Kikuchi-Fujimoto Disease with Bilateral Uveitis

Hope R. Garner[1], Hilary E. Fazzone[1], Daniel E. Meltzer[1*]

1. Department of Radiology, St. Luke's-Roosevelt Hospital Center, New York, NY, USA

* **Correspondence:** Daniel E. Meltzer, St. Luke's-Roosevelt Hospital Center, 1000 Tenth Avenue Suite 4B-14, New York, NY 10019, USA (dmeltzer@chpnet.org)

Radiology Case. 2009 Jul; 3(7):1-6 :: DOI: 10.3941/jrcr.v3i7.188

ABSTRACT

Kikuchi-Fujimoto disease (KFD), also called histiocytic necrotizing lymphadenitis, is rare condition that usually presents with lymphadenitis and fever. KFD has been associated with many infectious disease processes, predominantly viral. Association with systemic inflammatory processes has been described. Here we present a case of KFD with the rare ocular manifestation of bilateral anterior uveitis, and corresponding findings on magnetic resonance imaging (MRI).

CASE REPORT

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A 23 year old Hispanic male with no medical history presented to the emergency department with a primary complaint of sudden onset of painless blurry vision in both eyes. He had no past ophthalmic history and no family history of ophthalmic disease. He had been experiencing fever up to 40 degrees Celcius, weakness and weight loss of about 7 kilograms for approximately 3 weeks. The patient had documentation of a routine eye exam a few months prior that was normal with 20/20 vision in both eyes.

Physical examination revealed multiple, non-tender bilateral cervical and preauricular lymph nodes which were mildly enlarged. Ophthalmologic examination demonstrated visual acuity reduced bilaterally to counting fingers, and shallow anterior chambers with the iris bowing forward in both eyes. There was conjunctival injection with mild bilateral anterior uveitis. Evidence of posterior segment involvement was absent. B-scan showed no retinal detachment and no vitreous opacity or mass. Ophthalmoscopy demonstrated bilateral choroidal macular folds (figure 1). Fluorescein angiography showed areas of patchy delayed choroidal filling in the laminar phase (figure 2), which persisted in the late phase (figure 3), but with normal peripheral retina with slightly tortuous vasculature.

Laboratory testing showed mild leukopenia (2500cells/mm3) and an elevated lactate dehydrogenase level of 2000 IU/L. Immunological tests were negative for syphilis, toxoplasmosis, cytomegalovirus, Epstein Barr Virus and human immunodeficiency virus and just mildly elevated for parvovirus B19. Blood cultures were negative. Bone marrow biopsy was negative for any neoplasm or infection. Plain films and computed tomography of the chest showed no evidence of pulmonary tuberculosis or sarcoidosis. Angiotensin-converting enzyme was within the normal range and antinuclear, anti-double stranded DNA and anti-neutrophil cytoplasmic antibodies were negative. Rheumatoid factor and HLA B-27 were also negative. The patient went on to magnetic resonance (MR) imaging.

MR imaging of the orbits demonstrates symmetric abnormal thickening, irregular contour and enhancement of the choroid (figures 4, 5 and 8). The choroid is also mildly hyperintense on the noncontrast coronal T1 sequence (figure 6). These findings are consistent with choroidal inflammation and interstitial choroidal effusion. There is peripheral

T2/FLAIR hyperintense signal within the globes external to the choroid, consistent with suprachoroidal fluid collections (figures 4, 5, 6 and 7). There is also peripheral irregular enhancement surrounding the optic nerve sheath complexes in the retrobulbar spaces, consistent with inflammation involving the retrobulbar fat adjacent to the optic nerve sheath and possibly the dura, extending to the intracanalicular portions bilaterally (figure 8). Cervical lymph node biopsy was performed after the MRI, and showed necrotizing change with histiocytic and lymphocyte infiltration, without neutrophils: consistent with KFD (figure 9).

Treatment was started immediately with topical steroids to resolve the intra-ocular inflammation, and cycloplegic therapy. The patient was also treated with supportive measures for his symptoms and given an oral prednisone taper. The patient's ocular manifestations gradually dissipated and within 2 weeks. The fevers subsided spontaneously within 4 days and the lymph node enlargement subsequently resolved. During the follow-up period of six months the uveitis did not recur and the visual symptoms completely resolved.

