Kikuchi–Fujimoto disease is a rare lymphohistiocytic disorder that affects young women of Asian descent more frequently than persons of other ethnic groups.

Pathogenesis, Diagnosis, and Management of Kikuchi–Fujimoto Disease

Darcie Deaver, PhD, Pedro Horna, MD, Hernani Cualing, MD, and Lubomir Sokol, MD, PhD

Background: Kikuchi–Fujimoto disease (KFD) is a rare lymphohistiocytic disorder with an unknown etiopathogenesis. This disease is misdiagnosed as malignant lymphoma in up to one-third of cases and is associated with the development of systemic lupus erythematosus (SLE).

Methods: The medical literature between the years 1972 and 2014 was searched for KFD, and the data were collected and analyzed regarding the epidemiology, clinical presentations, diagnosis, management, and suggested diagnostic and treatment algorithms.

Results: Although KFD has been reported in other ethnic groups and geographical areas, it is more frequently diagnosed in young women of Asian descent. Patients with the disease typically present with rapidly evolving tender cervical lymphadenopathy, night sweats, fevers, and headache. Diagnosis is based on histopathological examination. Excisional lymph node biopsy is essential for a correct diagnosis. Apoptotic coagulation necrosis with karyorrhectic debris and the proliferation of histiocytes, plasmacytoid dendritic cells, and CD8+ T cells in the absence of neutrophils are characteristic cytomorphology features. Interface dermatitis at the onset of KFD may be a marker for the subsequent evolution of SLE. The natural course of the disease is typically benign. Short courses of steroids, nonsteroidal anti-inflammatory drugs, or hydroxychloroquine can be administered to patients with more severe symptoms.

Conclusions: Although KFD was described more than 40 years ago, the etiology of this disease remains unsolved. Infectious or autoimmune processes were proposed but have not been definitively confirmed. Clinical presentation with systemic B symptoms and adenopathy may lead to an erroneous diagnosis of malignant lymphoma. The introduction of modern methods into hematopathology, including immunohistochemistry, flow cytometry, and molecular clonality studies, has decreased the probability of misdiagnosis. Until reliable prognostic markers are available, patients with KFD should have continued long-term follow-up care due to their increased risk of SLE.

From the Departments of Malignant Hematology (DD, LS) and Hematopathology and Laboratory Medicine (PH) at the H. Lee Moffitt Cancer Center & Research Institute, Tampa, Florida, and IHCFLOW (HC), Lutz, Florida.

Dr Deaver is now affiliated with Celgene Corporation.

Submitted February 18, 2014; accepted July 2, 2014.

Address correspondence to Darcie Deaver, PhD, Celgene Corporation, 1503 Fogpiano Loop, Round Rock, TX 78665. E-mail: darciemarie2@hotmail.com

No significant relationships exist between the authors and the companies/organizations whose products or services may be referenced in this article.
Introduction
Kikuchi–Fujimoto disease (KFD), also known as Kikuchi disease, is a rare lymphohistiocytic disorder first described in 1972. KFD generally affects women of Asian descent between the ages of 20 and 35 years and has a male:female ratio of 1:2; however, new cases of KFD have also been described in non-Asian ethnic groups and children in Europe and the United States. The acute or subacute onset of adenopathy and systemic B symptoms in KFD has historically led to a misdiagnosis of malignant lymphoma, although modern hematopathological methods have made such misdiagnosis less likely. Following the resolution of KFD, concurrent autoimmune disorders have been reported; they may also be more frequently diagnosed.

Epidemiology
The precise incidence of KFD is unknown; however, a large review identified and analyzed 733 patients diagnosed worldwide since 1972. Of those cases, 140 (19%) were pediatric patients, and the male:female ratio was 1.4:1. It is worth noting that a higher propensity for male sex has only been observed in children younger than 12 years of age. The presenting symptoms in children are similar to adults, although fever and rash are more frequent in pediatric patients. Children younger than 18 years of age may also demonstrate bilateral cervical lymphadenopathy more frequently than adults.

