Kikuchi-Fujimoto disease is a rare histiocytic necrotizing lymphadenitis that was first described in 1972 and occurs most frequently in Asian populations. It affects predominantly young adults, but an increasing number of pediatric cases have been reported. Kikuchi-Fujimoto disease is known to have a self-limiting course. Lymphadenopathy is the most common clinical manifestation of this disease, and it can be associated with pyrexia, weight loss, night sweats, and hepatosplenomegaly. Involvement of the CNS has been described, in the form of aseptic meningitis and subdural hematoma or empyema in 2 case reports, both of which were in adult patients. Even though extranodal features are uncommon, it is very important to identify and treat these neurological conditions promptly, because they might account for significant morbidity in an otherwise benign pathological condition.

We report the case of a child in whom KFD had been recently diagnosed and who presented to a tertiary pediatric neurosurgical center with features of raised intracranial pressure due to subdural effusions. A biopsy revealed dural involvement in the disease process. The authors review the medical literature of this rare disease and highlight the paucity of documented cases with CNS involvement.

**Case Report**

**History.** A 13-year-old Asian girl presented to the emergency department with weight loss, night sweats, pyrexia, neck swelling, headache, and abdominal pain. There was no medical history. She had several tender cervical lymph nodes, but results of the rest of the systemic examination (including a neurological assessment) were unremarkable. She had been treated with 2 courses of antibiotics with no response. Her blood test results were normal, and a head CT scan was also normal. To establish a diagnosis she underwent a cervical lymph node biopsy, which showed vaguely nodular infiltrates of histiocytic cells with small foci of necrosis and conspicuous apoptotic nuclear debris typical of KFD (Fig. 1). Her symptoms subsided spontaneously and she was discharged. Two weeks following her discharge, she presented once more with headache, vomiting, and diplopia.

**Examination.** On examination, the patient had a divergent squint of her left eye and bilateral papilledema. She had no peripheral neurological deficits and was afebrile. Admission CT and MRI scans of the head showed bilateral subdural effusions as a result of dural involvement in the disease. To the best of our knowledge this has never been documented in the medical literature. We also discuss the possible mechanisms for the formation of intracranial collections and their management.

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Abbreviations used in this paper: KFD = Kikuchi-Fujimoto disease; SLE = systemic lupus erythematosus.
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It was not possible to differentiate if the collections were infective or noninfective.

**Operation.** A decision was made to drain the collection. The patient underwent drilling of a precoronal bur hole on the left side, drainage of the subdural collection, and dural biopsy.

**Pathological Findings.** Fluid analysis revealed that the collections were aseptic cellular effusions. The dural biopsy showed histiocytic necrotizing inflammation identical to that in the lymph node, confirming dural involvement in the KFD (Fig. 3).

**Postoperative Course.** Following surgery, the patient made a dramatic improvement and her neurological symptoms resolved. A postoperative MRI study performed 1 week after the operation confirmed resolution of the collections (Fig. 4). Six months after discharge the

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**Fig. 1.** Histological examination of the lymph node showing pale nodules of necrotizing histiocytic inflammation (*upper*) with abundant nuclear debris (*lower*).

**Fig. 2.** Preoperative MRI study showing subdural effusion with enhanced thickened dura mater.

**Fig. 3.** Photomicrograph of biopsy sample obtained for histological examination of the dura mater showing necrotizing histiocytic inflammation with abundant nuclear debris. H & E, original magnification ×20.

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patient attended a rheumatology outpatient clinic, reporting joint pain and swelling. Although an SLE workup was done, she did not meet the American Rheumatology Association diagnostic criteria for lupus. She improved clinically with a short course of steroid therapy.

Discussion

Kikuchi-Fujimoto disease was first described in 1972 by Kikuchi and Fujimoto et al. It is a benign histiocytic necrotizing lymphadenitis, which usually has a self-limiting course of illness, with recurrence and fatalities being very rare. Typically cases occur in Japanese and other Asian populations, usually affecting those younger than 30 years of age. The mean age at diagnosis is 25 years, but this disease is being reported more frequently in the pediatric population.