DISCUSSION

Kikuchi-Fujimoto disease (KFD), also called histiocytic necrotizing lymphadenitis, is an extremely rare, idiopathic, usually self-limited cause of lymphadenitis and fever. There is worldwide distribution, but a preponderance of cases in Asia (1,2). KFD has been reported in association with many infectious disease processes including cytomegalovirus, Epstein-Barr virus, human herpes virus, varicella-zoster virus, and parvovirus B19 (1,2,3) Women are affected more than men (although the female preponderance appears now to be less than originally thought) and, to date, most cases that have been reported are from East Asia (1,2). KFD has been associated with systemic lupus erythematosus, and indeed, its histopathologic findings may be indistinguishable from SLE, in which case correlation with serology is essential for correct diagnosis (3). Kim et al reported a case of KFD in which the patient developed bilateral anterior uveitis during the course of the illness (4). We present here a rare case of a patient presenting with uveitis as a manifestation of KFD, and the associated radiologic findings.

The ocular MR imaging findings in this case are compatible with an acute inflammatory process, and are consistent with the clinical impression of uveitis. The extension of the abnormal findings anteriorly to the level of the cilliary bodies favors inflammation of the choroid and associated fluid in the suprachoroidal space, rather than in the subretinal space, as the retina does not extend to the ciliary bodies (5). The crescentic/ringlike shape of the areas of choroidal signal abnormality and enhancement favor interstitial choroidal effusion over choroidal hematoma, which would have a lenticular morphology (5,6). In 1988, Mafee et al originally described the signal abnormality associated with the interstitial choroidal effusion as hyperintense on all sequences, including T1 and T2, in contradistinction to choroidal hematoma which would be of variable T2 intensity, depending on the age of the hemorrhage. In this case, there is mild intrinsic T1 signal hyperintensity of the choroid on the noncontrast images, and T2 signal of sufficient hyperintensity to be visually indistinct from the vitreous, in keeping with Mafee's original description (5). There is also high T2/FLAIR signal of the suprachoroidal fluid collections, with slight T1 hyperintensity compared to vitreous. This finding may be a manifestation of varying protein content between the interstitial effusion of the choroid and the fluid accumulating in the suprachoroidal space.

The contour irregularity of the choroid and the suprachoroidal fluid correspond to the ophthalmoscopic finding of macular folds. Ocular hypotony has been described as the mechanism for the development of interstitial choroidal effusion and resulting fluid accumulation in the suprachoroidal space, in the setting of inflammatory processes such as uveitis (6). The perineural signal change in the retrobulbar fat is a nonspecific finding which may be seen in a variety of inflammatory processes.

This patient's ophthalmic findings of macular folds, as a manifestation of choroidal effusion/suprachoroidal collection, are unusual, as is the dramatic demonstration of these findings on MRI. We speculate that the histiocytic and lyphocytic infiltration of the lymph nodes, consistent with KFD, also occurred in the choroid and ciliary body directly causing movement of the lens-iris diaphragm forward thereby shallowing the anterior chamber and causing a large refractive error, resulting in vision loss. In the case of KFD and associated anterior uveitis reported by Kim et al (4) a cell analysis was presented. 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. The authors speculate that these findings may be evidence of a shared pathogenesis between KFD and concomitant anterior uveitis (4).

The case presented here shows that KFD may present with ocular abnormalities, specifically uveitis and perineural inflammatory changes in this instance. While not specific to KFD, a potential complication of the inflammatory process in this case, if untreated, would be permanent vision loss caused by scarring and pigment changes from prolonged choroidal inflammation. Also, prolonged hypotony may in turn cause a maculopathy which can impair vision. Furthermore, severe choroidal inflammation may cause forward displacement of the iris and ciliary body, resulting in narrow angle glaucoma. Finally, perineuritis may need to be addressed with high dose steroids to avoid permanent damage to the optic nerve. MR was a key diagnostic modality in helping to highlight the extent of the choroidal and perineural involvement, thereby prompting immediate and appropriate treatment.

TEACHING POINT

Kikuchi-Fujimoto Disease is rare. Presentation with bilateral uveitis is even more rare. However, the radiologic manifestations of uveitis may be applicable to a variety of inflammatory processes and so are important for the radiologist to recognize. Detection of these findings may aid the radiologist, ophthalmologist and pathologist in arriving at the correct diagnosis.

