Acute respiratory distress syndrome precipitated by GCSF in undiagnosed *Pneumocystis jirovecii* pneumonia

RESEARCH WEEK
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INSPIRED RESEARCHERS
Northern Health

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Background

- Acute respiratory distress syndrome (ARDS) is a rapidly progressive condition characterised by the development of dyspnoea and inflammatory alveolar infiltrates, and occurs due to an inciting event[1].
- Granulocyte colony-stimulating factor (G-CSF) is used in haematology and oncology patients to promote innate immune reconstitution, however has been linked to inflammatory complications[2]. The development of ARDS has rarely been described[3].

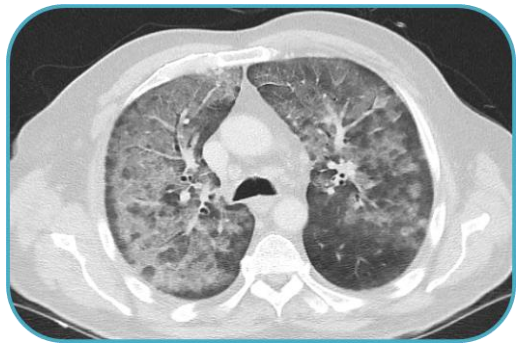

Figure 1: CT chest showing diffuse alveolar infiltrates

Case report

- 62yo male with rheumatoid arthritis presented with symptomatic anaemia and mouth ulcers. Investigations revealed neutropenia, mixed liver function test abnormalities and acute kidney injury.
- Diagnosed with methotrexate toxicity → calcium folinate rescue
- Persisting severe neutropenia → Day 5 given a single dose of GCSF
- Day 6 developed new hypoxia, cough and fevers
- CT chest showed diffuse alveolar infiltrates (**Figure 1)**
- Progressive elevation of inflammatory markers with blood film showing a leukaemoid appearance (**Figure 2**)
- Sputum PCR identified *Pneumocystis jirovecii*, and he was commenced on corticosteroids and co-trimoxazole
- Hypoxia and fevers rapidly resolved and he was discharged home with complete resolution on follow-up

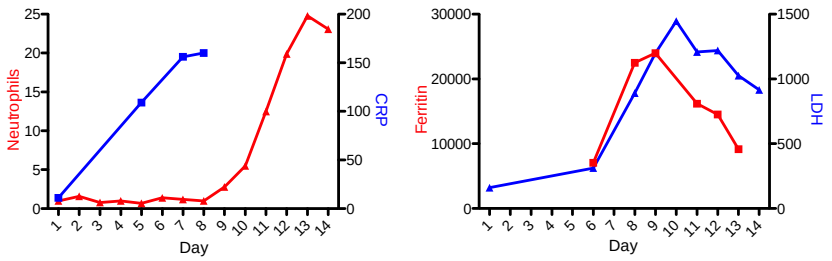

Figure 2: inflammatory markers

Discussion

- The development of ARDS following G-CSF highlights the risks of rapid innate immune reconstitution.
- The presence of a leukaemoid reaction provides evidence for a globally disproportionate immune response.

- Direct pulmonary toxicity from G-CSF is rare; however, in the presence of infections or other medications with pulmonary toxicity, the risk appears to be significantly greater[4].
- The development of ARDS has, in most cases, been associated with the presence of infections at the time of neutrophil recovery[5].

- Exogenous G-CSF, while useful, should be treated with caution as the upregulation of cytokines that increase alveolar permeability or neutrophil influx (such as TNF-a, IL-1b and IL-8) can exacerbate acute lung injury, such as we have become familiar with in the era of COVID-19.

1 The ARDS Definition Task Force, Acute Respiratory Distress Syndrome: The Berline Definition. JAMA 2012;307(23):2526-2533
2 Tigue CC et al, Granulocyte-colony stimulating factor administration to healthy individuals and persons with chronic neutropenia or cancer: an overview of safety considerations from the Reserarch on Adverse Drug Events and Reports project. Bone Marrow Transplantation 2007;40, 185-192
3 Karlin L et al, Respiratory status deterioration during G-CSF-induced neutropenia recovery. Bone Marrow Transplant 2005;36(3): 245-250
4 Iki S et al, Cytotoxic drug-induced pneumonia and possible augmentation by G-CSF: clinical attention. Ann Hematol 1993;66: 217-218.
5 Takahashi Y et al, Effect of granulocyte/colony-stimulating factor on the onset of the adult respiratory distress syndrome. Acta Haematol. 1999;101(3):124-9

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