PJI AND CANCER

PJI’s not only confer a mortality rate comparable to many cancers, but that joint infection and cancer share a number of biologic, genetic, psychological, and financial similarities.

“When I first put together this presentation, I thought the association between PJI and cancer would be esoteric and peripheral at best,” said Dr. Springer. “After examining the literature on both conditions, I was very surprised to find the exact opposite.”

Dr. Springer noted that during the past 150 years, infectious disease mortality has dropped precipitously, with the only real spike being the 1918 Spanish Flu epidemic. Likewise, mortality rates for the majority of cancers have declined. “What we have seen—and what is more concerning—is a rise in the mortality rate related to antimicrobial-resistant strains of bacteria,” he said.

For example, in one study cited by Dr. Springer, the mortality rate after septic versus aseptic revision TJA was five times higher (Fig. 1). Berend et al studied 205 infected total hip arthroplasties that went through a two-stage exchange and noted a 7 percent mortality in those patients in between stages.

As for cancer, Dr. Springer said, “Clearly when we look at mortality in PJI and compare it to mortality in cancer, you might be somewhat surprised to find out that the 5-year survivorship of a PJI is actually less than four of the five most commonly diagnosed cancers in our society today (Fig. 2).”

The T-cell connection

In biologic terms, the similarities center on the T cell and on T-cell homeostasis. “Both in cancer and in infectious organisms, proteins are expressed that are recognized by host T cells,” Dr. Springer explained. “Eventually, however, the upregulation of the T cell must be countered by a downregulation, which results in a T-cell exhaustion. Ultimately, there is a loss of T-cell response to fight both cancer cells and infecting organisms. The parallels between neoplasia and an early infection are virtually identical with regard to upregulation of the T cell,” Dr. Springer continued. “And when you look at mature tumor cells, and protracted or prolonged infections, you again see almost identical responses from the T cell with regard to upregulation, subsequent T-cell exhaustion, downregulation, and overpowering by either the infecting organism or the tumor.”

The similarities between the two disease processes do, however, have a potential therapeutic benefit, according to Dr. Springer. “The biggest one is targeted immunotherapy for treatment of both cancer and PJI,” he said. “This would enable the boosting of the host immune system without causing the overtoxic effect of overregulation of the T cells.”

The parallel approach to infection and neoplasm can be currently seen in clinical practice in the use of granulocyte-macrophage stimulating factor in treatment both for cancer and sepsis. “This really begs for collaborative efforts between oncology and infectious disease experts, because we are really working on very similar clinical presentations,” said Dr. Springer.

Another parallel between PJI and cancer is the familial clustering of the diseases. “This is defined as the occurrence of a disease within some families in excess of what would typically be expected in the general population,” Dr. Springer said. “Cancer is probably one of the best examples of this.”

Dr. Springer quoted a study by Gilliland et al presented at the 2016 American Association of Hip and Knee Surgeons annual meeting. That study examined familial clustering in a Utah population database identifying all patients with PJI. “The researchers found very specific groups within families that were at higher risk, particularly in first-degree relatives, of developing a PJI after undergoing a total knee or total hip arthroplasty. This is very interesting work that needs to be expanded on further,” he said.

In an interview, Dr. Springer explained that when he initially explored the topic, he focused on the lethality of PJI. “The high mortality rates in PJI are often not mentioned or are underreported,” he said. “The data that showed 5-year survival rates for PJI were lower than for four of the five most commonly diagnosed cancers in the United States was eye-opening. Because the overall incidence is low, we often underrepresent the issue of infection when discussing risk of PJI with our patients. However, the ramifications of a PJI after a total joint replacement are immense. When you put it in the same category as cancer, it really gets attention.”

The family ties

Aside from the shared biologic/genetic traits, Dr. Springer said, “The emotional investment is similar between patients and family who are...