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FIGURES

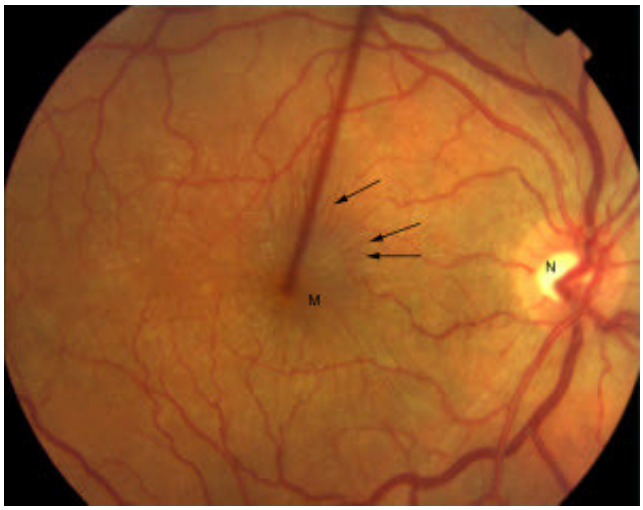

Figure 1: 23 year old male with Kikuchi-Fujimoto disease. Color fundus photograph of the right eye shows perimacular striae, indicating choroidal macular folds (arrows). This finding is consistent with choroidal effusion and accumulation of fluid in the suprachoroidal space. Similar findings were present in the left eye. The macula (M) and optic nerve (N) are indicated.

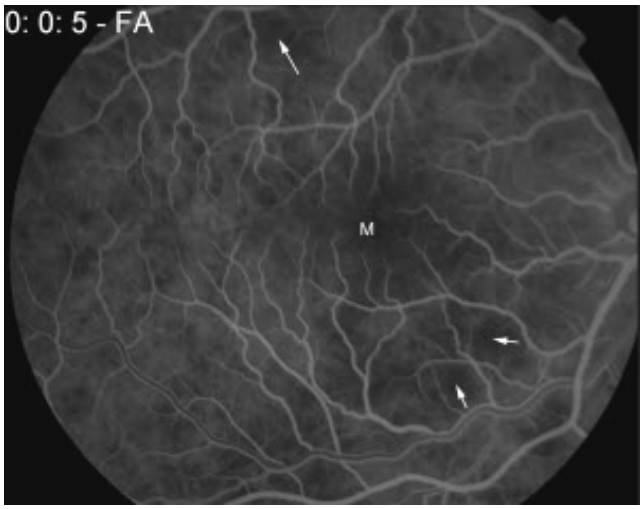

Figure 2: 23 year old male with Kikuchi-Fujimoto disease. Laminar phase fluorescein angiogram of the right eye shows heterogeneous fluorescence with areas of delayed choroidal filling (arrows), consistent with choroidal inflammation and effusion. The macula (M) is indicated.

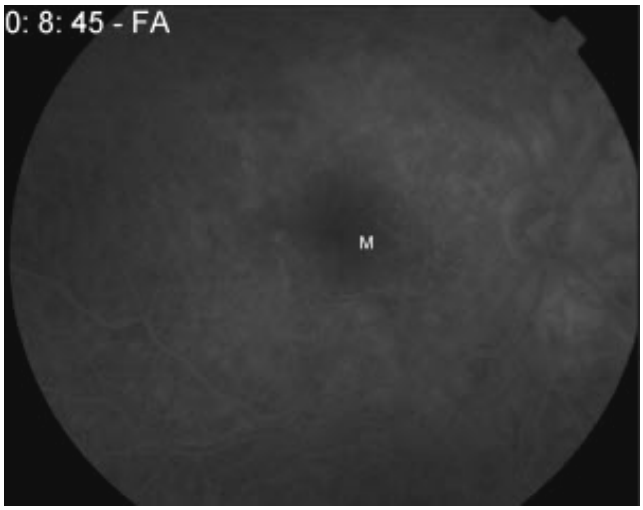

Figure 3: 23 year old male with Kikuchi-Fujimoto disease. Late phase fluorescein angiogram of the right eye shows persistent heterogeneous fluorescence. The macula (M) is indicated.

