

Tocilizumab, Anti-Inflammatory Effect: New Indications?

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Short Communication

Tocilizumab is a humanized monoclonal antibody that competitively inhibits the binding of interleukin-6 (IL-6) to its receptor. The inhibition of this receptor complex prevents IL-6 signal transduction to inflammatory mediators, hence to the entire pro-inflammatory properties of B and T cells [1,2]. Tocilizumab is indicated both for the treatment of moderately to severely active rheumatoid arthritis in adults and for the treatment of active polyarticular juvenile idiopathic arthritis and active systemic juvenile idiopathic arthritis in children older than 2 years of age [3].

Multicentric Castleman disease is associated with significant systemic symptoms, in part related to the underlying role of IL-6 in disease pathogenesis. Turcotte et al show a case who has shown sustained remission following multi-agent chemotherapy and targeted maintenance therapy with tocilizumab [4]. This drug has also been given as part of a immunosuppressive intervention for severe acute graft-versus-host-disease after allogeneic stem cell transplantation with improvement of the clinical symptoms within 48hr [1]. Although not yet explored, there may be also a window of opportunity to suppress other inflammatory processes. We present briefly the case of an adolescent girl with relapsed acute lymphoblastic leukaemia who was admitted to the hospital with neutropenic fever. She developed tachycardia and hypotension and was transferred to pediatric intensive care unit where she was started on inotropic support. Her blood cultures grew *Candida tropicalis* for which her Hickman catheter was

removed and extensive anti-microbial treatment including vancomycin, meropenem, caspofungin, ambisome and fluconazole, was initiated. Both G-CSF (ANC (=Absolute Neutrophil Count) 150) and methylprednisolone (2 mg/kg/day) were subsequently added to the treatment. However, her clinical course continued to worsen and developed multi-organ failure requiring maximal intensive care support, including high frequency oscillatory ventilation, nitric oxide inhalation, further extending inotropic support with epinephrine, norepinephrine and dobutamine, and continuous renal replacement therapy. While her neutrophil count improved (ANC 10.000, G-CSF was discontinued), her respiratory condition worsened, making it more difficult to ventilate her. Assuming the likelihood of the systemic inflammatory response due to ongoing IL-6 production (secondary to the systemic *Candida tropicalis* infection), Tocilizumab (10 mg/kg) was administered intravenously over 1 hour (72 hours after the G-CSF was discontinued). Within 12 hours, the chest X-ray showed a more convenient air distribution in the lungs (Figure 1) and the ventilatory support could be weaned. Unfortunately she experienced only a transient response. The next day her condition worsened, she became anuric and her cardiac function deteriorated further. Soon thereafter she passed away. Whether the administration of Tocilizumab in an earlier stage would have led to a better outcome, remains unclear. Conclusion: though our finding is limited to one single patient, the transient improvement of her condition may suggest potential efficacy of Tocilizumab in children with systemic inflammatory response of other causes.

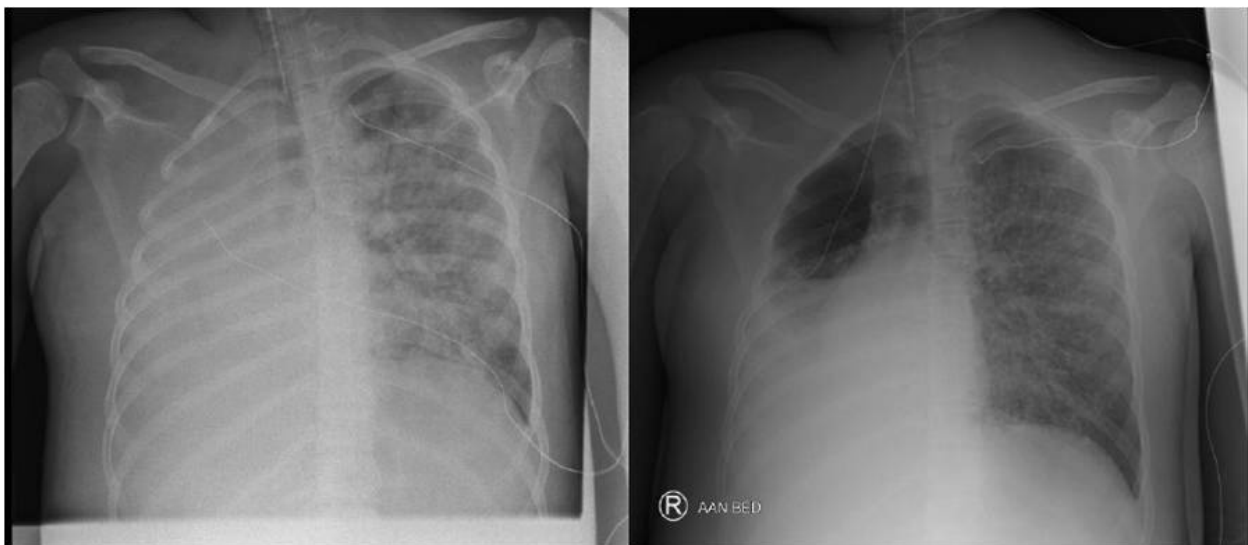


Figure 1: The chest X-ray showed a more convenient air distribution in the lungs.

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