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Anti-collagen type II antibodies in patients with very early synovitis

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Anti-type II collagen (anti-CII) antibodies have been reported in between 3% and 27% of patients with rheumatoid arthritis (RA).^{1–3} In contrast with anti-cyclic citrullinated peptide (anti-CCP) antibodies,^{4–5} anti-CII antibodies are absent before the onset of synovitis⁶ and decrease over the first few years of disease.^{2–3} Anti-CII antibody levels thus appear to peak around the time of diagnosis of RA when they are associated with active inflammation.³ The pathological processes operating in the joints of patients with very early synovitis who develop RA are distinct from those in other patients with early synovitis and are characterised by a cytokine profile that includes interleukins 2, 4 and 13.⁷ Consequently we sought to assess whether anti-CII antibodies were more prevalent in patients with very early synovitis who subsequently developed RA than in patients with other outcomes.

Patients with synovitis of < 3 months duration were recruited, and data collected from them, as previously described.^{7–8} Ethical permission was obtained and all patients gave written informed consent. Patients were followed for 18 months and assigned to their final diagnostic groups. Patients were classified as having RA according to established criteria.⁹

Antibodies against native human CII were measured in duplicate wells with enzyme-linked immunosorbent assay, as described previously, in serum samples that had been obtained at initial presentation and had been stored at –80°C.³ A level of < 29 U/ml (95th percentile among 100 healthy controls) was considered positive.³

A total of 177 patients were recruited (details shown in table 1); 64 patients developed RA and 113 did not (70 unclassified; 11 reactive arthritis; 10 psoriatic arthritis; 10 crystal arthritis; 12 other). Two patients without RA were anti-CCP antibody positive (both were classified as psoriatic arthritis, one was rheumatoid factor positive and neither had elevated anti-CII antibody levels).

Twelve of 177 patients were anti-CII antibody positive (fig 1). Three of these developed RA (two were rheumatoid factor positive and none were anti-CCP antibody positive), three developed a persistent unclassified synovitis and in six the synovitis resolved (three reactive arthritis; two gout; one unclassified). Of the nine non-RA patients, two were rheumatoid factor positive and none were anti-CCP antibody positive. The prevalence of anti-CII

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antibody positivity was not different between the patients with and without RA ($p = 0.40$; χ^2). There was no relationship between the ESR, CRP or swollen joint count and the anti-CII antibody level (Spearman test; data not shown).

The prevalence of anti-CII antibodies in patients who developed RA (5%) is towards the lower end of the range previously reported for patients with established RA. None of our patients had the very high levels of anti-CII antibody reported previously in a small subgroup (about 3%) of patients with early RA.³ These data suggest that the prevalence of anti-CII antibodies is no higher in patients with very early synovitis who develop RA than in those with other very early synovitides. The measurement of this antibody is unlikely to be useful in the prediction of outcome in patients with very early synovitis of less than 3 months duration.

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Figure 1. Anti-collagen II antibody levels in patients with very early synovitis divided according to final outcome (rheumatoid arthritis and non-rheumatoid arthritis).

Table 1

Characteristics of patients with very early synovitis divided according to final clinical outcome

	Very early RA	Other very early synovitis	p Value
Number	64	113	
Female; number (%)	38 (59%)	51 (45%)	0.07 [†]
Age, years; median (IQR)	61 (46–71)	43 (31–57)	<0.0001 [*]
Swollen joint count; median (IQR) (n = 177)	4 (2–7)	2 (1–3)	<0.0001 [*]
Tender joint count; median (IQR) (n = 177)	6 (3–13)	2 (1–5)	<0.0001 [*]
CRP; median (IQR) (n = 173)	21 (9–42)	23 (6–61)	0.73 [*]
ESR; median (IQR) (n = 159)	28 (14–50)	23 (9–60)	0.47 [*]
Rheumatoid factor positive; number (%) (n = 177)	36 (56%)	13 (12%)	<0.0001 [†]
Anti-CCP antibody positive; number (%) (n = 175)	31 (48%)	2 (of 111) (1%)	<0.0001 [†]
Anti-CII antibody positive; number (%) (n = 177)	3 (5%)	9 (8%)	0.40 [†]

CCP, cyclic citrullinated peptide; CII, collagen II; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; IQR, interquartile range; RA, rheumatoid arthritis.

^{*} Mann–Whitney test.

[†] χ^2 test.