VEXAS SYNDROME

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- It is a rare autoimmune genetic condition with grave prognosis
- Vexas means

V	Vacuoles are after seen in cells identified in bone marrow biopsy
E	E1 Ubiquitin activating enzyme I am code by the UBA1 gene which is mutated in patients
X	This gene is situated in the X chromosome
A	Patient have auto inflammation
S	Tax mutation in the genes are somatic that is mutation are required at same point in life and are inherited

- Pathogenesis :- variants in UBA1gene result in the production of enzyme ubiquitin activating enzyme D1 with reduced functions as a result damage protein build up inside the cells and this causes activation of immune cells or cells damage and death this leads to abnormal

inflammation impaired blood cells development and other features of vexas syndrome

- Clinical Features :-

- **Frequency** rare condition one in 13,000 people are affected typically older adults primarily males are affected
- **Age** 50 to 70 years
- **Joint involvement** generally fever fatigue inflammatory arthritis
- **Skin involvement** there is neutrophilic Dermotosis Leucocytoclastic vasculitis evidence of medium vessel vasculitis
- **Ocular involvement** inflammatory eye disease
- **Ear** relapseing chondritis and also sensorineural hearing loss
- P**ulmonary** Alveolitis pleural effusion
- C**ardiovascular System** myocarditis

- H**aematological** myelodysplastic syndrome multiple myeloma cytopenia vacuoles in myeloid and erythroid cells
- **GI system** hepato-splenomegaly and colitis

- **Diagnosis** genetic genetic testing looking for mutations in UBA1 gene located in X chromosome

- **Treatment** new standard treatment

- Inflammatory features are treated with steroids and other immunosuppressant
- Bone marrow transplantation
- Multidisciplinary approach where rheumatologist haematologist dermatologist are needed

- **Reference**

- Beck A B , Bodian AL ,Shah V el al prevalence and clinical manifestations of UBA1 variants associated with vexas syndrome in a clinical population JAMA 2023 Jan 24; 329 (4) 318-321

- Beck AB , Feradx MA , sibora RA et al somatic mutations on UBA1 and severe adult onset auto inflammatory disease NEJM 2020 Dec 31; 383 (27) 2628-2638

Sarilumab in adults with polymyalgia rheumatica

- Polymyalgia rheumatica is a painful delibitating disease affecting the proximal muscles of upper and sometimes lower extremities
- It is usually treated with high dose steroids
- But it may be a few laps in time and there may be a steroid resistant variant of poly myalgia Rheumatica
- It is in the these cases that saree new man which is and IL-6 receptor inhibitor find special place
- Phase 3 of the SAPHYR study findings suggest that IL-6 inhibition buy sarilumab is very efficacious
- It is well known that IL-6 is a key mediator in the pathophysiology of the disease it increases the remission rates and decrease inflammation

- Significant improvement and sustained remission were achieved in comparison to placebo treatment
- There was also less necessities of steroid
- Treatment emergent adverse events were not significantly higher among sarilumab patients
- Dose 200 µg subcutaneous once in 2 weeks
- Side effects site opinions ANC if between 50000-100000 hold treatment
- low platelet 50,000 to 1,00,000 hold treatment
- Liver enzymes AST ALT 3 times the normal hold the treatment

- Reference

- EULAR 2022 Lucy Pipers :- sarilumab shows treatment promise in relapsing poly myalgia rheumatica aunat of rheumatic disease 2022; 81 210 211