The occurrence of KFD in family members has rarely been described. A search for a link between KFD and human leukocyte antigen class 2 alleles in the Japanese population suggested the possibility of a positive relationship between DPA1*01 and DPB1*0202 alleles and the disease. Because these alleles are much more frequent in Japan than in Europe and the United States, this finding may explain the higher prevalence of KFD in patients of Asian descent, thus supporting a possible autoimmune pathogenic mechanism.

Viral Infections
Epstein–Barr virus (EBV), human herpesvirus (HHV) types 6, 7, and 8, herpes simplex virus, HIV, human T-lymphotrophic virus, and parvovirus B19 are the most frequently studied viruses in patients with KFD.

Human Herpesviruses
Cho et al studied HHV-6 and HHV-7 in 50 archival samples of KFD and 20 controls using nested polymerase chain reaction (PCR) and found no significant difference in the viral DNA sequences between the patient and controls. Labrador et al identified the DNA of HHV-7 in the affected lymph node of a young patient with KFD who presented with cervical adenopathy and maculopapular rash. However, no confirmatory studies or results from the control samples were available. Huh et al amplified sequences of HHV-8 from lymph nodes in 6 out of 26 patients with KFD (23%). They did not detect any viral sequences in the reactive lymph nodes of the study controls, suggesting that HHV-8 may play a role in the pathogenesis of KFD.

Parvovirus B19
Zhang et al searched for parvovirus B19 in 33 lymph node samples from patients with KFD and 16 controls using several different methods, including PCR, immunohistochemistry, and in situ hybridization (ISH). A significantly higher rate of B19 positivity was seen in samples from patients with KFD than in controls; B19 infected cells were mostly composed of lymphocytes and a small number of histiocytes.

Epstein–Barr Virus
Hudnall et al tested 30 lymph node samples of patients with KFD and 12 controls for the presence of EBV using real-time PCR, EBV-encoded RNA ISH, and EBV latent membrane protein with immunohistochemistry. Cells with apoptotic features positive for EBV-encoded RNA were found in the necrotic regions of many KFD cases, suggesting that the disease could be due to a hyperimmune reaction against EBV infection. Hollingsworth et al looked for EBV and HHV-6 using PCR and ISH in 20 patients with KFD, but the study results did not support a viral role in the pathogenesis of KFD. However, Yen et al reported EBV infection in a child with a cutaneous manifestation of KFD, supporting the pathogenic role of EBV infection, and Chiu et al detected EBV RNA sequences in all 10 tested samples of KFD but found only a single case of EBV-encoded proteins. No evidence of human T-lymphotrophic virus or parvovirus B19 was seen in the patient samples of this study.

Overall, the results of studies searching for a viral etiology of KFD have been inconsistent. Laboratory methods differed among laboratories, positive results were documented in a small number of samples, and confirmatory studies with control samples were often unavailable. Currently, no definitive evidence suggests that a known virus plays a key role in the pathogenesis of KFD.

Autoimmune Mechanism
Autoimmune disorders are frequently reported in patients with KFD, with systemic lupus erythematosus (SLE) being the most common disorder linked to KFD. In many reports, KFD preceded the development of SLE; however, the diagnosis of KFD has been reported to simultaneously occur or follow the diagnosis of SLE. In one study, patients with KFD were negative for antinuclear and anti-DNA an-
Moderate reactive follicular hyperplasia, scattered plasma cells and immunoblasts, increased vascularity with Azzopardi phenomenon associated with moderate reactive follicular hyperplasia, or varying degrees of coagulative necrosis with the presence of hematoxylin bodies (Table 1). A diagnosis of SLE requires at least 4 out of 11 criteria to be present, and lymphadenitis is not included in these criteria. Sopheña et al40 found several autoimmune disorders, including SLE, Sjögren syndrome, thyroiditis, and leukocytoclastic vasculitis, in 9 (53%) of 20 patients with KFD.

