New promising therapy against systemic sclerosis

June 14 2010

There is a new path to defeat systemic sclerosis, also called scleroderma because of the hardening of the skin of the patients (from Greek skleros, "hard", and derma, "skin"). This path involves the B-cell of the immune system, so far only considered "innocent spectators," as Catholic University rheumatologist Gianfranco Ferraccioli, among the authors of the important research, puts it.

Also Silvia Bosello, Maria De Santis, Gina Lama, Cristina Spanň, Cristiana Angelucci, Barbara Tolusso e Gigliola Sica, director of the Institute of Histology and Embryology, all working for the Catholic University of Rome, have all actively taken part in this research, published on the last issue of *Arthritis Therapy & Research*.

"What makes our work truly original," says Ferraccioli, "is that it clarifies the characteristics of a disease, very complex as all autoimmune diseases, whose patients have often no possibility other than having to undergo a long immunosuppressive cytotoxic therapy or a medullary transplant. Furthermore, this pathology often involves more organs and is doomed to high chance of failure with conventional therapies".

Scleroderma is characterized by a fibrosis - a thickening of tissues - due to the accumulation of matrix proteins that are not re-absorbed. By progressively hardening tissues and making them less elastic, these proteins alter the function of the organs. If, for example, the lung is involved, oxygen exchanges in the alveoli become more difficult. If the heart is involved, it gets harder and pumps blood inefficiently. If the

intestinal tract is involved, it is more difficult to void it. A very common effect is the thickening and hardening of the skin, which takes on a leather-like aspect.

"There are two different forms of this disease," explains Ferraccioli. "The first, and more frequent one, involves 80% of patients. This form is called limited, and has a slower and less aggressive progression. The second type, called diffuse, affects a fifth of the patients. This form is far more aggressive and involves younger patients, who normally are treated with high doses of cortisone and antitumoral drugs. Yet these drugs have very important side effects, like infertility or vesicle or pulmonary complications. Unluckily, as also proven by the last clinical trials, they also have a very limited effect".

In the study, involving only nine patients - although more are currently undergoing the same cure -, Ferraccioli's group has pinpointed the therapeutic objective that could change the fate of many of the patients affected by the most serious form of the disease.

There are three leading actors in the genesis of the diseases. First, the fibroblasts, cells producing connective tissue of all apparatuses, which are the responsible of the production of the tissue- and skin-hardening proteins. Secondly, the endothelial cells, the ones coating the interior part of the vessels and that provoke very dangerous occlusions. Finally, the immune system cells, which are exactly the ones causing an excessive response, that provoke the autoimmune disease.

"With the important contribution of the Institute of Histology," reminds Ferraccioli, "we have worked just upon those cells producing the antibodies against the constituents of the organism. We have eliminated the B-cell population, with a biological drug affecting the cells responsible of the autoantibodies, using only 50% of the doses of the drugs normally causing so many side effects. Thus we have obtained

better therapeutic results." Basically, the biological drug, together with a very low dose of immunosuppressant, has strikingly improved the effects of traditional drugs.

The Catholic University researchers, despite the low number of patients studied, have also identified the so-called window of therapeutic opportunity: if the drugs are employed within 2-3 years from the onset of the disease, results are significantly better.

"As suggested in the accompanying editorial which praised our results," concludes Ferraccioli, "we are working on more patients to confirm our first promising results. Yet there is something that we find really important. Whilst we previously felt that it was only the presence of the target cell in the organs what determined our chances of therapeutic success, we have shown that the effect of the therapy is systemic. In other words, we can improve the course of the disease modulating the immune system in the entire organism, without being forced to act upon the single organ."

Provided by Catholic University of Rome