PDGF ANTIBODIES IN SCLERODERMA

The autoimmune connection in systemic scleroderma
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In an article published in the NEJM, Italian researchers describe specific autoantibodies that contribute to the disease process in systemic scleroderma.

What is Scleroderma?

Systemic sclerosis (scleroderma) is an autoimmune disorder that causes a thickening of skin tissue and visceral organs known as fibrosis, which is perpetuated by a chronic inflammatory process.

The disease process in scleroderma, which is thought to be primarily caused by abnormal oxidative stress, is characterized by accumulations of excessive collagen deposits, excessive production of extracellular matrix, fibroblast cell (basic tissue cell that leads to fibrosis or hardening of tissue) activation, dysfunction of epithelial cells, and an altered immune tolerance. For more than 40 years antinuclear and other antibodies had been detected but not fully identified in patients with systemic sclerosis.

PDGF Autoantibodies

Recently, Italian researchers have identified these antibodies that react with extracellular-matrix and cell surface proteins, proteases, fibroblasts and endothelial cells as stimulatory autoantibodies to the platelet-derived growth factor (PDGF) receptor. These stimulatory PDGF receptor antibodies contribute to the disease process by activating collagen-gene expression and stimulating the production of reactive oxygen species. Therefore, the presence of stimulatory PDGF receptor antibodies can be used to determine if individual cases of scleroderma are limited (duration less than 5 years) or systemic disorders associated with late disease (more than 10 years). In addition, these antibodies appear to be hallmarks of disease, occurring before scleroderma becomes evident.

In the current Italian study, which was supported by a grant from the National Institutes of Health (NIH), five independent experiments demonstrated the presence of stimulatory PDGF receptor antibodies in patients with systemic sclerosis. These antibodies have also been demonstrated to cause myofibroblast (muscle fibroblast) conversion, type I collagen expression and reactive oxidative stress production.

PDGF Receptor Inhibitors
Inhibitors to the PDGF receptors in some of the patients prevented reactive stress indicating that natural inhibitors may modulate disease activity. The data also may imply that fibrosis in scleroderma is triggered by the accumulation of these stimulating antibodies.

**What are Cell Receptors?**

Cell receptors are proteins situated on the surface of nucleus of specific cells. These receptors act as gateways or locks allowing for activation by stimulatory molecules or blockage by inhibitory molecules. Cell receptors are affected or activated by various protein molecules, including hormones, medications and antibodies.

In autoimmune disorders, certain autoantibodies react with cell receptors. For instance, in Graves' disease, stimulating TSH receptor antibodies activate the thyroid cell receptor, causing excess thyroid hormone production, resulting in hyperthyroidism, whereas blocking antibodies prevent TSH from reacting with the TSH receptor, contributing to hypothyroidism.

**Fibroblasts in Scleroderma**

In scleroderma, the accumulated tissue fibroblasts undergo rapid deterioration or senescence marked by DNA and chromosomal changes. The early cell death of these fibroblast cells may explain why certain lesions in scleroderma show cell loss. Before fibrosis occurs in scleroderma, small blood vessel abnormalities and infiltration of tissue by lymphocyte white blood cells are seen, changes suspected of being induced by stimulatory PDGF receptor antibodies.

**Resources:**


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