Kim et al31 reviewed patients with KFD in the context of SLE and noticed an increasing number of case reports in the medical literature. Among 9 cases of KFD and SLE, 7 patients manifested with skin disease. Histological evaluation of skin biopsies was consistent with SLE in 3 of the 7 cases. Commonly, patients with a simultaneous onset of KFD and SLE have flare-ups of lupus; therefore, some researchers have suggested that concurrent KFD and SLE diagnoses are actually lupus lymphadenitis.31 Other researchers suggest that KFD is a forme fruste of SLE.32 Lymphadenitis is not included among the 11 diagnostic criteria of SLE, so it cannot establish a diagnosis of SLE as a sole pathological finding; however, the simultaneous manifestation of histiocytic necrotizing lymphadenitis with skin rash, cytopenias, arthralgias, and abnormal results on serological tests should raise suspicion of SLE and a comprehensive work-up should be completed.30 Paradela et al33 reported on a patient with KFD and interface dermatitis who subsequently developed SLE. They reviewed the medical literature and found an additional 27 cases of KFD with simultaneous nodal and cutaneous involvement, 9 of whom subsequently developed SLE. Skin biopsy was consistent with interface dermatitis in all of the KFD cases that evolved into SLE. The authors suggested that interface dermatitis could be a valuable marker of evolution of KFD into SLE.33 However, due to differing opinions about the possibility of concurrent diagnoses of KFD and SLE, further research is necessary to reach a definitive conclusion.

SLE adenopathy is usually mild, generalized, and nontender. The cytomorphology of enlarged lymph nodes in SLE consists of scattered plasma cells and immunoblasts, increased vascularity with Azzopardi phenomenon associated with moderate reactive follicular hyperplasia, or varying degrees of coagulative necrosis with the presence of hematoxylin bodies (Table 1).4,10,27 These features can help differentiate involvement with SLE compared with KFD.27,34 SLE is also associated with higher antinuclear antibody titers and organomegaly, which is a rare finding in KFD.35

### Molecular Biology

Molecular pathways implicated in the pathobiology of KFD are not well understood. Ishimura et al36 reported on a noninvasive method for diagnosing KFD using gene expression profiling on peripheral mononuclear cells. The top 5 up-regulated genes included IFI44L, CXCL10, GBP1, EPSTI1, and IFI27. All 5 genes belong to the family of interferon-induced genes. Ohshima et al37 investigated apoptosis and cell-cycle-associated gene expression in lymph nodes from patients with KFD and nonspecific lymphadenitis (NSL). The up regulation of nearly all apoptosis-associated genes, including caspase, and the down regulation of apoptosis inhibitory genes, such as BCL2, was seen in samples with KFD. Cell-cycle–associated genes were up regulated in all patients with KFD, which is in contrast to patients with NSL.37 Ohshima et al38 studied cytokine pathways in 10 lymph node samples from patients with KFD and 4 controls with NSL using immunohistochemistry and reverse transcriptase PCR. Results of the study suggested that the cytokine and chemokine pathways of interferon γ, interleukin 18, MIG, and interferon γ–induced protein 10 play an important role in the pathogenesis of apoptosis associated with KFD.38

