Tumour necrosis factor inhibition causing psoriasis? A more plausible explanation exists

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I read with interest the report by Kary *et al.*¹ who reported nine patients who developed psoriatic skin lesions after treatment with tumour necrosis factor (TNF) α antagonists. Their diagnosis was psoriasis palmo-plantaris pustulosa or psoriasis vulgaris, and they proposed that this was an adverse reaction to the TNF α antagonists. Interestingly, they specifically report that six of nine patients had psoriatic-like lesions on their palms and soles. In only one patient do they specifically state that the lesions did not involve the palms and soles.

This same paradoxical adverse reaction to treatment with TNF α antagonists was recently postulated by Sfrikakis *et al.*² They described five patients who developed apparent psoriasis after treatment with a TNF antagonist. None of these patients had a personal or family history of psoriasis. They also referenced 20 other similar patients. They believed that psoriasis is heterogeneous and concluded that psoriasis is a paradoxical adverse reaction to TNF α inhibition.

Although psoriasis is heterogeneous, instances where a specific treatment can ameliorate or exacerbate a certain disease state are rare. Further, there are no known treatments in modern medicine that have been proved to both treat and cause the same disease. A more plausible explanation exists.

Keratoderma blenorrhagicum is both grossly and histologically indistinguishable from pustular psoriasis.³ It almost always involves the soles and palms, but also involves the nails, scalp and extremities.⁴ Keratoderma blenorrhagicum causes onycholysis, subungual keratosis and nail pits.³⁻⁵ Keratoderma blenorrhagicum occurs in the setting of reactive arthritis after exposure to certain causative bacteria such as *Chlamydia trachomatis*.

Six of the nine patients reported by Kary *et al* and four of the five patients presented by Sfrikakis *et al* had lesions on the soles and palms. Most of the referenced patients presented in a similar fashion. Three of the five patients described by Sfrikakis *et al* had onycholysis and subungual keratosis. All of these conditions are common for keratoderma blenorrhagicum. One patient without lesions involving the palms and soles, and the two not specified in the report by Kary *et al* had lesions involving their extremities, which is described in keratoderma blenorrhagicum.³

It is well established that patients receiving TNF α antagonists are at increased risk of infections. They are also at risk of reactivation of persistent obligate intracellular bacteria such as *Mycobacterium tuberculosis*. Interestingly, *C trachomatis* and *Chlamydia pneumoniae* are also persistent obligate intracellular bacteria.⁶⁻⁷ This persistent state has also been suggested with *Yersinia*, another causative organism of reactive arthritis.⁸ Further, in vitro data suggest that *C trachomatis* replication is inversely related to TNF α levels.⁹ This applies to both the acute and persistent forms of infection.

This paradoxical adverse reaction probably represents a manifestation of reactive arthritis—that is, keratoderma blenorrhagicum. These cases could be interpreted as new exposures to these causative organisms or re-activation of the persistent state. TNF inhibition would increase the risk of developing symptoms in either scenario. This would also explain why the skin lesions resolved in those patients who stopped the drugs, persisted in those who continued taking

the drug, and was not unique to a specific TNF α antagonist—that is, a class effect.

I propose that these cases represent keratoderma blenorrhagicum rather than TNF inhibition paradoxically causing psoriasis in a subset of patients as the authors have suggested. However, I agree that this is a very interesting and important observation. Perhaps we need to be more vigilant about recognising and monitoring other persistent infections such as *Chlamydia* when treating patients with TNF α antagonists.

Competing interests: None declared.

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