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Title: Ferritin, CRP, and serum CD25 distinguish between HLH and TAFRO

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Background: Hemophagocytic lymphohistiocytosis (HLH) and the thrombocytopenia, anasarca, fever, reticulin fibrosis, and organomegaly (TAFRO) subtype of idiopathic multicentric Castleman disease (iMCD) are rare cytokine storm syndromes which are difficult to diagnose and often fatal without treatment. Ferritin, CRP, and serum CD25 levels are elevated in these diseases, however no studies compare the extent of elevation between TAFRO and HLH.

Methods: A retrospective cohort of patients with HLH and iMCD-TAFRO were identified from Vancouver General Hospital and the ACCELERATE Castleman disease database. Ferritin, CRP, and serum CD25 were obtained and compared using ROC curves to determine cut-off values for optimum sensitivity and specificity.

Results: 113 patients were identified with HLH (n=44) and iMCD-TAFRO (n=69 total, n=24 for sCD25). The optimal cut-off for CRP is 128.6 with sensitivity 60.4% and specificity 90.9% (AUC 0.75). The optimal cutoff for ferritin is 1854 with a sensitivity 93.1% and specificity 97.7%, (AUC 0.94). The optimal cutoff for sCD25 is 3354 with sensitivity 95.8% and specificity 76.7%, (AUC 0.89). The combined optimal cutoffs are CRP >80, ferritin <4900, and sCD25 <3300 with a sensitivity 100% and specificity 68.4% for TAFRO over HLH.

Conclusions: These findings suggest that HLH and TAFRO can be reliably differentiated based on ferritin, CRP, and sCD25. Given the severe morbidity and mortality associated, and the diagnostic challenge they present, these findings serve to aid in accurate and rapid diagnosis and therefore earlier administration of disease-directed treatment.