### Table 1. — Histopathological Features of Kikuchi–Fujimoto Disease and Systemic Lupus Erythematosus

<table>
<thead>
<tr>
<th></th>
<th>Cytomorphology</th>
<th>Immunohistochemistry</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kikuchi–Fujimoto Disease</strong></td>
<td>Distorted nodal architecture with cortical and paracortical nodules with proliferation of histiocytes and immunoblasts, coagulative necrosis, abundant apoptotic karyorrhexis, and crescentic histiocytic nuclei</td>
<td>CD68+&lt;br/&gt;CD123+&lt;br/&gt;CD4+&lt;br/&gt;CD8 T-cell predominance&lt;br/&gt;Myeloperoxidase positive&lt;br/&gt;Lysozyme positive&lt;br/&gt;T-cell immunoblasts</td>
</tr>
<tr>
<td><strong>Systemic Lupus Erythematosus</strong></td>
<td>Moderate reactive follicular hyperplasia, scattered plasma cells and immunoblasts, with increased vascularity or varying degrees of coagulative necrosis with Azzopardi phenomenon and presence of hematoxylin bodies</td>
<td>CD4+ with predominance over CD8+ T cells&lt;br/&gt;Lymphoid follicles are mixture of small- and medium-sized lymphocytes&lt;br/&gt;Germinal centers of the B cell are BCL2+</td>
</tr>
</tbody>
</table>
Clinical Manifestation
KFD frequently manifests as an acute or subacute illness with systemic B symptoms and painful posterior cervical lymphadenopathy (Table 2).\textsuperscript{1,2,4,10,39} Lymph nodes are usually smaller, ranging from 0.5 to 4.0 cm.\textsuperscript{10,27,40} Approximately 1% to 22% of patients develop generalized lymphadenopathy.\textsuperscript{4,39} Kucukardali et al\textsuperscript{41} analyzed 244 patients between 1991 and 2006, most of whom were from Taiwan (36%); 15 (6%) were from the United States. Fever was the most common systemic symptom (presenting in 35% of patients). Lymphadenopathy was observed in 100% of patients, erythematous rashes in 10% of patients, and hepatosplenomegaly in 3% of patients.\textsuperscript{32} An association with SLE was seen in 13% of patients and viral infections in 10% of patients, although SLE was more frequent in patients from Asia than Europe (28% vs 9%).\textsuperscript{32} The disease was self-limiting in most patients (64%), and treatment with corticosteroids was necessary in 16% of patients.\textsuperscript{32}

Cheng et al\textsuperscript{41} studied 195 patients who were diagnosed with KFD between 1989 and 2006 in the largest retrospective study reported from a single institution. In this study, 53% of patients presented with tender adenopathy, 38% with fever, and 17% with headaches.\textsuperscript{41} A benign course with a spontaneous resolution of systemic symptoms and adenopathy was observed in 183 patients (94%); 14 patients (15%) developed recurrent disease within 6 months of follow-up; 5 patients (3%) developed autoimmune diseases, including SLE (2), Graves disease (2), and mixed connective tissue disease (1); and 1 patient with recurrent KFD died of intracranial hemorrhage secondary to thrombocytopenia.\textsuperscript{41}

Extranodal Manifestation
The most commonly affected extranodal organ is the skin (30%–40%).\textsuperscript{42,43} Nonspecific variable lesions, including papules, facial malar erythema, plaques, or nodules, are typically observed.\textsuperscript{43} Histology of the skin biopsy often resembles that of KFD. Case reports have also indicated an association of KFD with various inflammatory disorders, such as hemophagocytic syndrome, cerebellar ataxia, meningitis, conjunctivitis, arthritis, and myocarditis.\textsuperscript{39,44-49}

Laboratory Tests
No specific laboratory test is available for diagnosing KFD. A complete blood count is usually within normal range.\textsuperscript{27} Two large reviews observed leukopenia in 19% to 43% and anemia in 23% of people with KFD. Other laboratory abnormalities include elevated levels of erythrocyte sedimentation (40%–79%), lactate dehydrogenase (53%), and alanine aminotransferase (23%).\textsuperscript{32,41} Circulating atypical lymphocytes have also been reported in the peripheral blood film of approximately 25% of patients with KFD.\textsuperscript{50}

