comparisons, P = 0.03 in the unadjusted model and P = 0.05 in the adjusted model. Among the five subjects who achieved ACR20 in Tai Chi group, all had improvement in joint tenderness (20–81%), joint swelling (25–80%) and physician’s global assessment of disease activity (44–80%). Four subjects had improvement in pain measurements (20–84%), HAQ score (71–100%) and CRP (36–89%). Two Tai Chi subjects had 20% improvement in almost all the variables in the ACR20 criteria even without considering the two variables (HAQ and CRP) that were not balanced between the study groups at baseline, and thus could have biased the statistical analysis.

Overall, the Tai Chi group improved in all 25 secondary outcomes, while the control group improved in only some and never by as great an amount. The Tai Chi group improved significantly more than the control group only on the HAQ disability index (P = 0.01), the vitality subscale of SF-36 (P = 0.01) and the CES-D (P = 0.003). Physical function variables (chair stand and 50-foot walk) improved in both groups (within-group comparisons, P < 0.05), but between-group comparisons were not statistically significant. No adverse events were observed.

No patients withdrew from the study.

This preliminary study suggests that group Tai Chi is a safe and potentially promising complementary therapy for adults with functional class I or II RA. Furthermore, the results demonstrate that Tai Chi seems to be associated with trends to improvement in disease activity that relates to both symptoms of pain and the cognitive coping process, which in turn is related to physical and psychological disability. Our results are consistent with two non-randomized studies of Tai Chi for RA that reported that there was no significant exacerbation of joint symptoms for 10 weeks of Tai Chi [9]. It is also consistent with other Tai Chi studies in which Tai Chi had beneficial effects on tension, anxiety and depression [3].

The study was limited in that the sample size was small and the Tai Chi group appeared to have had more severe RA, as measured by higher HAQ, CRP and tender joint count at baseline and therefore may have had a greater chance for improvement in the outcome measures. The Tai Chi group also weighed less than the controls (Table 1), so we cannot exclude the possibility that Tai Chi may help joint symptoms in non-obese more than in obese individuals. In spite of these limitations, the rigour of the study design and our results warrant further investigation into the potential complementary role of Tai Chi for treatment of RA.

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lymphoid tissue (MALT) B-cell lymphoma with focal areas of activation and Epstein–Barr virus (EBV) latent membrane protein-1 (LMP-1) expression. The patient’s RA flared 3 months later and after counselling MTX 7.5 mg/week with folic acid 5 mg/week were recommenced with regular surveillance (monthly clinical review of weight and constitutional symptoms for the first year, then 3 monthly; monthly CRP and ESR; annual chest X-rays; yearly chest CT, for the first 5 yr). The patient remains well without evidence of recurrence at 8 yr follow-up.

This report contributes three novel findings: (1) pulmonary MALT lymphoma can exist in RA without SS; (2) it may be associated with very high serum IL-6, which could be useful for surveillance; (3) control of inflammatory activity may be more important than avoidance of MTX therapy in such cases.

Primary pulmonary lymphoma represents 3–4% of extra-nodal lymphomas and only 0.5% of primary lung malignancies [1]. It is usually of the MALT type, which is normally found in intestinal Peyer’s patches. Chronic inflammation associates with development of MALT in ectopic areas: this is thought to be important in the development of MALT lymphomas in salivary glands in SS [2], thyroid in Hashimoto’s thyroiditis [3], and the stomach in chronic Helicobacter pylori infection [4]. MALT lymphomas are of B-cell type, and are usually indolent, though they may cause local effects or constitutional upset. Surgery, radiotherapy and chemotherapy have all been used but there is no consensus regarding optimal therapy.

MALT lymphomas have only been described in RA patients with SS [5], which was excluded in this case. Lymphomas are commoner in RA than the general population [6], and associations have been found between MTX therapy and lymphoma development [7]. A recent survey of lymphomas in patients with RA, however, did not find this association and suggested that disease activity was the risk factor [8]. EBV has also been implicated in the pathogenesis of several lymphomas, including those in RA [9] and the expression of LMP-1, the protein identified in this patient’s tumour, may be important in B-cell transformation [10]. Cases thought to be related to EBV have regressed on withdrawal of MTX [9, 11]. It remains unclear whether such mechanisms or chronic uncontrolled inflammation are more important for the development of lymphomas in RA. The risk of MTX therapy may be counterbalanced by beneficial suppression of the inflammatory response. This patient had not been exposed to MTX prior to the identification of the tumour. Post-operative deterioration of her RA required the use of disease-modifying drugs and, in view of previous therapeutic failures, options were limited. Treatment with MTX after counselling has proved successful and continuous long-term surveillance has not revealed tumour recurrence.

The authors have declared no conflicts of interest.

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FIG. 1. CT scan showing soft tissue masses in the left lower lobe.

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**Dramatic improvement with anakinra in a case of chronic infantile neurological cutaneous and articular (CINCA) syndrome**

**Sir,** Chronic infantile neurological, cutaneous and articular (CINCA) syndrome, also known as neonatal-onset multisystem inflammatory disease (NOMID), is a rare genetic systemic autoinflammatory disease characterized by mutation in the CIAS1 (cold autoinflammatory syndrome-1) gene [1, 2]. Renal AA-amyloidosis, severe arthropathy and neurological complications are long-term disabilities with this disease. CINCA syndrome is poorly treatable and steroids do not completely eliminate the disease and can cause harmful side-effects. We report a case of CINCA syndrome which was dramatically improved with anakinra, an interleukin-1-receptor antagonist (IL1-RA).

