Junctional adhesion molecule-A is abnormally expressed in diffuse cutaneous systemic sclerosis skin and mediates myeloid cell adhesion

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ABSTRACT

While the pathogenesis of systemic sclerosis (SSc) is incompletely understood, vascular changes play a role. Junctional adhesion molecules (JAMs) are novel members of the immunoglobulin superfamily expressed by endothelial and other cells. JAMs facilitate the formation of junctions and serve as cell-adhesion molecules. Here we determined the role of JAM-A in the pathogenesis of SSc.

Methods. Samples from proximal and distal arm skin and venous blood were obtained from patients with SSc and normal NL skin. sJAM-A was measured by ELISA and immunostaining was performed. JAM-A expression was assessed by immunochemistry in NL, SSc proximal arm, and SSc distal arm skin. Immunofluorescence and U937 cell binding assays were performed.

Results. The stratum granulosum and dermal endothelial cells from distal arm SSc skin exhibited significantly decreased expression of JAM-A compared to NL. Distal SSc skin has fewer blood vessels than NL skin. JAM-A mediates U937 cell binding to SSc skin, and JAM-A expression is correlated with increased adhesion of U937 cells to SSc dermal fibroblasts. JAM-A was expressed at a significantly higher portion of U937 binding to SSc dermal fibroblasts. In addition, JAM-A mediates U937 adhesion to SSc skin.

Conclusions. Elevated sJAM-A in SSc serum may reflect disturbed engagement with a compensatory increase in the SSc skin. JAM-A may serve to regulate and remodel skin leading to disordered skin architecture and vascular function of the skin affected by SSc.

INTRODUCTION

Junctional adhesion molecule-A (JAM-A) is a member of the immunoglobulin superfamily and has been implicated in angiogenesis in the skin. JAM-A expression is associated with angiogenesis in various diseases, including cancer, diabetes, and cardiovascular disease. JAM-A is expressed on endothelial cells, pericytes, fibroblasts, and leukocytes. JAM-A has been implicated in the regulation of immune responses, and its expression is regulated by various factors, including cytokines and growth factors. JAM-A expression is associated with angiogenesis in various diseases, including cancer, diabetes, and cardiovascular disease. JAM-A has been implicated in the regulation of immune responses, and its expression is regulated by various factors, including cytokines and growth factors. JAM-A expression is associated with angiogenesis in various diseases, including cancer, diabetes, and cardiovascular disease. JAM-A has been implicated in the regulation of immune responses, and its expression is regulated by various factors, including cytokines and growth factors.

MATERIALS AND METHODS

Within pathogenetic and pathological skin samples were obtained from subjects with SSc in diffuse disease and control subjects.

Cell surface ELISA was used to detect JAM-A expression in cell lines with/without stimulation by TNF-α, IL-1 or IFN-γ.

Cellular adhesion molecules play a role in mediating cell-cell and cell-matrix interactions. JAM-A expression is correlated with angiogenesis in various diseases, including cancer, diabetes, and cardiovascular disease. JAM-A has been implicated in the regulation of immune responses, and its expression is regulated by various factors, including cytokines and growth factors.

RESULTS

sJAM-A in normal and SSc serum

Distal SSc skin has fewer blood vessels than NL skin

JAM-A mediates U937 cell binding to SSc dermal fibroblasts

JAM-A mediates U937 cell binding to SSc skin

CONCLUSIONS

JAM-A expression is increased in SSc dermal endothelial cells compared to normal NL dermal endothelial cells.

Taken together, these results may help to understand disordered angiogenesis in SSc.

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