date the mainstay of treatment is steroids with good long-term response rates observed. However, recurrences have occurred on cessation of steroids and side-effects are well documented. The response to steroids, combined with similarities microscopically with granulomatous thyroiditis and orchitis [4], have led to an autoimmune process being implicated. We describe our experience with three cases, and the use of immunosuppressive therapy.

The three women ranged in age from 31 to 39 yr (mean 35.3), all were parous (1–3 children) and had breastfed (cessation varying from 42 to 90 months from presentation). Two presented with single painful breast lumps and one with multiple lumps in both breasts, confirmed on ultrasound and mammography. There was no evidence on examination or investigation of generalized granulomatous or vasculitic disease. All underwent an ultrasound guided core biopsy, and in two cases this was repeated for clarification of the diagnosis. The histology was compatible with granulomatous mastitis in all three cases, showing non-caseating granulomatous inflammatory changes centred on the lobules. All cases were negative for microbiological cultures, stains for tuberculosis and serological investigations for other granulomatous and vasculitic diseases. All three patients responded well to 60 mg daily of oral prednisolone, but relapsed on dose reduction. Case A was started on methotrexate, and after 7 months of treatment with 15 mg weekly was able to stop steroids without relapse. Twelve months later she is still controlled on 12.5 mg, but has not been able to reduce this dose. Case B was treated with 8 months of methotrexate at 10 mg weekly, during which time she stopped steroids successfully. She has been off all treatment for 6 months and has had no relapse of granulomatous disease, but suffers with chronic breast pain that was never eased by treatment. During treatment she underwent surgery for a benign pituitary tumour. She is now treated with thyroxine. Case C felt short of breath on methotrexate at 7.5 mg and was changed to azathiprine, although clinically she had no evidence of methotrexate-induced pneumonitis. She has had long-term steroids and her management has been complicated by the development of cushingoid features and mood disturbances attributed to the steroids, and hyperprolactinaemia secondary to paroxetine. Having started immunosuppressive therapy 4 months ago she has clinically improved, and decreased her steroids from 15 mg to 7.5 mg daily.

In conclusion, granulomatous mastitis is a troublesome condition that presents management problems due to side-effects of steroids. Rheumatologists may well be asked to help in the management of these patients. Our experience with the use of methotrexate and azathioprine as steroid-sparing agents in these cases indicates that remission may well be attainable without long-term steroid use. These findings are consistent with a recent series of five patients treated in Australia [5] with methotrexate. Immunosuppressive therapy can be effective in reducing steroid use, controlling the inflammatory process and thus preventing further complications.

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Bilateral anterior uveitis as an unusual manifestation of Kikuchi–Fujimoto disease

Sir, Kikuchi–Fujimoto disease (KFD) is a subacute necrotizing lymphadenitis of unknown origin and is usually a self-limited cause of fever and lymph node enlargement [1]. KFD may be associated with a wide spectrum of immune diseases, such as polymyositis [2], systemic lupus erythematosus [3], arthritis [4] and uveitis [5]. However, as far as we are aware the simultaneous development of KFD and uveitis has not been reported. Here, we present the first case of KFD involving the development of bilateral anterior uveitis during the disease course, and compare fluorescence-activated cell sorting (FACS) assay results of inflammatory cells in aqueous humor with those of lymph node tissue immunohistochemical staining.