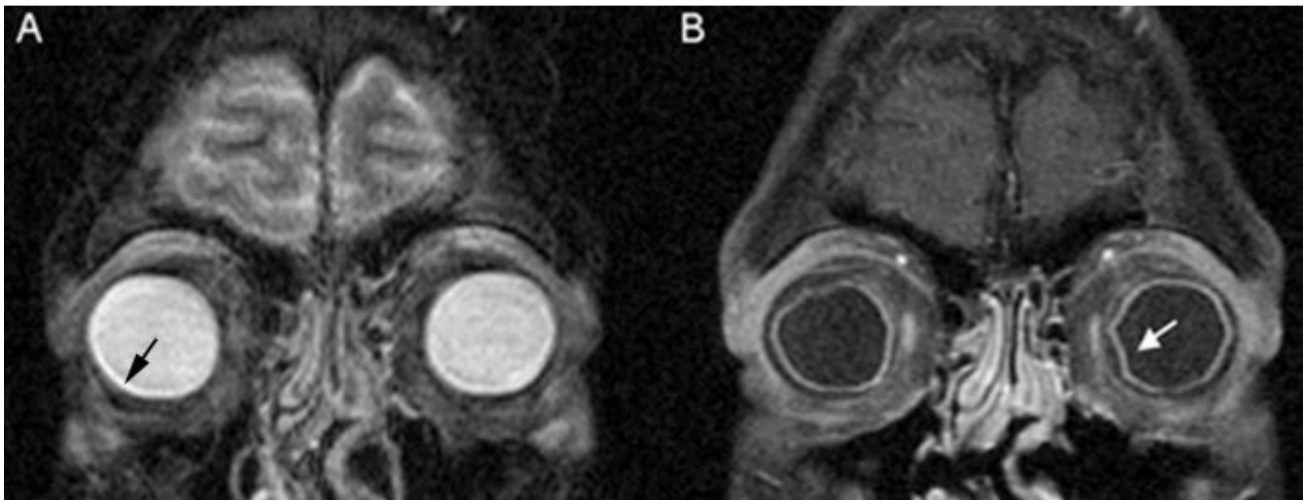

Figure 4: 23 year old male with Kikuchi-Fujimoto disease. High resolution coronal STIR (2650/63) (A) and T1 post contrast (416/13) with fat saturation (B). Suprachoroidal fluid is hyperintense to the vitreous on the STIR (arrow in A). T1 post contrast with fat saturation (B) demonstrate irregular contour of the abnormally enhancing choroid, in a bilateral symmetric fashion. Note areas of inward buckling of the choroid (arrow in B).

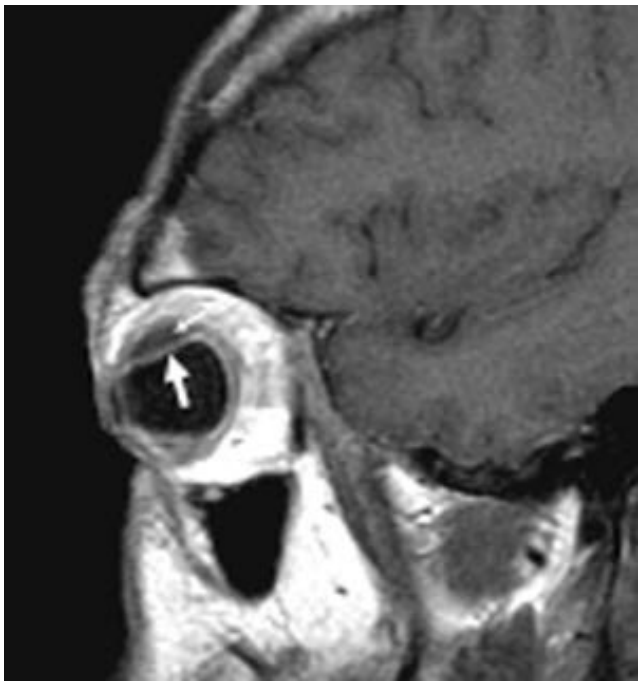

Figure 5: 23 year old male with Kikuchi-Fujimoto disease. Sagittal post contrast T1 (500/13) image shows ringlike enhancement of the choroid (thick arrow) and suprachoroidal fluid (thin arrow) which is slightly hyperintense to vitreous.

