

Quiz

CORRECT ANSWER TO THE QUIZ. CHECK YOUR DIAGNOSIS

HISTIOCYTIC NECROTISING LYMPHADENITIS IN MEDIASTINUM MIMICKING THYMOMA OR LYMPHOMA – CASE PRESENTATION AND LITERATURE REVIEW OF KIKUCHI FUJIMOTO DISEASE

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Kikuchi Fujimoto disease (KFD) as a rare self-limiting lymphadenopathy of short and benign course concerns most frequently the lymph nodes of the neck. The most common symptoms are painfulness of the diseased area, fever and night sweating. The etiology is not well understood, but in the role of pathogenesis viral, autoimmune and genetic factors are taken into account. In the presented case of 37-year-old female it was necessary to exclude diseases such as lymphoma or thymoma because of atypical mediastinal location of Kikuchi Fujimoto disease. After multidisciplinary consultation the lymph node was resected from the mediastinum with videothoroscopic approach. The diagnosis was difficult for the pathologist because of the large percentage of necrosis of the lymph node but the image was typical for histiocytic necrotizing lymphadenitis. Two cases of patients with KFD limited to the mediastinum have been previously reported in the literature. This article presents the world's first reported case of this disease in the topographic location of the thymus. Furthermore, a review of current literature was made.

Key words: histiocytic necrotizing lymphadenitis, mediastinal lymph node.

Introduction

Kikuchi Fujimoto disease also called histiocytic necrotizing lymphadenitis is self-limiting disease. The name comes from the names of two authors from Japan who described it independently of each other in 1972 [1, 2]. Kikuchi Fujimoto disease is more common in Asians and in women. In Europe, it is extremely rare. In Poland only 11 cases were described in literature [3, 4, 5, 6, 7, 8]. The etiology is not well understood but genetics, autoimmune and inflam-

matory factors are taken into account. There are a lot of similar symptoms of Kikuchi Fujimoto disease and of lymphomas. Also myasthenia symptoms similarity, as in the described case, can be a cause of problems with differential diagnosis. Lymphadenopathy in the form of enlarged lymph nodes may also occur in the case of metastases of solid tumors. Therefore, despite the self-limiting nature of the disease, decision of surgery was made. We present a case of histiocytic necrotic lymphadenitis in an exceptional location.

Case presentation

37-year-old Caucasian female came in February 2014 to a primary care doctor with symptoms of chronic malaise, muscle weakness, recurrent headache and somnolence. She smoked cigarettes in the past during 5 years, she had an episode of rash as an allergy to penicillin and periodically she had episodes of depression. She did not lose any weight. As a white-collar worker she was exposed to stress in the work environment. In some work situations she felt the sensation of stinging and crushing behind the sternum. Physical examination showed only the scars after cesarean section and appendectomy and no abnormalities in cervical and supraclavicular lymph nodes. Primary care doctor performed basic examinations and he excluded the cardiac causes of the ailment. In the meantime, the patient underwent bronchitis which has been successfully treated with antibiotics given empirically. Laboratory tests revealed anemia (Hgb concentration = 10.5 g/dl) and Westergren ESR = 51 mm, the concentration of CRP = 76.96 mg/l. In the chest radiography performed in March 2014 widening of middle shade on the left side was observed (Fig. 1). It was recommended to perform computed tomography of the chest and the patient was directed to neurologist. An oval tumor sized 6,5 × 4,7 × 5,3 cm with smooth contours in the upper front mediastinum was found in the CT. The remaining mediastinal and lung hilum lymph nodes were not enlarged. The image of the CT suggested thymoma.

