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YKL-40 (HCgp-39) in giant cell arteritis

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Keywords

Giant cell arteritis, giant cells, HCgp-39, polymyalgia rheumatica, vasculitis, YKL-40

Context

YKL-40, also known as human cartilage glycoprotein-39 (HCgp-39), is a mammalian member of the family 18 glycosyl hydrolases. Its function is unknown but it is a heparin- and chitin-binding lectin which is secreted in large quantities by articular cartilage and synoviocytes in patients with rheumatoid arthritis (RA). It is recognized by T cells in over 50% of patients with RA, although the pathological significance of this is unclear. YKL-40 is also secreted by differentiating vascular smooth muscle, some cancer cells, neutrophils and human macrophages at a late stage of differentiation. The pattern of secretion of YKL-40 in humans, and of its homologues in other mammals, has led to the proposal that it is involved in tissue remodelling. GCA and polymyalgia rheumatica (PMR) are related (overlapping) vasculitic diseases, characterised by an inflammatory infiltrate of T cells, macrophages and multinucleated giant cells. However, the expression of YKL-40 in inflammatory lesions in these patients has not previously been explored. To assess whether YKL-40 levels are elevated in patients with GCA or PMR and whether YKL-40 can be detected in macrophages and giant cells in the inflammatory lesions.

Significant findings

The 27 patients in the study yielded 14 temporal artery biopsies with characteristic changes of arteritis, and 13 biopsies with no signs of inflammation. In the inflamed arteries, YKL-40 was evident in a subset of $CD68^{+}$ giant cells and macrophages which were located around the internal elastic lamina. The YKL-40 staining in giant cells was cytoplasmic and granular.

The median serum YKL-40 concentration in GCA patients was significantly higher (256 ?g/l) than the median for age matched controls (118 ?g/l). This had fallen to within the normal range in 15 of the 19 patients with GCA after treatment with prednisolone for 1 month. The serum YKL-40 concentration was not significantly elevated in the PMR group overall, although three individuals had elevated levels.

Comments

YKL-40 (and its homologues in other mammals) is secreted by a range of cells in tissues during inflammation or involution. Although this study does not demystify the function of this protein, it does demonstrate the very restricted cellular distribution of YKL-40 in phagocytic cells around the internal elastic lamina, precisely at the site of tissue destruction. The study also shows that YKL-40 is not merely a local factor, since it is elevated in serum from giant cell arteritis (GCA) patients. It is rather surprising, therefore, that the authors could not detect the secreted protein in the extracellular matrix of the arteritic lesion. YKL-40 has now been documented in several inflammatory disorders and, at least in some patients, is an autoantigenic target for T cells. It will be interesting to see whether this protein proves to play a role in the immunopathogenesis of these diseases, and/or whether it can be harnessed as an immunomodulatory target to ameliorate them.

Methods

Nineteen patients with GCA and eight patients with PMR were studied. In all cases, a temporal artery biopsy was obtained prior to starting corticosteroid therapy and was assessed histologically. Adjacent tissue sections were used for immunohistochemical analysis with polyclonal rabbit anti-YKL-40 immunoglobulin (Ig) G or monoclonal anti-CD68 and second layer alkaline phosphatase conjugated anti-rabbit antibody (Ab). Double-labelling immunofluorescence was also performed on sections for YKL-40 (FITC-conjugated second layer Ab) and CD68 (Texas red-conjugated second layer Ab). Serum C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) were determined by conventional methods and the serum levels of YKL-40 were determined by radioimmunoassay. The patients were followed for 1 year, with serial measurments of ESR, serum CRP and YKL-40.

References

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