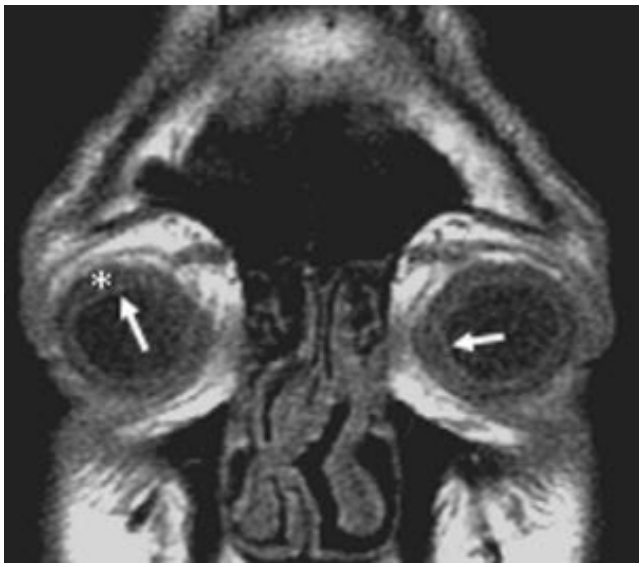

Figure 6: 23 year old male with Kikuchi-Fujimoto disease. High resolution coronal noncontrast T1 (450/13) image shows hyperintensity of the choroid, consistent with interstitial choroidal effusion (arrows). The suprachoroidal fluid is slightly hyperintense (asterisk) with respect to the vitreous.

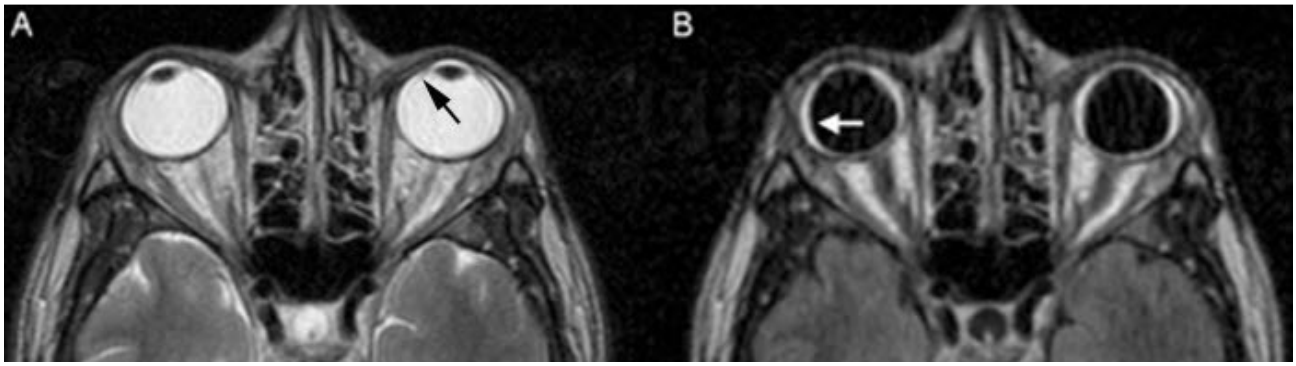

Figure 7: 23 year old male with Kikuchi-Fujimoto disease. Axial T2 (2950/89) (A) and FLAIR (10002/126) (B) images demonstrate crescentic high signal along the periphery of the ocular globes bilaterally (arrows), reaching the level of the ciliary body, consistent with suprachoroidal fluid collections.

