Psoriatic uveitis is not an exploded myth

Carla Enrica Gallenga
Francesco Parmeggiani
Paola Monari
Paolo Perri

Department of Biomedical and Specialist Surgical Sciences, “Antonio Rossi” Eye Clinic, University Hospital, Ferrara, Italy

Address for correspondence:
Carla Enrica Gallenga
Eye Clinic, University Hospital
Department of Biomedical and Specialist Surgical Sciences
Section of Ophthalmology
Via Aldo Moro 8
44124 Ferrara, Italy
E-mail: gilch@unife.it

Summary

Psoriatic uveitis, a distinct clinical entity quoted for 7 to 25% in psoriatic ophthalmic patients with spondyloarthritis, and for 25.1% ± 2.3 in a meta-analysis of rheumatic patients with a prevalence of HLA-B27 quoted as for 40 - 50%, is often misdiagnosed. The model proposed by Conti et al. [Clinical Dermatology 2017;5(1):30-36] merits also to drive the attention of Dermatologist, Radiologist, General Practitioner to submit those psoriatic patients to an ophthalmological screening.

We read with attention and appreciated very much the paper “Possible role of mast cells and IL-37 in the pathogenesis of psoriasis” by Conti et al. [Clinical Dermatology 2017;5(1):30-36]; the paper follows the scientific filum led by T. Theoharides (1) in Tufts University School of Medicine in Boston and in the Immunology Division, Postgraduate Medical School at the G. d’Annunzio, University in Chieti-Pescara, charging the mast cells (MC) as contributor for psoriasis (PsA) pathogenesis, caused by the generation of pro-inflammatory cytokines, in a cooperative crosstalk with skin keratinocytes to amplify the inflammatory cutaneous disorders, releasing TNF, IL-6 and other cytokines, causing recruitment of leukocytes mediating inflammation (2).

Skin and partially the eye (cornea, lens, retina) both are ectodermic. Ophthalmology started in XIX century in many countries as a specialty collateral to dermatology: i.e. the “Ospedale Oftalmico” in Turin was built in 1859 by senator Casimiro Sperino, ophthalmologist & dermatologist involved in Syphilis; Eye & Skin is still a chapter for university and postgraduate medical students. Uvea (iris, ciliary body, choroid) is mesodermic as it is for vitreous body. Loeping and Gartner (quoted by Rossi and Gallenga PE, 1969) (3) correlate the mesodermic vitreous body to the synovial fluid, opening the hypothesis of a common genetic pathway and a common participation to ‘rheumatic’ diseases, also for endocrine-metabolic pathology secondary to an exaggerated GH secretion (4).

The Anterior Chamber (AC) and the Vitreous Chamber (VC) have a privileged associated immuno-deviation (AID): ACAID and VCAID regulate the suppression of delayed hypersensitivity and the production of complement-fixing antibodies, both for endogenous and exogenous antigens; they require the presence of cells presenting ocular antigens and NKT CD1d-restricted cells that, when activated, produce immune-suppression factors (IL-10 and TGF-β).

Normal aqueous humour (AH) contains immunomodulatory substances:
- α-MSH which inhibits the production of IFN-γ;
- TGF-β1 and 2 which inhibit activation and proliferation of T lymphocytes;
- VIP that suppresses the secretion of TNF-α and the proliferation of T lymphocytes, by regulating ACAID.

Resident macrophages, antigen-presenting and polynuclear cells act in a medium that reduces and controls their functions with various mechanisms, reducing the possibility of generating an immune response, due to the limited expression of molecules of the major histocompatibility complex of class I and II, for inhibition by direct contact between infiltrating lymphocytes and resident cells (retinal Muller cells, anterior uvea epithelium, and corneal endothelium), due to the presence in AH of locally produced immunosuppressive molecules such as VIP, α-MSH, CGRP, somatostatin and trombospondin (5).

This balanced equilibrium is changed when a systemic disease (like PsA) introduces a trouble. Even though the psoriatic uveitis could be a distinct clinical entity, having distinguishing clinical features: mean age of presentation higher in HLA-B27+ PsA patients versus non-PsA, bilateral in 62% and prolonged (>11 weeks), requiring to add oral NSAIDS more often than HLA-B27- (6), few studies have been conducted to evaluate the association between uveitis and psoriasis when the joints are not affected. Luckily, psoriasis without arthropathy does not appear to be
Psoriatic uveitis is not an exploded myth

an high risk factor for the development of uveitis, being more likely to develop in patients with arthropathy or psoriasis pustulosa compared to other forms of psoriasis (7) but the presence of HLA-B7 may be associated with more severe uveitis: these positive patients tend to develop a more resistant, recurrent form of uveitis that is more difficult to control.

Anterior uveitis (AU) is quoted as for 7 to 25% in psoriatic ophthalmic patients with spondylarthritis (8) and for 25.1% ± 2.3 in a metaanalysis of rheumatic patients (9), with a prevalence of HLA-B27 quoted as for 40 to 50% (10) and two genes (the Arts1 and IL23R) correlated to the ankylosing spondylitis, were detected by the WTCCC (Wellcome Trust Case-Control Consortium Study). But the HLA-B27 AU, associated for more than half of cases (49 to 90% according to Monnet) (10), is often misdiagnosed (11).

So, the Authors statement “PsA is a common immunomediated chronic inflammatory skin disease... that occurs in 2 to 3% of the worldwide population ... (that induces) risks of depression, cardiovascular disease and arthritis” is correct but seems insufficient, even though they cover the proposed pathogenesis as a “chronic relapsing autoimmune disorder wich presents excessive keratinocyte proliferation, abnormal differentiation, elevated MC number, enhanced type I IFN, angiogenesis and over-expression of several chemokines and cytokines which contribute to the disease pathogenesis”: iridocyclitis (AU) is a correlated pathology that should be reported.

We would like to congratulate Authors not only for their deep analysis showing this new possible balancing role of IL-37 as pro-inflammatory cytokines suppressor in the pathogenesis of psoriasis, but also because the paper should open mind to increase the basic research on uveitis, where this MC model merits new researches that could apply to an olistic view (12) and to stress the attention of Dermatologist, Rheumatologist, Radiologist, General Practitioner to submit those psoriatic patient to an ophthalmological screening for AU.

References