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.

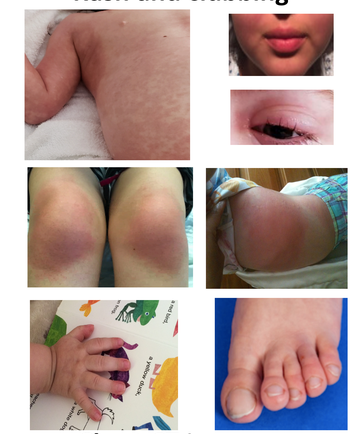
Cytokine blockers and fatal lung disease

AAAAI 2020 Annual Meeting

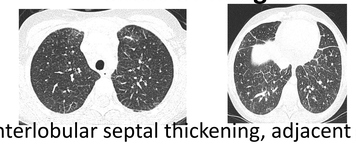
Features of 15 cases scoring as DReSS by RegiSCAR[1]	
Peak eosinophil values[2]	
Peak eosinophils (med absolute count(IQR))	1654(1298,4257)
Peak % eosinophils (med % of WBC(IQR))	17(12.4,31)
Oral prednisone dose at time of eosinophilia (med mg/kg/d(IQR))	0.4(0.1,1)
Rash characteristics (n,(%))	
Pruritic and non-evanescent	15(100%)
Covering >50% of body	13(87%)
Known to have included the face	13 (87%)
Delayed reaction: Implicated medication[3,4] (n reacting/n exposed,(%),(n as first of class))	
Anakinra	14/15 (100%)(11)
Canakinumab	5/7(71%)(2)
Rilonacept	2/2(100%) (1)
Tocilizumab	3/12(25%)(1)
Immediate reaction (anaphylaxis) (n reacting/n exposed,(%), (n as first of class))	
Tocilizumab	4/12(33%) (1)
Fatality (n,(%))	
Overall	10/15 (67%)
During treatment with implicated medication	10/10 (100%)
After discontinuing implicated medication[5]	0/4 (0%)

[1] RegiSCAR classification: Maximum score is 9 with a score of 6-9 defined as 'definite'(Kardaun et al 2007).
[2] Upper limit of normal: absolute eosinophilis <500 cells/ul, eosinophil % of WBC <5-6%
[3] Other ongoing medication (>2weeks): methotrexate in 2/15
[4] 12/15(80%) were exposed to > 1 cytokine blocker, 8/12(67%) exhibited features consistent with drug reaction to a subsequent cytokine blocker.
[5] One surviving case continues the implicated medication and requires multiple medications to manage ongoing disease. The remaining four survivors are doing well on other treatments. Each surviving case has been followed for at least 2 years after developing lung disease.

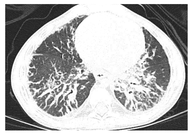
Rash and clubbing



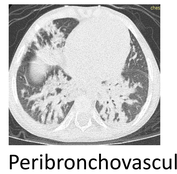
Chest CT images



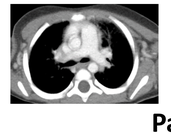
Interlobular septal thickening, adjacent ground glass opacities, lower &upper lungs



Peripheral consolidation



Peribronchovascular/ perihilar consolidation



Hyper-enhancing lymph nodes

Pathology

Patchy variant alveolar proteinosis/ endogenous lipoid pneumonia, often with vascular involvement