Diagnosis

Lymph Node Biopsy
Although fine-needle aspiration biopsy (FNAB) is a valuable tool for the diagnosis of some lymphoproliferative disorders, particularly in relapse settings, excisional biopsy is the preferred diagnostic tool in patients presenting with new adenopathy.\textsuperscript{27} Tong et al\textsuperscript{51} analyzed 44 cases of patients with confirmed KFD or suggested by FNAB. The false-positive and false-negative rates were 37.5% and 50%, respectively. The overall accuracy of FNAB was about 56%.\textsuperscript{51} Das et al\textsuperscript{42} compared FNAB smears of lymph nodes between patients with KFD and reactive nodal hyperplasia and showed overlapping cytological features in both conditions, which suggests the limited diagnostic potential of this method. Up to 30% of patients with KFD are initially misdiagnosed, so lymphoma excisional biopsy should be the requested diagnostic method used for patients with suspected KFD.\textsuperscript{4,10}

Histology and Immunohistochemistry
KFD is characterized by a distortion of the normal nodal architecture with cortical and paracortical nodules with coagulative necrosis and abundant apoptotic karyorrhectic debris.\textsuperscript{1,2,4,10,27} Additional characteristic features include the proliferation of histiocytes and immunoblasts with an abundance of CD8\textsuperscript{+} T cells and an absence of neutrophils (Fig 1). Immunohistochemical stains reveal histiocytes expressing CD68, myeloperoxidase, and CD4 markers. A predominance of CD8\textsuperscript{+} T cells in affected lymph nodes of patients with KFD has also been described.\textsuperscript{53} The expression of the CD123 marker on plasmacytoid dendritic cells also supports a diagnosis of KFD (see Table 1).\textsuperscript{53}

Kuo et al\textsuperscript{50} studied 79 cases with KFD and stratified KFD into 3 stages according to histopathologi-

<table>
<thead>
<tr>
<th>Table 2. — Diagnostic Criteria for Kikuchi–Fujimoto Disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical</strong></td>
</tr>
<tr>
<td>Localized lymphadenopathy</td>
</tr>
<tr>
<td>Systemic symptoms</td>
</tr>
<tr>
<td>Fever</td>
</tr>
<tr>
<td>Fatigue</td>
</tr>
<tr>
<td>Headache</td>
</tr>
<tr>
<td><strong>Pathological</strong></td>
</tr>
<tr>
<td>Laboratory studies</td>
</tr>
<tr>
<td>Leukopenia</td>
</tr>
<tr>
<td>Elevated C-reactive protein</td>
</tr>
<tr>
<td>Erythrocyte sedimentation rate</td>
</tr>
<tr>
<td>Biopsy of the lymph node</td>
</tr>
<tr>
<td>Aggregates of CD68\textsuperscript{+} histiocytes with occasional crescent-shaped nuclei</td>
</tr>
<tr>
<td>Foci of cell death ranging from isolated apoptotic cells to large areas of geographical necrosis</td>
</tr>
<tr>
<td>Proliferation of plasmacytoid dendritic cells</td>
</tr>
<tr>
<td>No accumulation of eosinophils or neutrophils</td>
</tr>
</tbody>
</table>
cal features. The proliferative stage is characteristic for the expression of various histiocytes, plasmacytoid monocytes, and lymphoid cells containing karyorrhectic fragments and eosinophilic apoptotic debris. The necrotizing stage can be recognized based on the presence of a various degree of coagulative necrosis; the xanthomatous stage manifests with foamy histiocytes.

The minimum criteria for a pathological diagnosis of KFD include the presence of crescent-shaped histiocytes and plasmacytoid monocytes with scattered karyorrhexis (see Table 2). It may be histiocytic proliferation, not necrosis alone, that is more characteristic of KFD.

**Differential Diagnosis**

A differential diagnosis of KFD is wide and should include infections such as tuberculosis, toxoplasmosis, *Bartonella henselae*, HIV, and EBV, as well as connective tissue disorders (eg, SLE) and lymphoproliferative disorders (Table 3). The proliferation stage of KFD may present with features similar to lymphoma and may lead to misdiagnosis. The presence of large atypical cells and immunoblasts of T-cell lineage origin cause confusion because these cells are also characteristic of aggressive lymphoma.