Despite this suggestion after neurological examination consulting neurologist excluded myasthenia gravis. Anti-acetylcholine receptor antibodies (AChR-Ab) were negative. Finally, the patient was referred

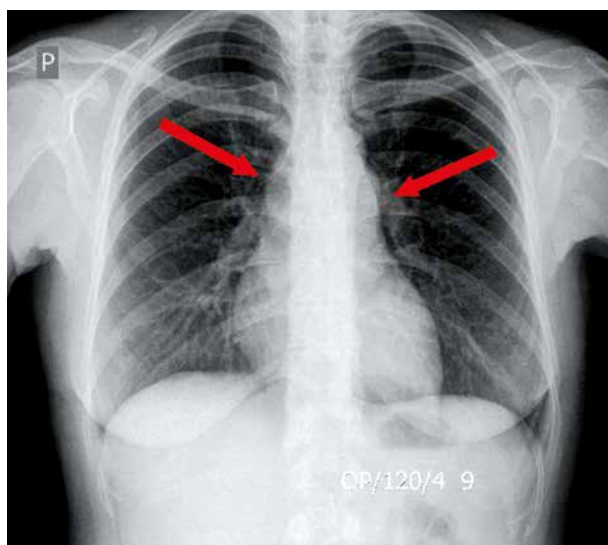


Fig. 1. Chest radiography – nodular opacity in the upper part of the central shadow (arrows)

to the Department of Thoracic Surgery of the Lower Silesian Center for Lung Diseases in Wrocław with purpose of diagnosis and surgical treatment of mediastinal tumor. In May 2014 under general anesthesia with the left video-assisted thoracoscopic surgery approach the patient underwent complete resection of the tumor. It had a diameter of 5 cm and it was sent for histopathological examination (Fig. 2). The study was much more difficult due to the fact that almost the entire tumor was necrotically changed. In addition, immunohistochemistry was performed. Antibodies were tested: Bcl-2(+), EMA(-), CD3(+), CD20(+), CD68(+), MAC 387(+), Ki67(+). Apart from fragments of thymus and extensive karyorrhexis, necrosis in the formulation the inflammatory infiltrate consisting of histiocytes, plasma cells and lymphocytes were also found (Figs. 3, 4). The image was typical for histiocytic necrotizing lymphadenitis that is called Kikuchi Fujimoto disease. In the differential diagnosis changes in the course of nodal systemic lupus erythematosus (SLE) were also taken into account, but consulting rheumatologist excluded this disease based on the physical examination and negative antinuclear antibody test. Clinically, the postoperative course was uncomplicated. The woman was discharged from the hospital in good general condition on the third day after surgery. The 18-months follow-up period was not complicated. Currently, she has no evidence of chronic fatigue symptoms or discomfort signs behind the sternum. There are no signs of recurrence in current radiography.

Discussion

The most common cause of mediastinal lymph node enlargement are neoplastic diseases of the lymphatic system or metastatic solid tumors [7, 9, 10, 11]. In order to make a proper diagnosis the pathologically altered lymph node must be taken by surgical biopsy and histopathology must be performed [12]. It is often required to perform additional immunohistochemistry. A typical feature of the microscopic image of lymph node affected with Kikuchi Fujimoto disease is the presence of numerous, irregular, sharply demarcated foci of necrosis with nuclear debris or extensive karyorrhexis. The surroundings of these foci are filled with the full number of characteristic CD68-positive plasmacytoid histiocytes containing comma-shaped nuclei and transformed lymphocytes (immunoblasts). Neutrophils, eosinophils or plasma cells are completely absent [3, 10, 13].

Laboratory examinations of patients with Kikuchi Fujimoto disease show no specific findings except mild leukocytopenia [10, 13].

Kikuchi Fujimoto disease most often occurs in the lymph nodes of the neck, but it has been also described in other locations: cervical parotid space,

