true number of cases may be slightly underestimated because the condition is so rare that it may be overlooked. Most experts also agreed that ALCL is not seen within the first six months following breast implantation and is often not seen until many years later.

Uncertainty About Risk

The experts also were uncertain regarding factors that might increase a woman's risk of developing ALCL after receiving an implant. They expressed little agreement regarding the potential for family history, other genetic factors, obesity, smoking, or the type of implant to influence risk.

Diagnosis and Management

The panelists were also asked to weigh in on how a suspected case of ALCL should be handled. Agreement was strong that the buildup of fluid in the space surrounding an implant (called a *seroma*) six months or more after surgery or the recurrence of these seromas should lead to a thorough diagnostic evaluation using aspiration and cytological examination. They further agreed that the diagnosis of ALCL should result in a complete evaluation to rule out spread of the disease outside of the breast capsule (the lining that forms around the implant), followed by removal of the implant and capsule. However, agreement was much lower on the management of the breast that is not affected, namely whether the other breast's implant, capsule, or both should be removed as a preventive measure. In addition, there was significant uncertainty about the risk of ALCL progression if another implant is inserted immediately in place of the affected implant after it is removed.

There was greater agreement on follow-up treatment. Experts did not believe that localized disease (confined to the implant capsule) warrants radiation treatment or chemotherapy after surgery. Most experts expressed the belief that the risk of recurrence or development of systemic disease following removal of the affected implant and capsule is low, but that clinical follow-up is necessary.

What's Next?

Definitively proving whether or not breast implants cause ALCL and determining the optimal management of the disease will require years of research. However, in the meantime, the results of the literature review combined with expert panel input offer some guidance to women and

their surgeons, pathologists, and oncologists. Although the findings suggest the need for vigilance to detect this rare disease, they also provide reassurance that the condition has a very slow course and does not require aggressive treatment for localized disease, which may be controlled by surgical removal of the affected implant and capsule alone. Recently, the Food and Drug Administration announced plans to collaborate with the American Society of Plastic Surgeons to develop a prospective registry that will follow women with implants to gather information, which should help increase our understanding of this disease. ■

NOTE: This report summarizes research findings and should not be construed as offering medical advice to any individual patient or physician. As with any decision relating to medical care, individual patients need to make their own decisions, in consultation with their physicians, based on all of the risks and benefits of the contemplated treatment.

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