In 2002, a 36-yr-old man consulted for a diagnosis of Muckle-Wells syndrome (MWS). He had suffered from birth from a generalized urticarial skin lesion with episodes of fever and conjunctivitis. He complained of arthritis which was particularly severe during childhood and involved knees, ankles and wrists, and required long-standing steroid treatment. He developed progressive sensorineural deafness and required bilateral prosthesis at the age of 15. He also suffered from mild mental retardation and left school early. Headaches related to chronic meningitis with papilloedema were diagnosed during childhood. Numerous blood tests throughout his life had revealed persistent massive neutrophilia, anaemia and intense acute phase response. No proteinuria was found. Faced with urticarial skin lesion, fever and deafness, an initial diagnosis of MWS was made during childhood. However, when we met the patient we noticed a dysmorphic facial appearance characterized by frontal bossing of the skull, saddle nose, micrognathia and clubbing of the fingers. After genetic advice, a diagnosis of CINCA syndrome was made which could explain the dysmorphic appearance, the mental retardation and the chronic meningoencephalopathy—a classical features of this syndrome [3]. Sequencing of CIAS1 revealed that the patient was heterozygous for the D303N mutation in exon 3. At the time of this result in 2002, CIAS1 gene analyses in CINCA syndrome had not yet been published but were published soon afterwards [1, 2]. The patient was used to be treated with steroids when crises were severe, but only a high dose (1 mg/kg) could decrease the level of inflammation. At the time we met the patient, the steroid dose was 10 mg/day. Colchicine was added with celecoxib (200 mg/day). However, the patient still had arthritis of wrists, knees and ankles, urticarial rash and fatigue. Biological evaluation in May 2004, immediately before the institution of anakinra treatment, revealed a severe inflammatory process (Table 1). The patient was informed of the therapeutic trial and subcutaneous anakinra (100 mg/day) was started in May 2004. At the same time, celecoxib was discontinued. Within 1 week of commencement of treatment he noted a dramatic clinical change: fatigue, rash, conjunctivitis and arthralgia had disappeared. Steroids were progressively tapered and discontinued in June 2004. Follow-up at 6 months showed a persistent good response to anakinra; the patient felt very well and only had one mild flare with fever and arthralgia which regressed with analgesic treatment and did not require steroids. He no longer complained of asthenia and headaches, and urticarial rash did not occur. He was able to play badminton once a week without any articular complaint. His friends and mother clearly noticed the improvement in health. Biological evaluation showed a regression of the inflammatory process (Table 1). Anakinra treatment was tolerated very well and the initial dose was maintained.

The two other autoinflammatory syndromes related to CIAS1 mutations are MWS and familial cold autoinflammatory syndrome (FCAS) [4, 5]. All three syndromes have some common features such as fever, urticarial rash, biological inflammatory process and risk of renal amyloidosis but also have different characteristics: cold triggering for FCAS and articular, neurological and dysmorphic symptoms in CINCA syndrome. CIAS1 encodes a member of the pyrin superfamily of death domain fold proteins called ‘cryopyrin’ that is involved in inflammation and apoptosis. It is expressed in polymorphonuclear cells, monocytes, chondrocytes and activated T cells [1, 6]. Cryopyrin has been shown to be an activator of caspase 1 that cleaves pro-IL-1β into biologically active IL-1β and has been shown to activate NF-kB [7]. Thus, a hypothesis explaining the inflammatory events in CINCA syndrome involves a hyperactive state with release of IL-1β and influx of polymorphonuclear cells to the site of inflammation. Moreover, high secretion of IL-1β by peripheral blood cells, spontaneously and after stimulation, has been evidenced in CINCA syndrome [8]. Thus treatment with anakinra is particularly interesting in CINCA syndrome as it targets the main cytokine involved in the inflammatory process. Dramatic response to anakinra in CINCA syndrome has already been observed, similar to our observation, by Hawkins et al. [9], and was initially reported in three cases of MWS [10].

**Table 1. Biological evolution before and after anakinra treatment**

<table>
<thead>
<tr>
<th>Data</th>
<th>January 2004</th>
<th>May 2004</th>
<th>August 2004</th>
<th>September 2004</th>
<th>December 2004</th>
</tr>
</thead>
<tbody>
<tr>
<td>White blood cell count (10⁹/μl)</td>
<td>13.7</td>
<td>21.5</td>
<td>10.4</td>
<td>13</td>
<td>8.8</td>
</tr>
<tr>
<td>Haemoglobin level (g/dl)</td>
<td>12.4</td>
<td>12.3</td>
<td>15.7</td>
<td>15.8</td>
<td>15.4</td>
</tr>
<tr>
<td>Platelet count (10⁹/l)</td>
<td>429</td>
<td>425</td>
<td>246</td>
<td>267</td>
<td>308</td>
</tr>
<tr>
<td>C-reactive protein (mg/l, n &lt; 5)</td>
<td>No</td>
<td>Yes (start in May)</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Anakinra 100 mg/day</td>
<td>10</td>
<td>Progressive tapering and discontinued in June 2004</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Steroid (mg/day)</td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Celecoxib (mg/day)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>Colchicine (mg/day)</td>
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</tr>
</tbody>
</table>

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