The origin of KFD is unclear. An infectious or autoimmune hypothesis has been suggested, based on the clinical manifestations (especially the viral-like prodrome and atypical lymphocytosis) and certain histopathological features such as T cells, as revealed by immunological marker studies. Yersinia enterocolitica, Epstein-Barr virus, Paramyxovirus, and the rubella and parainfluenza viruses have been suggested as etiological agents. Kikuchi-Fujimoto disease has also been recorded in HIV-positive and human T-cell lymphotrophic virus type I-positive patients. Some authors have hypothesized that KFD may reflect a self-limited autoimmune condition induced by virus-infected transformed lymphocytes. Moreover, it is possible that KFD may represent an exuberant T-cell-mediated immune response in a genetically susceptible individual to a variety of nonspecific stimuli.

The disease manifests with cervical lymphadenopathy in 56%–98% of patients, and 50% also have pyrexia. Lymphadenopathy can occur in the intraparotid, supraclavicular, mediastinal, abdominal, and pelvic lymph nodes. Other features include weight loss, night sweats, and hepatosplenomegaly. Extranodal manifestations are less frequent and include cutaneous rash, myalgias, arthralgias, bone marrow disease, and interstitial lung disease. Laboratory findings include leukopenia, a raised erythrocyte sedimentation rate, lactate dehydrogenase, and transaminitis. However, diagnosis is confirmed based on histopathological findings of hyperplastic changes; increased phagocytic histiocytes and apoptotic plasmacytoid monocytes with variable degrees of necrosis in cortical and paracortical areas; and prominent karyorrhectic debris, proliferation of histiocytes, and immunoblasts surrounding the area of necrosis. Infiltration of the tissues surrounding the lymph nodes and perivascular spaces by inflammatory cells may occur. A mortality rate of 2% has been reported.

There is a recognized association of KFD with connective tissue diseases, particularly SLE; KFD can present before, simultaneously, or after the presentation of SLE. Worldwide, 17 cases have been reported and there are similarities in histological findings. The lymphadenitis of SLE, like KFD, is characterized by necrosis. However, hematoxylin bodies are present in patients with SLE. It is recommended that patients with KFD should be assessed for SLE as part of their long-term follow-up.

Treatment for KFD is symptomatic, with analgesics, antipyretics, NSAIDs, and (rarely) corticosteroids. A case series of 16 patients in whom biopsy-proven KFD was diagnosed showed that prednisolone shortened the duration of fever. Antibiotics are not shown to provide beneficial effects in the treatment of KFD.

Involvement of the CNS has been reported, mostly as aseptic meningitis. In a series of 69 cases in patients with an age range of 12–58 years, 2 patients developed aseptic meningitis. Another report describes 11 cases of KFD in Japanese patients presenting with headaches, in whom the age range was 8–38 years. Analysis of CSF typically shows a lymphocytic pleocytosis (with white cell counts that can go up to 1685 cells/μL), and slightly elevated glucose and protein levels. Aseptic meningitis is believed to be secondary to an autoimmune response in which infiltration of the neural tissue by lymphocytes occurs.

Neurosurgical complications have been described in 2 adult patients who were initially thought to have aseptic meningitis. Gros et al. reported the case of a 50-year-old woman with aseptic meningitis who developed a right frontoparietal subdural abscess with mass effect and mild brain edema. Allmendinger et al. had a case of a middle-aged Hispanic patient with cervical lymphadenopathy and bilateral chronic subdural hematomas. Both were primary manifestations of KFD and required surgical drainage due to neurological deterioration.

To the best of our knowledge, a child presenting with subdural effusions secondary to histologically confirmed dural involvement in KFD has never been described in the medical literature. Our patient also presented with features of raised intracranial pressure following hospi-
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talization 2 weeks earlier for pyrexia of unknown origin. She had received courses of antibiotics during her time in the hospital. Based on her imaging results we were unable to exclude subdural empyema with certainty. In such a situation, one should keep an open mind as to the differential diagnosis of KFD with aseptic effusions as well as the possibility of partially treated subdural empyema.

Furthermore, intraoperatively we found an abnormal dura mater that was thickened and fibrotic, and histopathological analysis showed typical features of KFD confirming that the dura was involved in the disease. Thus, dural biopsy may be beneficial in suspected cases, because it provides additional information that can confirm CNS involvement in the disease process.

Kikuchi-Fujimoto disease is a rare histiocytic necrotizing lymphadenitis that usually has a benign course. It can affect the CNS in the form of aseptic meningitis and subdural collections. Prompt identification and management of the possible neurosurgical conditions related to KFD is of paramount importance to prevent morbidity. The clinical and histopathological features of KFD are frequently nonspecific, and radiological imaging might be inconclusive; therefore, biopsy of the dura mater in selected cases can be helpful in establishing CNS involvement.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

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