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A case of refractory adult-onset Still's disease that responded to sequential therapy with anakinra and tocilizumab

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INTRODUCTION

Adult-onset Still's Disease (AOSD) is a systemic auto-inflammatory disorder with unknown aetiology. We report a case of refractory AOSD that responded to sequential treatment with anakinra (IL-1 antagonist) and tocilizumab (IL-6 inhibitor).

CASE DESCRIPTION

A 31-year-old lady was diagnosed with AOSD based on the Yamaguchi criteria which included the presence of fever ≥39oC, arthritis, leucocytosis, elevated liver enzymes, lymphadenopathy and hepatomegaly, and negative tests for antinuclear antibody and rheumatoid factor, with exclusion of other aetiologies. There was associated hyperferritinaemia, at 37,396 µg/L. Her disease showed poor response to high-dose corticosteroids and intravenous immunoglobulin, and she was subsequently treated with a biologic agent, subcutaneous anakinra. Despite the recommended dose of 2mg/kg daily and background oral prednisolone, she continued to have daily high-grade fever, hyperferritinaemia, leukocytosis and transaminitis. Transaminitis and leukocytosis eventually resolved after 8 months of treatment with anakinra.

Nonetheless, fever persisted, and arthritis recurred. This prompted an addition of methotrexate (MTX) to control the arthritis, and optimization of anakinra dose to 200mg daily. Despite this, her symptoms did not improve, prompting a switch of biologic agent from anakinra to intravenous tocilizumab.Fever resolved after the first dose of tocilizumab, followed by gradual resolution of her symptoms and improvement in hyperferritinaemia. Tocilizumab was discontinued after 1 year of treatment as there was no recurrence of clinical manifestations. Prednisolone was also stopped but MTX was maintained to keep her disease in remission.

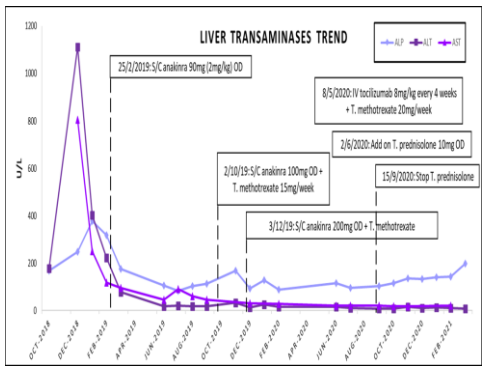

Figure 1(A)Liver transaminases trend

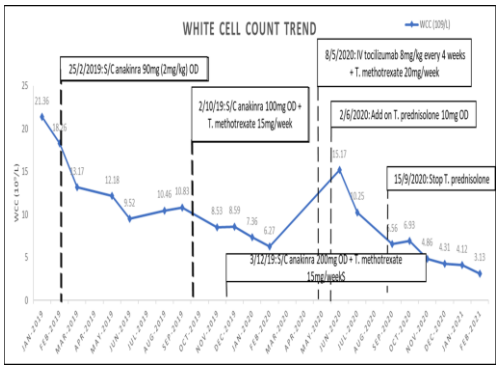

Figure 1(B) White cell count trend

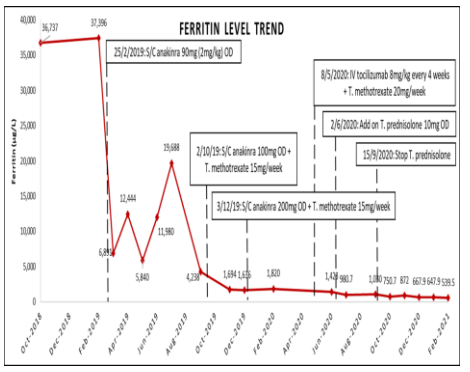

Figure 1(C) Ferritin level trend

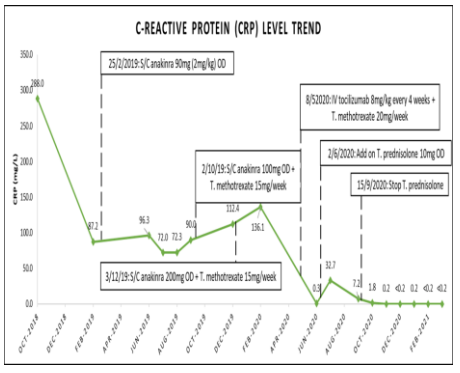

Figure 1(D)CRP level trend

DISCUSSION

- Proinflammatory cytokines like interleukin (IL)-6, IL-1 and IL-18 and tumour necrosis factor α (TNFα), are implicated in the pathogenesis of AOSD[1].
- Treatment includes non-steroidal anti-inflammatory drugs(NSAIDs), systemic corticosteroids, conventional disease-modifying antirheumatic drugs (csDMARDs) and biologics that target the proinflammatory cytokine pathway[2-3]

Table 1 : Anakinra vs. Tocilizumab in This Case

Feature	Anakinra (IL-1 Receptor Antagonist)	Tocilizumab (IL-6 Receptor Antagonist)
Justification for Use	Chosen initially due to severe transaminitis; safer hepatic profile[4].	Selected after refractory response to anakinra; liver enzymes normalized.
Mechanism of Action	Blocks IL-1, a key driver in systemic inflammation of AOSD[3,5,6,7].	Blocks IL-6, involved in both systemic and articular inflammation[3,8,9].
Response	Partial: Biochemical improvement, but persistent fever and arthritis.	Excellent: Fever and inflammatory markers normalized after first dose.
Limitations/Challenges	Off-label use in Malaysia: Required special approval, interrupted due to infection, sepsis, and drug supply issues.	Off-label use in Malaysia: Required special approval, but no major clinical complications.
Outcome	Resolution of transaminitis and leucocytosis, but disease remained active.	Achieved sustained remission; allowed steroid cessation.
Safety Profile in This Case	Shorter half-life and less hepatotoxic potential, making it a safer option in the context of liver dysfunction[4].	No significant adverse effects reported.

Key Learning Points & Conclusion

- Stepwise escalation to biologics targeting IL-1 or IL-6 is critical in refractory AOSD.
- Anakinra selection was justified due to concerns about hepatotoxicity and its rapid onset of action, with a favorable safety profile in cases of liver dysfunction. Tocilizumab was appropriately selected when the hepatic enzymes normalised and the disease remained active despite optimized anakinra therapy. Hence, the sequential therapy with both Anakinra and Tocilizumab has successfully induced remission in this patient.

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