Drug Reaction and High Fatality Lung Disease in Systemic Onset Juvenile Idiopathic Arthritis (sJIA)

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**RATIONALE**: Diffuse parenchymal lung disease (DLD) is not a known feature of sJIA. Coincident with the introduction of anti-IL-1 and anti-IL-6 medications as treatment of sJIA, a subset of children with this illness have developed an unusual high-fatality DLD. Since this is often preceded by extensive rash and eosinophilia or with drug related anaphylaxis, the contribution of drug reaction is considered.

**Methods**: Retrospective details of 63 cases of sJIA with DLD were assessed for delayed drug hypersensitivity (DReSS by RegiSCAR) or drug induced immediate (anaphylaxis). A REDCap database was used to collect details.

**Results**: Cases were collected worldwide. Serious drug reactions to immunomodulating medications occurred only among cases exposed to cytokine blockers (48/63). RegiSCAR for DReSS scored 15/48 as definite. At the time of scoring, all were treated with one of anakinra, tocilizumab, canakinumab or rilonacept; no other medications were implicated. Among those classifying as DReSS, anaphylaxis to the IL-6 inhibitor, tocilizumab, occurred in 3/12 (25%) exposed cases. In 4/15 with DReSS, the implicated drug was discontinued after lung disease developed; 4/4 survived. Among those continuing the drug, 10/10 (100%) are deceased. Lung disease was noted a median of 1 year after the drug reaction occurred.

**Conclusion**: Delayed drug hypersensitivity scoring as DReSS precedes the development of an unusual lung disease. Fatality is high, particularly in the group where drug hypersensitivity can be recognized. Unrecognized drug hypersensitivity may account for poor outcome in other cases.

Cytokine blockers and fatal lung disease