Risk of tuberculosis from arthritis medication examined

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Treatment with anti-tumor necrosis factor (TNF) agents is recognized as a risk factor for tuberculosis (TB) in patients with immune-mediated inflammatory diseases such as rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, psoriatic arthritis and psoriasis. Most TB cases develop as a result of reactivation of a latent TB infection, and health authorities worldwide recommend screening for latent TB and treating patients before initiating anti-TNF treatment.

A new study examined cases of TB associated with anti-TNF therapy and found that the risk of TB is higher for patients receiving anti-TNF monoclonal antibody therapy (infliximab or adalimumab) than for those receiving soluble TNF receptor therapy (etanercept). The study is published in the July issue of *Arthritis & Rheumatism* (http://www3.interscience.wiley.com/journal/76509746/home).

Led by Xavier Mariette of the Université Paris-Sud, researchers set up a national registry in France to collect all cases of TB occurring during a three-year period in patients receiving anti-TNF therapy for any reason. Researchers collected data on 69 cases of TB, assessing risk factors for TB before anti-TNF therapy began and anti-TNF treatment history.

The results showed that the risk of TB for patients receiving anti-TNF therapy compared with the French population differed depending on the anti-TNF agent used; those receiving monoclonal anti-TNF therapy had a higher risk than those receiving sTNFR therapy. The risk of TB was

higher during the first year of anti-TNF treatment, which favored the reactivation of latent TB. None of the patients who received correct prophylactic treatment for TB which is in France in most of the cases the association of INH and rifampicione for 3 months. Two thirds of TB cases occured in patients with negative skin tests.

The authors note that other countries have set up registries to investigate the safety of anti-TNF agents, but TB rates were so low that it was difficult to discern a difference in risk between the different types of anti-TNF agents; the current study, however, clearly demonstrates this difference. This study examined TB cases in the entire French population and researchers were therefore able to collect many more cases. In addition, it is the only registry to collect safety data for patients receiving anti-TNF therapy for any indication.

The mechanism by which TNF antagonists reactivate latent TB is not fully understood, but the authors suggest that differences in the action of the two types of anti-TNF agents in specific T helper cells (which play an important role in maximizing the capabilities of the immune system) and T regulatory cells (which suppress activation of the immune system) may help explain the differences in the risk of TB that were observed. The authors conclude that the differences seen with the two types of anti-TNF treatment may also explain the better efficacy of monoclonal antibody therapy in certain diseases, such as Crohn's disease, sarcoidosis and uveitis.

More information: "Risk of Tuberculosis Higher with Monoclonal Antibody Therapy Than with Anti-Soluble Tumor Necrosis Factor Receptor Therapy," F. Tubach, D. Salmon, P. Ravaud, Y. Allanore, P. Goupille, M. Bréban, B. Pallot-Prades, S. Pouplin, A. Sacchi, R.M. Chichemanian, S. Bretagne, D. Emilie, M. Lemann, O. Lorthololary, X. Mariette, *Arthritis & Rheumatism*, July 2009.

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