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Title: TAFRO syndrome without pathology supporting Castleman disease: treated as iMCD-TAFRO or a distinct disease entity?

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Summary: TAFRO syndrome was previously considered a subtype of idiopathic multicentric Castleman disease (iMCD-TAFRO), requiring pathology supporting Castleman disease. However, obtaining lymph node biopsies could be difficult for TAFRO patients (TAFRO without pathological evidence, TAFRO-w/op-iMCD), and sometimes these biopsies do not confirm iMCD (TAFRO-w/o-iMCD). To compare the clinical features and prognosis of these subgroups, we retrospectively analyzed 50 iMCD-TAFRO and 11 TAFRO-w/o-iMCD patients from May 2015 to April 2024. Both groups showed no significant differences in clinical presentations and laboratory data. Most of the patients were treated with iMCD-targeted strategies addressing cytokine storm. With a median follow-up of 21.4 (range, 0.5-107.0) months, there were no significant differences between iMCD-TAFRO and TAFRO-w/o-iMCD patients in 3-month response rate (72.1% vs. 88.9%, P=0.525), 6-month response rate (70.0% vs. 83.3%, P=0.849), or the best overall response rate (77.6% vs. 90.0%, P=0.645). The estimated 3-year progression-free survival rate (65.8% vs. 90.0%, log-rank P=0.163), and the estimated 3-year overall survival rate (77.0% vs. 100%, log-rank P=0.145) were also not significantly different. Univariate logistic analysis showed that decreased eGFR (< 60ml/min/1.73m2) was associated with increased risk of disease progression (OR=5.556, 95%CI: 1.653-18.672, p=0.006). Therefore, iMCD-TAFRO and TAFRO-w/o-iMCD patients could be considered the same entity and treated promptly, targeting the cytokine storm with similar strategies.