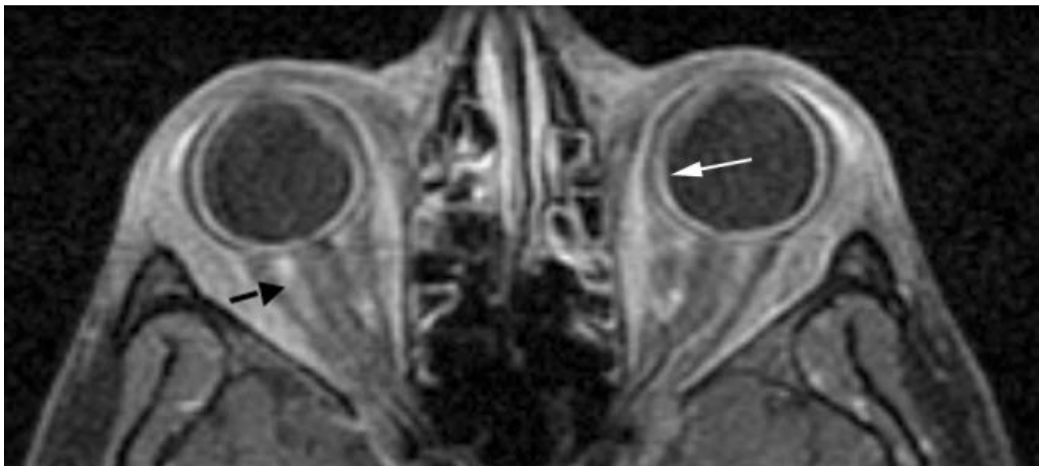

Figure 8: 23 year old male with Kikuchi-Fujimoto disease. High resolution axial T1(650/12) post contrast with fat saturation demonstrates abnormal enhancement in the retrobulbar fat adjacent to the optic nerve sheath complexes bilaterally (black arrow). Again appreciated is abnormal enhancement of the choroid within the ocular globes (white arrow).

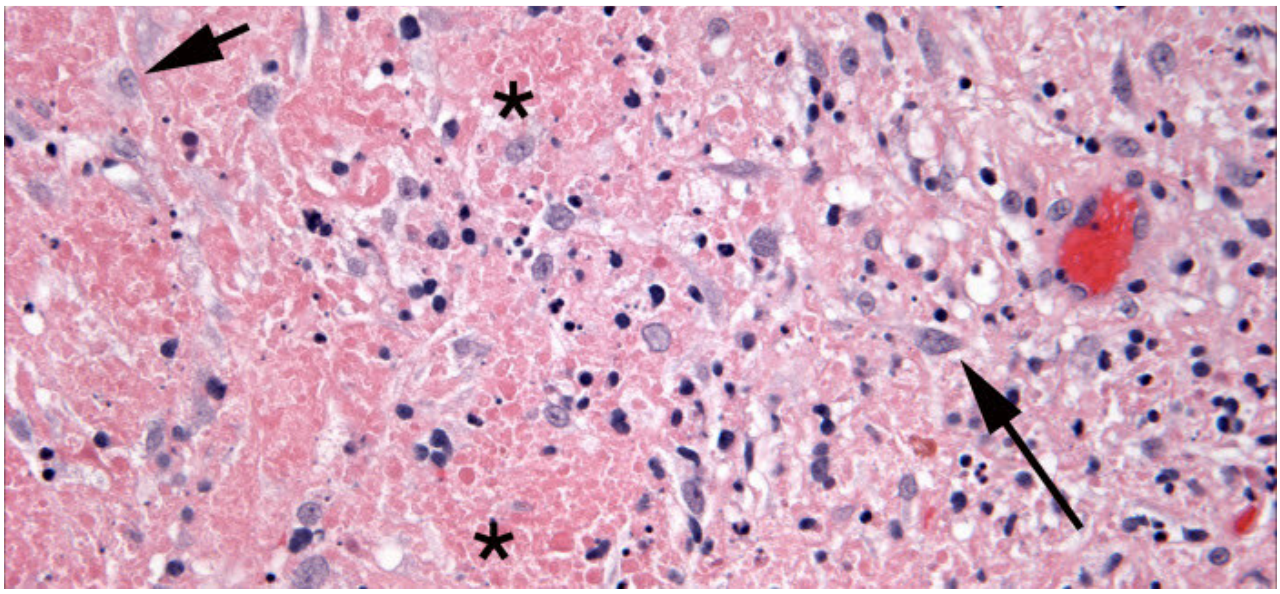

Figure 9: 23 year old male with Kikuchi-Fujimoto disease. 40X hematoxylin and eosin stain showing "crescentic" histiocytes with irregular nuclear contour (long arrow) admixed with plasmacytoid monocytes (short arrow). The cells are surrounded by amorphous necrotic material (asterisks).

ABBREVIATIONS

KFD: Kikuchi-Fujimoto Disease
MRI: Magnetic Resonance Imaging
MR: Magnetic Resonance

KEYWORDS

Kikuchi-Fujimoto, uveitis, magnetic resonance imaging, MRI