Genetic variants and phenotypic features of childhood large vessel vasculitis and vasculitis-like

Shahad Alansari[1], Alhanouf AlSaleem[1], Sulaiman M Al-Mayouf[1, 2]
Pediatric Rheumatology, King Faisal Specialist Hospital and Research Center[1],
College of Medicine, Alfaisal University [2]
Riyadh, Saudi Arabia

Background
Large vessel vasculitis (LVV) rarely affects children. Clinical characteristics, disease progression and outcomes vary based on the size of blood vessel and organ involved. The precise etiology remains incompletely defined. Recently, genetic variants gained more attention and shed more light on the underlying pathomechanism involved in the various systemic vasculitis.

Objectives
To report the phenotypic, genetic findings and outcome of children with LVV.

Methods
This is a cross-sectional retrospective cohort study from a single tertiary medical center and systematic review of childhood LVV associated with genetic variants.

Results
Four patients (three males) were enrolled, all presented before two years of age. Two patients had recurrent chest infection, skin abscesses and eczema proved to have DOCK8 variants. One patient with FOXP3 variant presented with very early onset inflammatory bowel disease; and one patient had skeletal dysplasia and inflammatory bone disease with homozygous ZNF469 variant and de novo variant in KDM5B. All patients had progressive extensive LVV, affecting mainly aorta and its branches. Our comprehensive systematic review revealed 15 (out of 70 articles) eligible articles were included. Data of 17 patients extracted and reviewed. All included patients had childhood onset of inherited disorders, including hyper-IgE syndrome, Blau syndrome, Wiskott–Aldrich syndrome and FMF. Eleven patients had genetically proved diagnosis while the diagnosis was based on the expert physician's opinion and fulfilling the diagnostic criteria. Seventeen out of 21 patients, (including our patients), received immunosuppressive treatment, 13 patients treated with corticosteroids and 11 received DMARDs, one patient completed hematopoietic stem-cell transplantation. Six of them underwent surgical intervention. Most of them showed a reasonable therapeutic response. However, three patients had neurological complications. There were five deaths.

Conclusion
This study shows a wide spectrum of underlying inherited disorders with genetic variants, associated with early onset LVV, which might allow to propose monogenic LVV as a distinct entity. We hope that these findings will increase the awareness of the association between LVV with genetic variants. Early recognition can lead to a better understanding of the disease pathophysiology and earlier effective intervention in order to improve the outcome.