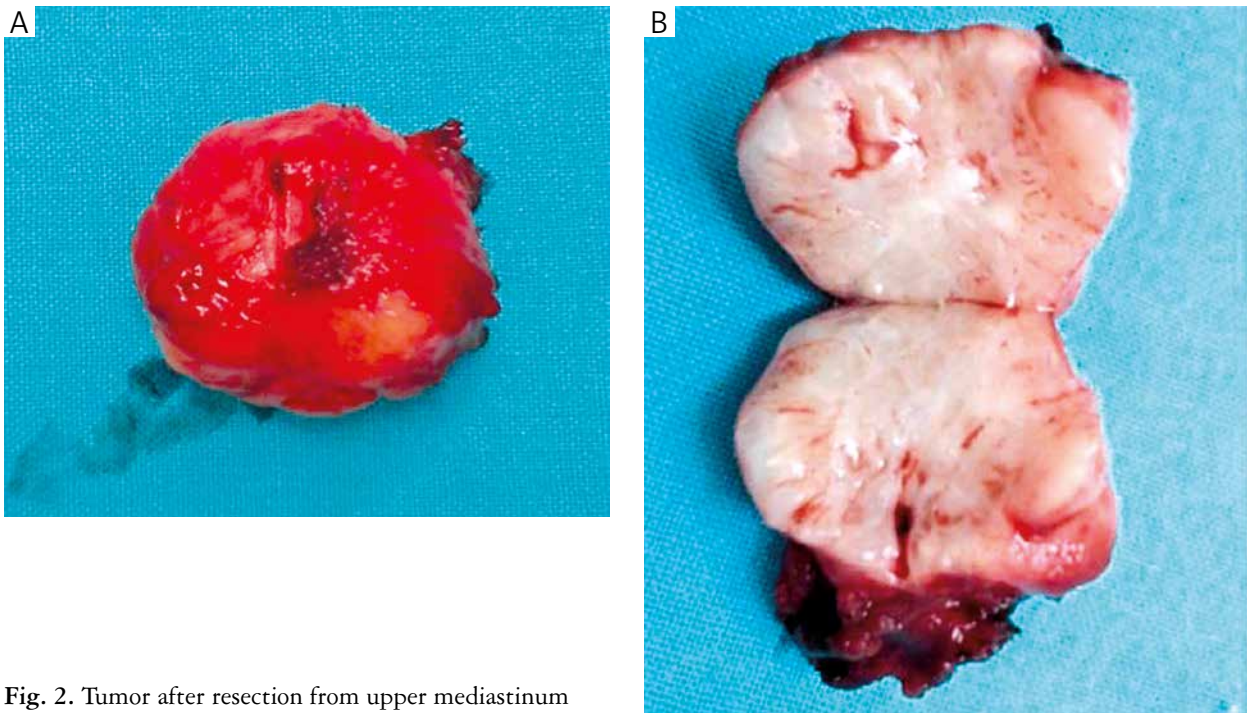


Fig. 2. Tumor after resection from upper mediastinum

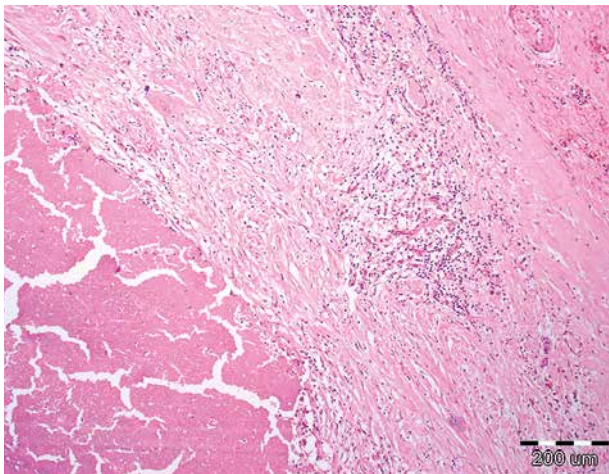


Fig. 3. The area of effacement of the normal nodal architecture with histiocytes and plasmacytoid monocytes infiltration, focal coagulative necrosis with cellular debris without infiltrates containing neutrophils; hematoxylin and eosin staining

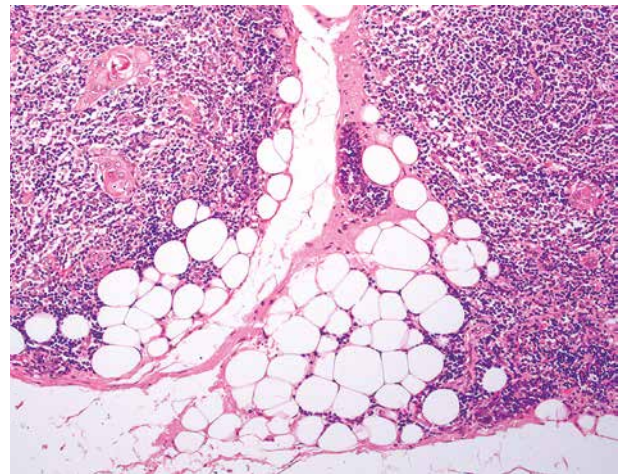


Fig. 4. HE stain. Thymus with necrosis (on the right) without neutrophils and with numerous histiocytes

supraclavicular, axillary, intra-abdominal, and retroperitoneal regions [9, 14, 15, 16]. There are a few cases of chest location. There were only two cases described that were limited to the mediastinal lymph nodes.

