

ASPS members take part in ALCL advisory panel

BY JIM LEONARDO

ASPS members played key roles in an advisory panel convened by the RAND Corp. on March 26-27 in Arlington, Va., to advance the exchange of medical information relating to breast implant-associated anaplastic large-cell lymphoma (BI-ALCL) – a rare condition of which relatively little is known.

Mark Clemens, MD, Houston, and V. Leroy Young, MD, St. Louis, participated in a rigorous roundtable discussion alongside researchers and clinicians from medical oncology, hematopathology, molecular pathology, and surgical and radiation oncology during RAND's Scientific Advisory Panel on BI-ALCL. The group employed the "Delphi" method developed by the RAND Corp. in the 1950s to complete an evidence review and supply consensus, where possible, given the information learned throughout the two-day event.

The RAND-sponsored effort, moderated by Soeren Mattke, MD, RAND Health

Advisory Services managing director, is another step in the process of investigating the etiology and epidemiology of BI-ALCL, to more quickly and efficiently identify the condition as well as potential courses of treatment. The gathering was aimed at reexamining BI-ALCL literature and updating the RAND review of the disease that was first undertaken during a similar panel commissioned by ASPS in 2010.

Initial reports in 1995 on the emergence of large T-cell lymphoma in proximity to breast implants led to an AMA article review and discussion in 2008 with industry and science experts. In March 2010, ASPS President Michael McGuire, MD, The PSF President William Kuzon Jr., MD, and the presidents of ASERF and ASAPS announced the formation of an advisory council that included the FDA to study BI-ALCL.

At Plastic Surgery The Meeting in September 2011, ASPS President Phil Haec, MD, led the President's Panel "ALCL and Breast Implants – Plastic Surgery's Proactive Response, State of the Science and

Collaboration with the FDA," during which expert speakers provided updated information on the condition and related issues, and on the positive working relationship with the federal agency.

These and additional partnership arrangements with the FDA have led to the construction of the Patient Registry and Outcomes For breast Implants and anaplastic large cell Lymphoma etiology and Epidemiology (PROFILE) data registry vehicle – a joint and unprecedented partnership between ASPS/PSF and the FDA (*for more on PROFILE, see sidebar*).

The study is led by ASPS member Colleen McCarthy, MD, assistant attending physician in the Memorial Sloan-Kettering Cancer Center (New York) Department of Surgery, Plastic and Reconstructive Service. At PSN press time, 31 ASPS members had contacted the PROFILE registry since its launch in late 2011 to report BI-ALCL cases.

"Excitement over this investigatory process is tempered by the fact that we're only in the infancy of understanding this disease," says Dr. Clemens. "Our ultimate goal is to find a cure for BI-ALCL. We must encourage physician and public education – similar to the lead taken by ASPS and The PSF. The Foundation is working to provide supportive avenues for laboratory and clinical research – and at this potentially seminal moment, this strategy is critical to establish tissue banking and model cell lines, and to define diagnostic and therapeutic options."

'Solve the mystery'

"The disease of BI-ALCL is a mystery, and the medical profession has been trying to recognize its impact and understand its molecular genesis in order to prevent a single further case," says Dr. Clemens, who leads a multidisciplinary research team and tissue repository for BI-ALCL treatment at MD Anderson Cancer Center. "The mission of RAND is, through quality and objectivity, to support innovative research on crucial issues that require policy debate. Our panel's task was to review and then fully exploit very limited data to discuss consensus recommendations for diagnosis, treatment and follow-up."

BI-ALCL differs from systemic ALCL in significant ways, perhaps the most important of which is its treatment: When isolated to breast implant capsules, the disease generally doesn't require chemotherapy or radiation therapy, according to panelists at the "Management of Complications in Plastic Surgery" symposium held in late March in Rosemont, Ill. As a result of this difference, the World Health Organization is considering BI-ALCL for its own classification, Dr. Clemens tells PSN.

Data and other information gleaned from the panel will be codified and analyzed by the RAND Corp.'s BI-ALCL leadership, with the results to be published in the summer or fall of 2014, according to a RAND spokesperson.

"One of the big issues with BI-ALCL is that there's little information and little known for certain," says Dr. Young, who's authored several BI-ALCL articles for *PRS* – and been extensively involved in research on breast implants at Washington University. "So we took very seriously our charge to add clarity to the issue in the midst of that limitation."

"Considering the pre-panel work and the two-day discussions in Arlington, we did a lot of work," he adds. "But it really paid off. I feel confident that we added clarity to an important issue where data are limited."

Working preview

In the weeks prior to the conference, the 12

panelists received from RAND a BI-ALCL literature review, as well as 65 consensus statements from which – following the Delphi method – they would choose among the responses "Disagree," "Unable to Judge or Unsure," and "Agree." For the March panel, participants met early in the morning over breakfast – and then became immersed in each question, with the recognized discipline-specific person or persons taking the lead in their respective field of expertise.

"There was a multidisciplinary collection of experts in the room who led the discussions – for instance, oncologists addressed the chemotherapeutic recommendations, and surgeons defined operative treatment," Dr. Clemens says. "Some of the relatively obvious questions we answered immediately; others demanded 30 minutes or more. But we were allowed as much time as was necessary on each topic."

