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WOUND HEALING INFLAMMATORY MARKERS PREDICT PROGNOSIS AND SURVIVAL IN EARLY BREAST CANCER

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Introduction: Cancer is likened to a non-healing wound. There is limited evidence on the expression of wound healing tissue inflammatory markers, CD68(pan-macrophage marker), HO-1(tumour cell marker) and FAP(cancer-associated fibroblast marker) in human breast cancer.

Method: In 201 invasive breast cancer and 58 DCIS patients, CD68+TAM expression, tumour HO-1 and fibroblast FAP expression, quantified by immunohistochemistry(dichotomised: high/present vs low/absent), was correlated with tumour factors (grade, proliferation(Ki67), ER, HER2); demographic factors, behavioural factors (smoking, alcohol) and survival status(DFS, OS)

Result: High CD68+macrophage expression was increased in invasive breast cancer, compared to DCIS, and normal tissue distant from the tumour(59%,41%and 6% respectively; $p<0.001$).In invasive cancer,CD68+TAM expression increased with increasing tumour grade(Grade 1:42%, Grade 2:58%, Grade 3:72%; $p=0.006$), high Ki67(71%vs.47%; $p=0.004$), ER negativity(79.4%vs.55.4%; $p=0.01$) and HER2(HER2 positive 81.8% vs. HER2 negative 56.3%; $p=0.03$). CD68+TAM expression was higher in high compared to low/intermediate grade DCIS(44% vs. 31% $p=0.52$). CD68+TAM expression was increased in patients who self-reported alcohol intake(non-drinker 43% vs. drinker 62%; $p=0.01$). HO-1 was associated with shorter DFS(HR:3.22, $p=0.027$) and OS(HR:2.86, $p=0.029$).FAP fibroblast expression correlated with longer DFS (HR:0.296, $p=0.029$) and OS (HR:0.271, $p=0.008$).

Conclusion: Tumour inflammation as assessed by CD68+TAM expression shows utility in identifying aggressive breast cancer sub-types. The association reported between CD68+TAM density and alcohol intake suggests a possible mechanism for alcohol as a risk factor for breast cancer. The prognostic value of HO-1 and FAP expression demonstrated here suggests a functional role of these wound healing markers in breast cancer. HO-1:Heme-oxygenase-1; FAP:Fibroblast activation protein; TAM:Tumour associated macrophage; DCIS: Ductal carcinoma in situ

Take-home message: Wound healing pathways of inflammation may be implicated in early breast cancer development