NEW HORIZONS

TNF Blockers in Gout

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TNF blockers (Etanercept, infliximab, adalimumab) are recommended and commonly used presently for the treatment of active RA, Psoriatic arthritis and active Ankylosing spondylitis. In addition etanercept finds place in treatment of Juvenile idiopathic arthritis of the polyarticular type and mucocutaneous manifestations of Behçet's syndrome .Whereas, infliximab finds place in treating granulomatous inflammatory diseases such as luminal and fistulising Crohn's disease, Sarcoidosis, or Wegener granulomatosis (1). In addition, Recoganisation of their role in treatment of gout is being discussed in the present article.

Recent findings regarding the pathogenesis of acute gouty arthritis illuminate that monosodium urate crystal are Internalised by phagocytes & stimulate inflammatory cytokines such as TNF-alpha, IL-1, IL-6 and IL-8 and this drives gouty arthritis. These cytokines can activate vascular endothelial cell expression of E-selectin, ICAM-1 and VCAM-1 and thereby stimulate both recruitment of neutrophils to the site of crystal deposition and amplification of inflammatory response. TNF-alpha and IL-1 can induce chondrocytes to release IL-8 and mono chemoattractant protein-1(2-4). Moreover, increased concentrations of TNF is also detectable in joints of gouty arthritis. On this hypothesis, anti-tumour necrosis factor has been tried as a new therapeutic option in gout, recently.

The use of etanercept (25 mg subcutaneously twice weekly) produced a noticeable decrease in all the pathological clinical and laboratory findings of severe gouty arthritis refractory to anti-inflammatory drugs (5).

Similar case of a patient with refractory chronic tophaceous gout treated with infliximab 400 mg i.v. (5 mg/kg) in weeks 0, 2, 6 and every 8th week resulted in a fast improvement of the polyarticular inflammation. The patient experienced fast relief from pain (VAS from 7.0 cm to 0 cm), joint inflammation (tender joint count from 9 to 0 and swollen joint count from 7 to 2) and a reduction of CRP (63.2 mg/dl to 2.2 mg/dl) and platelet counts (912/nl to 613/nl) in the peripheral blood. However, parameters of secondary renal amyloidosis did not respond to the treatment (6).

As in contrast to acute gouty arthritis, the lowering of blood uric acid in chronic tophaceous gout often does not result in permanent remission. Although treatment with glucocorticoids or colchicine has been described as effective in some patients, no other established therapy for chronic tophaceous gout is available. Thus, TNF-Inhibitors theoretically might be a further treatment option.

However, criticizing the above treatment, Reinders *et al*(7) suggest that for a case of severe tophaceous gout, when an expensive treatment is indicated, rasburicase should be considered as a potentially very effective treatment before using costly anti-TNF therapy.

The experience however of these drugs in gout remains scanty but future ongoing research in this direction and sharing of clinical experiences will definitely provide another important option in the form of anti TNF alpha drugs for clinicians in refractory gout and enrich the therapeutic arramamentarium for treating gout.

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