Necrosis may or may not be present in lymphoma. Immunohistochemical staining, flow cytometry, and molecular clonality studies can help in the differential diagnosis of these 2 disorders. Melikoglu et al reported lymphadenopathy in 23% to 34% of patients with SLE. The lymph nodes were small, nontender, and generalized in the majority of patients, which is in contrast to patients with KFD. Compared with KFD, other clinical and laboratory findings are necessary to diagnose SLE.

---

**Fig 1 A-D.** — (A) Low power view of a lymph node with involvement by Kikuchi histiocytic necrotizing nonsuppurative lymphadenitis. The pathognomonic pale foci are clues to the collection of histiocytes located in the center between the benign germinal centers located on the left and right sides of the image. (B) Medium power view showing necrosis and pink debris among histiocytes with round- to sickle-shaped nuclei. Well-formed granulomas are not typically seen. (C) Oil magnification showing sheets of pale histiocytic nuclei with violaceous hue and pink cytoplasm showing early findings of the disease with crescentic histiocytes appearing as tingible bodies. This stage is the most often histological appearance mistaken for large cell lymphoma because of the solid appearance of these large cells. Most of these are plasmacytoid monocytes that derive from plasmacytoid dendritic cells. (D) A more advanced stage of Kikuchi–Fujimoto lymphadenitis recognized by pathologists that shows the typical pink necrotizing nodules composed of histiocytic debris. Note the absence of neutrophils or suppurative abscess, which is a hallmark distinguishing this process from the class of suppurative granulomas.
**Imaging Studies**

Imaging studies may be useful in the assessment of patients with peripheral adenopathy. Computed tomography helps to differentiate tuberculous lymphadenitis from KFD. Lee et al\(^5\) compared computed tomographic imaging of the lymph nodes of 24 patients with KFD and 45 lymph nodes from patients with tuberculous lymphadenitis. Histologically, differences were seen between KFD and tuberculous lymphadenitis regarding the type of necrosis within the lymph nodes. By contrast to tuberculous lymphadenitis, which manifests with caseation necrosis surrounded with granulomatous tissue, KFD is characteristic for coagulation necrosis with apoptosis of various cell types. These differences may be responsible for changes seen on imaging studies. Indistinct margins of necrotic foci independently predicted the diagnosis of KFD with 80% accuracy in a multivariate analysis.\(^5\) Calcifications within the lymph nodes were observed in tuberculous lymphadenitis alone compared with KFD and other lymphoproliferative disorders.

Tsujikawa et al\(^5\) compared the size of lymph nodes and the maximum standardized uptake value in 8 patients with KFD and 14 patients with non-Hodgkin lymphoma using 18F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT). The sizes of the lymph nodes were smaller in patients with KFD compared with patients with indolent or aggressive lymphomas. The maximum standardized uptake value was also higher in cases of KFD compared with indolent non-Hodgkin lymphoma. A high maximum standardized uptake value in patients with KFD has been a contributing factor to misdiagnosis with aggressive lymphoma (see Table 3).\(^5\)

Lo et al\(^5\) examined ultrasonographic characteristics (size, shape, rims, matting, and echotexture) in 137 lymph nodes from 21 patients with KFD and 89 lymph nodes from 20 patients with malignant lymphoma. Results of this study suggested that cervical lymphadenopathies in patients with KFD are smaller in size, have a shape that is less round, a reticular echotexture that is less micronodular, and additional signs of matting and cortical widening than those with lymphoma.