First case on this atypical site was described by Yoshida *et al.* in 2011. The pathologically altered right lower paratracheal and subcarinal lymph nodes showed a significantly increased tracer uptake in PET [17]. The patient besides a fever that lasted one week did not have any symptoms and physical examination was without any deviation. Due to suspicion of cancer

surgical biopsy of those lymph nodes was performed and histopathology confirmed necrotizing histiocytic lymphadenitis. After surgery, the body temperature normalized without treatment.

The second mediastinal-site case was described by Gupta *et al.* in 2014. The 27-year-old native American woman was diagnosed due to isolated mediastinal lymphadenopathy of lower right paratracheal, subcarinal and para-oesophageal lymph nodes [18]. The patient underwent Quantiferon test, which was positive. Patient required performance of differential diagnosis of tuberculous adenitis of mediastinum.

Mediastinoscopy was performed and samples of pathologically changed nodes were taken. Histopathology confirmed Kikuchi Fujimoto disease. Stains for mycobacteria and fungi were negative. In this case, all symptoms resolved after using steroids.

Another case with no evidence of cervical or supraclavicular adenopathy was reported recently by Fernández *et al.*, in which CT showed not only enlarged mediastinal and subcarinal lymph nodes but also small peripherally distributed subpleural nodules [15].

The overwhelming majority of patients with Kikuchi Fujimoto disease described in the literature did not require treatment. Kucukardali *et al.* examined 244 cases in which the majority did not require any treatment while only 16% of patients required treatment with steroids [9].

In the pathogenesis of Kikuchi Fujimoto disease the role of autoimmune factors is taken into account. In view there are frequent simultaneous occurrences of autoimmune diseases with histiocytic necrotizing lymphadenitis. The most common are systemic lupus erythematosus, Hashimoto's disease and rheumatoid arthritis [3, 19].

Also in a group of patients with Kikuchi Fujimoto disease there were a lot of cases with simultaneous viral infection. Therefore, an infectious agent is taken into account in the pathogenesis of histiocytic necrotizing lymphadenitis. The highest frequency of co-infection belongs to parvovirus B19, but detailed pathogenic mechanisms governing this virus and Kikuchi Fujimoto disease have not been elucidated yet [19, 20, 21, 22].

The increased disease incidence of Asian race has been associated with a group of HLA class II genes, such as DPA1 * 01, and DPB1 * 0202, predisposing to the development of Kikuchi Fujimoto disease [3, 13, 23].

FDG-PET is a convenient tool widely used now to investigate the location of malignancy. This method utilizes the feature of amplified glucose activity and glycolysis in malignant cells. In many cases patients showed increased uptake of FDG in PET. Due to high percentage of false positive results, eg. in sarcoidosis, benign lesions, some inflammatory diseases it is not possible to distinguish malignant from benign disease, SUV at a single time point [14, 24, 25, 26, 27].

Kikuchi Fujimoto disease recurrences were rarely described [28]. In the treatment prednisolone was used with good and rapid effect.

Conclusion

Although Kikuchi Fujimoto disease is self-limiting, due to the similarity to other diseases of worse prognosis without proper treatment, an accurate a diagnosis is required. The disease is usually not

taken into consideration in the differential diagnosis, because it is very rare. Asia is the continent where the disease occurs most frequently, but nowadays it is diagnosed more and more often in other areas which may be associated with migratory flows. Because the Kikuchi Fujimoto disease is self-limiting and of benign course, it is possible that many cases of this disease have not been identified and have been self-cured, or have been diagnosed as infectious diseases and cured with antibiotics or anti-inflammatory drugs.

The authors declare no conflict of interest.

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