A 16-yr-old Asian boy was referred to the Department of Internal Medicine with a spiking fever of unknown origin of up to 40 °C of 3 weeks’ duration. Physical examination revealed multiple, non-tender right cervical lymph node enlargements of diameter 0.5–1 cm. Laboratory testing showed mild leucopenia (2140/mm³) with elevated C-reactive protein (6.11 mg/dl) and an erythrocyte sedimentation rate of 41 mm/h. Immunological tests were negative for syphilis, toxoplasmosis, cytomegalovirus, parvovirus B19 and human immunodeficiency virus. IgG antibodies for Epstein–Barr virus (EBV) were positive but IgM antibodies were negative, suggesting a previous EBV infection. Blood culture was negative and no specific finding was observed by bone marrow biopsy. Chest computed tomography showed no evidence of pulmonary tuberculosis or sarcoidosis. Acid-fast staining for tuberculosis was negative and angiotensin-converting enzyme was within the normal range. Antinuclear and anti-double stranded DNA antibodies were negative and the clinical features of systemic lupus erythematosus were absent. Anti-neutrophil cytoplasmic antibodies (ANCA), rheumatoid factor and human leucocyte antigen (HLA) B-27 were negative. Neck computed tomography revealed multiple lymph node enlargements with necrosis in the right side of the neck. Lymph node biopsy showed findings compatible with KFD, including necrotic change and pronounced karyorrhexis, and histiocyte and lymphocyte infiltration without neutrophils. Immunohistochemical staining revealed that most lymphocytes stained as CD3+ T cells and that there were increased numbers of CD8+ cytotoxic-suppressor T cells. CD56+ natural killer cells were rare, and histiocytes were positive for CD68 and myeloperoxidase.

Two days after the diagnosis, he consulted an ophthalmologist complaining of conjunctival injection and visual blurring in both eyes, which had developed during the previous night. He and his family members did not have any history of uveitis. An ocular examination showed bilateral anterior uveitis and aqueous cells were graded as 4+; however, keratic precipitate or hypopyon was not noted. Evidence of posterior segment involvement, such as retinal vascular sheathing or vitreous cell, was absent. Fluorescein retinal angiography showed normal findings. Aqueous humor was sampled from both eyes at the ophthalmic presentation, and was negative for EBV by the polymerase chain reaction. A FACS
assay of inflammatory cells in the aqueous humor showed that lymphoid cells were mainly T cells, with predominance of CD8+ cells over CD4+ helper T cells. The proportion of CD56+ natural killer T cells was increased, which were mainly CD8+ cytotoxic cells. The proportion of CD56+ T cells was increased, and they were mainly CD8+ cells (Fig. 1). His best corrected visual acuity was 20/25 in both eyes. After 3 weeks of topical steroid therapy, the intraocular inflammation resolved completely and visual acuity improved to 20/20 in both eyes. The fever subsided spontaneously 2 weeks after the ophthalmic consultation and the lymph node enlargement subsequently resolved. During the follow-up period of 6 months, the uveitis did not recur.

Kikuchi–Fujimoto disease, first described by Kikuchi and Fujimoto in 1972, is a benign, self-limited disease of unknown origin that often manifests as enlarged cervical lymph nodes and fever [1]. Laboratory abnormalities are usually non-specific and leucopenia is frequently observed. The histological features are characteristic but are occasionally confused with SLE or lymphoma. An immunohistochemical study revealed an increase in cytotoxic-suppressor T cells and myeloperoxidase [6,7]. The cause of this disease is unknown, though autoimmune or various infectious origins, including EBV and human herpes virus type 6, have been suggested [7,8].

The patient we describe here had clinical and pathological features compatible with KFD and simultaneously developed bilateral anterior uveitis. As far as we know, only one case of KFD developing uveitis has been reported. However, in that case bilateral panuveitis developed some 2 yr later. Furthermore, no cell analysis was presented. In our case, bilateral anterior uveitis developed during the course of KFD and subsided with the disappearance of fever and lymphadenopathy. In addition, a FACS assay of aqueous humor showed findings similar to those obtained by the immunohistochemical staining of lymph node tissue, although the proportion of CD56+ natural killer T cells was increased in the aqueous humor. This may be evidence for a shared pathogenesis between KFD and concomitant anterior uveitis.

In conclusion, we present a case that developed bilateral anterior uveitis as a rare manifestation of KFD. A full ophthalmological examination is needed in patients with KFD to reveal the presence of uveitis.

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