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Daclizumab-induced sarcoidosis

Sarcoidosis is a multisystem granulomatous disease of unknown immunopathogenesis. However, patients with sarcoidosis have been found to have an increased number of natural killer (NK) cells with CD56 activation markers. Several drugs have been associated with drug-induced sarcoidosis-like reactions that are clinically indistinguishable from sarcoidosis. It is not clear whether these drugs truly cause sarcoidosis, render the immune system more susceptible to the development of sarcoidosis, or exacerbate subclinical sarcoidosis.

Daclizumab, a humanised monoclonal antibody that binds to the alpha subunit of interleukin-2 receptor on activated T cells, has been associated with the development of sarcoidosis. The mechanism is unclear; however, it is known to increase the number of CD56 NK cells, and this could be a plausible mechanism. Understanding the mechanisms of drug-induced sarcoidosis may yield important insights into the immunopathogenesis of sarcoidosis. Daclizumab is used for the treatment of relapsing forms of multiple sclerosis.

During the clinical trials of daclizumab between June 2013 and November 2016, 12 subjects developed clinical conditions consistent with sarcoidosis. Subsequently, an independent adjudication committee (comprising a pulmonologist, radiologist and pathologist) was set up to determine the likelihood that the cases represented sarcoidosis. The committee unanimously confirmed sarcoidosis in 11 patients. Biopsies were available in 7/11 and 4/11 who did not have biopsies had clinical findings and/or laboratory findings that were highly suggestive of sarcoidosis. Alternative causes for these findings were reasonably excluded in all cases. The lung (n=8/11) and skin (n=6/11) were the most common organs involved. The median time to the development of sarcoidosis from the first dose of daclizumab was 996 days. The incidence rate in those participating in the clinical trials was 154/100 000 patient-years compared with incidence rates of sarcoidosis in the USA of 3.2 - 17.8/100 000/year, therefore it was unlikely that they developed sarcoidosis by chance only. These data suggest that the cases may have represented drug-induced sarcoidosis related to daclizumab therapy.

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1. Judson MA, Elicker BM, Colby TV, et al. The development of sarcoidosis in patients receiving daclizumab: A case series from multiple clinical trials. Resp Med 2019;149:23-27. https://doi.org/10.1016/j.rmed.2019.01.015