ABNORMAL OVEREXPRESSION OF MASTOCYTES IN SKIN OF FMS PATIENTS

Ignacio Blanco et al. Biohealth Research Office [OIB-FICYT], Oviedo, Asturias, Spain

OBJECTIVES

To test if a skin low grade inflammation can underlay in fibromyalgia Syndrome (FMS)

METHODS

Open skin biopsies from no-tender point of the gluteus region from a matched cohort of 63 FMS females and 49 volunteers. Blind IHC analysis by two external pathologists. Formalin-fixed, paraffin-embedded sections were examined for the broad spectrum inhibitor alpha1-antitrypsin (AAT), the proteinases elastase and tryptase, the cytokines Monocyte Chemoattractant Protein 1(MCP1) and Tumor Necrosis Factor alpha (TNFa), the endothelium biomarker Vascular Endothelial GF (VEGF), and the nociception-related receptor Proteinase Activated Receptor 2 (PAR2)

Table 1. Demographic data

Sample (n)	Age Mean (SD)[Range]	Female-to-male Ratio (%)
Volunteers (49)	51 (7) [39-67]	94%
FMS (63)	53 (9) [34-67]	98%

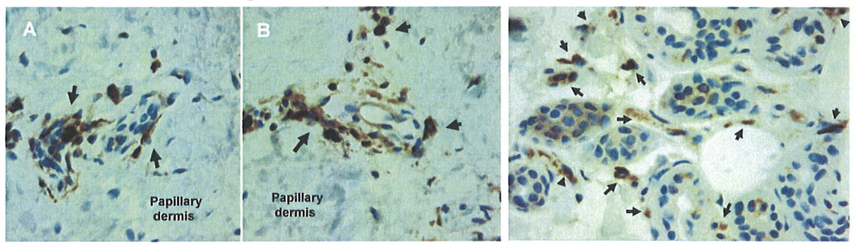
Table 2. Clinical data

Test	Score Mean (SD)	Values range
FIQ	63.9 ±3.4	0-80
HAQ	1.7 ±0.4	0-3
TPs	16.9 ±1.1	0-18

RESULTS

The most relevant finding was a significantly increased number of mast cells (MCs) in the papillary dermis of 100% FMS patients (5-14 per microscopic high power field) vs. 0-3 in controls ($p<0.001$). MCs strongly stained with tryptase, AAT and PAR2 antibodies, and were distributed around blood vessels and appendages. MCs also stained with Tolouidine blue and Bismark brown. Subsequently, a double staining with the cell activation marker CD63 and the C-kit receptor marker CD117 showed activation in about 50% of MCs. No significant differences for the remaining biomarkers neither histological difference between AAT deficiency and normal AAT samples were found.

Fig. 1 Representative TRYPTASE staining in the papillary dermis of FMS patients.

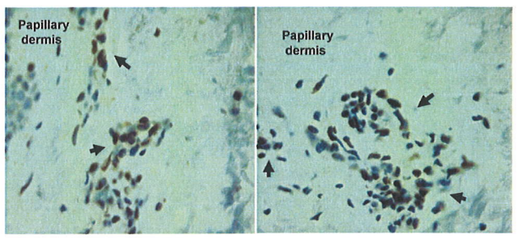


A,B: Mast cells tryptase+ (dark brown) in capillary vessels (x 40)

Mast cells tryptase+ (brown) in appendages (x 40)

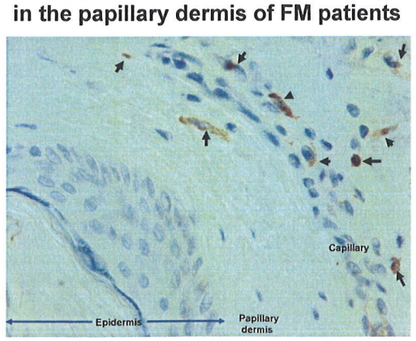
As a whole, tryptase + cell counting gave a FM : CONTROL proportion *of 10 versus 1 cell (10:1)*

Fig. 2 -PAR2 diffusely stained MAST CELLS around small vessels and appendages in 83% of FMS vs. 43% of controls, with strong intensity.
-Focal positivity was occasionally found in epidermis, endothelium, appendages, small muscles and nerves of the dermis.



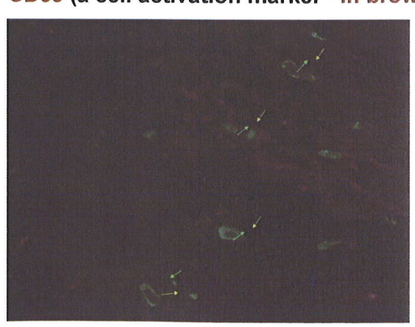
Representative PAR2 staining in the papillary dermis of FM patients.
Mast cells PAR2+ (dark brown) in the capillary of the papillary dermis (x 40)

Fig. 3 Representative AAT staining in the papillary dermis of FM patients



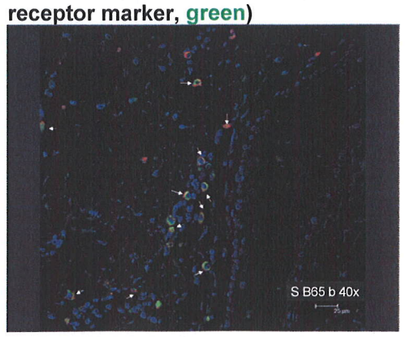
Mast cells AAT+ (brown) around capillary vessels (x 40)

Fig. 4 Double staining with anti-CD117 (a C-kit receptor marker –in green-) & anti-CD63 (a cell activation marker –in brown-)



Antibodies stained different antigens of Mast cells.
Activated cells stained in green and brown

Fig. 5 Confocal microscopy.
Triple staining with DAPI (it binds strongly to DNA –blue-), anti-CD63 (a cell activation marker red) and anti-CD117 (a C-kit receptor marker, green)

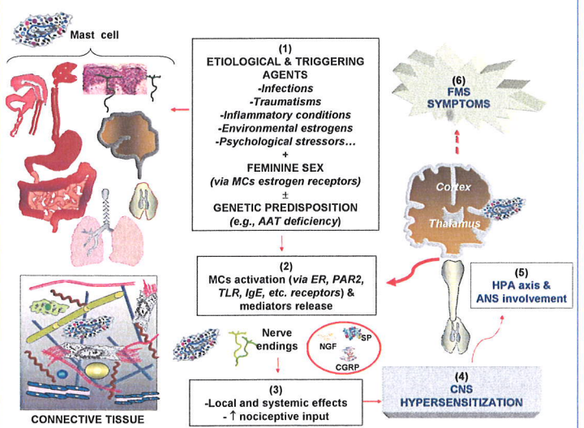


All nuclei from skin cells stained in blue. Activated mastocytes stained in green and red

CONCLUSIONS

Our results indicate that FMS is a MCs associated condition. MCs are present in skin, mucosal surfaces and nervous system (i.e., nerves, meninges, choroid plexus, area postrema of the medulla, pineal body, hypophysis, thalamus, sympathetic glanglia), and are easily stimulated by a number of physical, psychological, and chemical triggers to degranulate, releasing several products which are able to generate peripheral and central stimuli causing Central Nervous System (CNS) hypersensitivity, local and systemic symptoms. Our findings open new lines of research on FMS mechanisms, diagnosis and therapy.

PROPOSED ROLE OF MAST CELLS IN FMS PATHOGENESIS



REFERENCE

Blanco I, Béritze N, Argüelles M et al. Clin Rheumatol. 2010.