Early treatment of systemic onset JIA with anakinra restores the IL-18 response

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First line treatment with anakinra (an interleukin-1 (IL-1) receptor antagonist), results in a 'good' clinical response (ACRp90) in patients newly diagnosed with systemic onset juvenile idiopathic arthritis (SoJIA), and restores the deficient IL-18 response of natural killer (NK) cells, according to a new study.

During the six month study, numbers of NK cells slightly increased initially but remained stable throughout treatment with anakinra, although specific lysis (the death of a cell by breaking of the cellular membrane) was restored to normal within just three days. Interestingly, the NK cell response after IL-18 stimulation was restored and sustained at normal levels, as seen in healthy children, during the follow up period - suggesting that anakinra was able to mediate levels of cells involved in the immune response.

JIA is the most common form of persistent arthritis in children under the age of 16 years. It differs significantly from arthritis commonly seen in adults (such as osteoarthritis and rheumatoid arthritis) as, in addition to inflammation of the joints, there may also be inflammation of the eyes and internal organs, as well as skin rash (exanthema) and fever. Children with SoJIA, a subtype of JIA, are known to have defective NK cell function which compromises their immune systems, since NK cells (a type of cytotoxic lymphocyte, or white blood cell, that is capable of killing infected cells) play a major role in the rejection of cells infected by viruses and malfunctioning cell types including those commonly found in tumours.

Dr Wilco de Jager of the University Medical Centre Utrecht, The Netherlands, who led the study, said: "In patients with SoJIA, the essential cell-based regulatory systems that make up cell based immunity are impaired. Our study has shown that, once NK cell levels and function are restored to normal, the cytokine pathway specifically involving IL-18 is restored, which elicited a good clinical response in this patient group. The underlying processes involved in auto inflammatory diseases are complex and these results suggest a potential new treatment strategy for children with newly-diagnosed SoJIA."

Researchers in this study recruited ten children with newly-diagnosed SoJIA, initiating treatment with anakinra prior to steroids. During a six month follow-up period, absolute NK cell numbers and function, cytokine profiles, and NK cell response after IL-18 stimulation, were monitored.

Following treatment, clinical parameters such as fever, exanthema and arthritis resolved after 3 days. A rapid decrease in ESR (erythrocyte sediment rate; an indication of inflammation), CRP (C reactive protein; a marker for inflammation), ferritin (a test of iron stores in the body) and sIL-2R (soluble interleukin 2 receptor) was observed. No differences of IL-1alpha, IL-1beta and IL-33 were observed, but levels of IL-6, IL-1RA and IL-18 returned to normal, as observed in healthy controls. During follow-up, two patients flared following anakinra treatment.

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NK cells are a type of cytotoxic lymphocyte that constitute a major component of the innate immune system. NK cells play a major role in the rejection of tumors and cells infected by viruses. The cells kill by releasing small cytoplasmic granules of proteins called perforin and granzyme that cause the target cell to die by apoptosis or necrosis.

Source: European League Against Rheumatism