Managing Myeloma

What is cytokine-release syndrome and how is it treated?

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I am frequently asked, “What is cytokine-release syndrome (CRS)?” Overall, cytokine-release syndrome is a massive outpouring of inflammatory cytokines in response to an inflammatory stimulus. Now, this is seen in haploidentical transplants where there is only a half match between donor and recipient, and there is an outpouring of inflammation due to this recognition. Cytokine-release syndrome is also seen in chimeric antigen receptor therapy where the targeted cells, the tumor cells, are being attacked by the T cell that has been modified to attack a particular antigen that is expressed on the surface of the cancer cell. This leads, again, to a massive outpouring of cytokines which need to be managed.

Cytokine-release syndrome, especially in the context of chimeric-antigen receptor therapy, is an inflammatory condition that interestingly enough leads to very high levels of interleukin-6. Now, the original study done by the Penn group showed that these patients with very high IL-6 levels can be treated with tocilizumab, an anti-IL-6 receptor antibody. It binds to the IL-6 receptor, preventing IL-6 from activating end-stage cells or endothelial cells, inflammatory cells, and a variety of things that can be upregulated in terms of inflammation by IL-6. Tocilizumab is a critical component of the treatment of cytokine-release syndrome. If it is getting worse, in other words the patient is not responding to tocilizumab, steroids are now the gold standard treatment that follows patients who were not responding well to tocilizumab, or who have accelerated CRS such that it is life-threatening. CRS can be very life-threatening and thus it is very important to recognize and treat this syndrome.