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The TNF-a antagonist infliximab partially impairs the in vitro tuberculosis-specific immune responses of severe psoriasis patients and healthy individuals with positive tuberculin skin-test

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TNF-α antagonists are recommended for treating severe psoriasis. However, these drugs, particularly infliximab (IFX), led to increased incidence of tuberculosis (TB). Surprisingly, epidemiological data suggest that the rate of TB in patients taking IFX in São Paulo, Brazil, does not differ from that from developed, non-endemic countries. To better understand the effect of TNF-α blockade with IFX on the susceptibility to TB reactivation in severe psoriasis patients in a TB endemic setting (Brazil), we evaluated the in vitro Mtb-specific immunity of severe psoriasis patients and controls, both with latent TB, in the presence/absence of IFX. Patients selected had active severe psoriasis, no co-morbidities or treatments that affect the immune responses and were strong tuberculin skin test (TST) reactors (> 10mm). Healthy individuals also TST+ served as controls. PBMC cultures from both groups were stimulated with different *Mycobacterium tuberculosis* (Mtb) antigens (ESAT-6, 85B and a Mtb lysate) and PHA, in presence or not of therapeutic IFX concentration (5 μg/ml). First, we verified that IFX almost abolished the TNF-α levels in PBMC' supernatants of both groups. IFX also significantly reduced patients and controls proliferative responses to PHA and the Mtb antigens, as well as the levels of IFN-γ released into 5 days supernatants. To verify whether these decreases were due to exaggerated IL-10 secretion, its supernatants levels were measured but were either further decreased or unaffected by IFX. Overnight ELISpot was also carried out and showed that, contrasting with the central-memory responses above, effector-memory INF-γ-releasing T-cell numbers were not affected by IFX. Thus our results show that IFX affected some, but not all aspects of the in vitro anti-TB immune responses tested. The preserved effector-memory responses, putatively related to exposure to environmental mycobacteria, may help to explain the lower than expected susceptibility to Tb reactivation in our setting.

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