Discussion centered on sets of questions that targeted characteristics of the disease; its biology; recommended diagnostic approaches; recommended treatment, including chemotherapy and adjunctive treatment; and its surveillance.

Naturally, Dr. Clemens and Dr. Young took the lead and directed the conversation on plastic surgery-related consensus statements which involved "questions such as surgical technique with implants, common disease presentations and operative management applied directly to a plastic surgeon's perspective of the disease process, management and surveillance," Dr. Clemens says. "My particular contribution was to convey my experience operating on and treating BI-ALCL patients, to impart knowledge gained from direct discussions with plastic surgeons worldwide about their experience, and share The PSF initiatives such as the PROFILE patient registry."

The process lasted approximately 14 hours, after which the participants were informed that they would be asked again in the following week to address those same 65 statements, again choosing from the same set of three responses – this time using new information gained through the roundtable process to inform their current positions.

All for one

Drs. Clemens and Young agreed that the 12 panelists worked together exceedingly well, dispelling the notion that the likelihood of disagreement rises in proportion to the number of medical experts assembled to discuss any issue.

"It was one of the most collegial groups I've had the pleasure to work with," says Dr. Clemens. "My perception was that no one came in with a pre-set agenda. We worked well together, exchanging and analyzing a massive amount of information in a relatively short amount of time. We maintained momentum and progress throughout the talks – and, for the most part, we obtained consensus on most things. That is remarkably rare."

Dr. Young says the group's singular approach created an efficient process on an important issue. "These folks simply wanted to get the right answers to important questions," he says. "It was a good-sized group, but we had a strong moderator and a clear goal, which kept everyone on the right path. It was a very refreshing way to interact – and it wasn't about egos or personal gain and loss. It was about solving the mystery."

For more information on BI-ALCL or to report a case, contact ALCL@plasticsurgery.org or visit The PSF's PROFILE webpage at the-psf.org/research/clinical-impact/profile.htm. PSN

PROFILE registry

ASPS/FDA collaboration collects, offers information on BI-ALCL

BY JIM LEONARDO

The information currently available on breast implant-associated anaplastic large-cell lymphoma (BI-ALCL) is as scarce as the disease is rare. According to the Surveillance, Epidemiology, and End Results (SEER) Program of the National Cancer Institute, 1 in 500,000 U.S. women is diagnosed with ALCL each year, while the projected annual rate of incidence for BI-ALCL is approximately three in 100 million. This low number of cases makes the data-gathering process related to its etiology and epidemiology difficult, but its uniqueness to women with breast implants also makes it a priority for both the aesthetic and reconstructive aspects of the specialty.

The PSF's Patient Registry and Outcomes For breast Implants and anaplastic large cell Lymphoma etiology and Epidemiology (PROFILE) registry – an unprecedented joint partnership between ASPS and the FDA – was launched in 2011 to better understand BI-ALCL through the accumulation and analysis of clinical data. In addition to providing crucial etiology and epidemiology data on this rare disease, the PROFILE registry can bring plastic surgeons who encounter BI-ALCL into a network of colleagues with prior experience in the disease. By contacting PROFILE, plastic surgeons can receive recommendations on the evaluation of their patient, as well as suggestions on the procedures and additional specialty consults that might be needed.

In other words, rather than face this mysterious disease isolated and within an information vacuum, patients unfortunate enough to contract the disease will at least have a plastic surgeon who knows where to find guidance and data.

No help without data

Truly significant information, however, can only come from plastic surgeons who contribute data to the PROFILE registry – and The PSF President Kevin Chung, MD, implores ASPS members who encounter BI-ALCL to contribute their data.

"The medical community as a whole clearly needs all the data it can get on BI-ALCL," Dr. Chung says. "It's such a rare disease that the data-gathering process has been quite slow, naturally. But we need to get as much as we can, as soon as we can. Because of its relative rarity, the methods of approaching BI-ALCL are still being sorted out. Only through data submission can we really begin to take a rigorous, academic look at this disease – and PROFILE is really a quick and easy registry to work with to get that done."

Data are being collected both retrospectively and prospectively on confirmed cases of primary BI-ALCL (including localized or systemic disease, and of any anatomic site and ALCL cell phenotype) – Dr. Clemens says there have been 83 identified cases worldwide. While one main goal is to better understand the role of breast implants in the etiology of primary BI-ALCL, the research also will focus on identifying potential risk factors, detection and management of this disease.

"Getting in contact with PROFILE and sharing that diagnosis will bring plastic surgeons – who may feel isolated due to a lack of wide colleague experience, and at somewhat of a loss for a treatment approach – into this network of people who have information on, and experience with, BI-ALCL," says Mark Clemens, MD, who leads a multidisciplinary research team and tissue repository for BI-ALCL treatment at MD Anderson Cancer Center, Houston. Dr. Clemens was a participant in a recent RAND Corp. panel on the disease.

Dr. Clemens is available to assist physicians who encounter BI-ALCL. "I'm happy to speak to anyone who's encountered a case, as will the PROFILE leaders," he adds. "The process of contributing data to PROFILE is quite simple; the registry itself can direct them."

"It may seem a small contribution by the plastic surgeon who encounters a BI-ALCL patient, but the return is potentially quite large," he says.

For more information on BI-ALCL or to report a case, contact ALCL@plasticsurgery.org. Dr. Clemens can be reached at mwclemens@mdanderson.org. PSN