**Treatment**

Treatment guidelines have not been established for KFD, and recommendations are based on case reports and expert opinion alone. Due to the self-limited, benign course of KFD, observation is the most common approach in management. Patients with symptoms or with involvement of the extranodal tissues, such as the central nervous system, skin, and eyes, can benefit from treatment with short pulses of corticosteroids, nonsteroidal anti-inflammatory drugs, and antipyretics (Fig 2). In patients with complicated KFD, glucocorticoids or hydroxychloroquine might be useful. Chen et al\(^6\) reported a rapid response to hydroxychloroquine in a child with symptomatic KFD. Yoshioka et al\(^6\) treated 13 patients with KFD and prolonged fever with a short course of methylprednisolone (0.5 g/day for 3 days). A dramatic resolution of fever was seen in all patients within 24 hours. Four out of 13 patients (40%) relapsed.\(^6\) Rezai et al\(^6\) treated a patient with KFD who had systemic symptoms with a 4-day course of chloroquine and achieved a rapid response. The patient was then re-treated with oral hydroxychloroquine 200 mg twice a day for 14 days for recurrent KFD; the patient's symptoms resolved within 12 hours.\(^6\) Yalcin et al\(^6\) administered methylprednisolone 1 m/kg for 8 days in a symptomatic patient with KFD who achieved a complete resolution of symptoms. The researchers tapered treatment with steroids by 8 mg every 3 days, leading to the regression of lymphadenopathy.\(^6\) Rezayat et al\(^6\) reported on a patient who initially responded to therapy with steroids; when the disease recurred, the patient was treated with single-agent hydroxychloroquine. However, following the discontinuation of each agent, the disease relapsed and the patient required dual therapy.\(^6\)

---

<table>
<thead>
<tr>
<th>Variable</th>
<th>Kikuchi–Fujimoto Disease</th>
<th>Aggressive Lymphoma</th>
<th>Systemic Lupus Erythematosus</th>
<th>Tuberculosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Onset</td>
<td>Rapid</td>
<td>Rapid</td>
<td>Slow</td>
<td>Slow</td>
</tr>
<tr>
<td>Presence of pain</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Anatomical distribution</td>
<td>Localized</td>
<td>Generalized</td>
<td>Generalized</td>
<td>Localized</td>
</tr>
<tr>
<td>Size of lymph nodes by CT, cm</td>
<td>2–4</td>
<td>&gt; 2</td>
<td>2–4</td>
<td>2–5</td>
</tr>
<tr>
<td>FDG/PET avid</td>
<td>Yes/High</td>
<td>Yes/High</td>
<td>Yes/Low, if active disease</td>
<td>Yes/Low, if active disease</td>
</tr>
</tbody>
</table>

CT = computed tomography, FDG/PET = 18F-fluorodeoxyglucose positron emission tomography.
Recurrence
In a single study, the recurrence rate of KFD was approximately 4%; however, in a more recent review, the recurrence rate was observed to be 15%. Bogusz et al identified 65 patients with recurrent KFD in the published literature until 2013. However, because approximately 800 cases of KFD have been reported thus far, the estimated frequency of recurrent KFD could be less than 10%. Recurrences can occur as long as 8 years after the initial presentation; therefore, long-term follow-up is necessary to assess the recurrence rate in KFD.

Pregnancy
Few cases have been reported of KFD manifesting during pregnancy. Two reports suggest that treatment with antibiotics, steroids, or both have no adverse impacts on the mother, fetus, or throughout the course of pregnancy. One miscarriage was described in a patient with KFD and evolving SLE.

Prognosis
In most patients with KFD, the course of disease is benign, with a spontaneous resolution of systemic symptoms and adenopathy typically occurring in 1 to 4 months. The association of KFD with SLE ranges between 3% and 28% and is higher in Asian populations.

In rare instances KFD has a fatal course. The mortality rate of KFD was reported in 2 large studies to be between 0.5% and 2.1%. The fatal course was due to an infiltration of the myocardium, cerebral hemorrhage secondary to thrombocytopenia, and an association with SLE and hemophagocytic syndrome.

Conclusions
Kikuchi-Fujimoto disease is an idiopathic, rare, benign lymphadenopathy that primarily affects younger people. Since its original description in young Japanese females, the disease has been diagnosed in other geo-


