Barw Medical Journal | 2025;3(2):65-69
Journal home page: https://barw.krd/index.php/BMJ

Case Report

Kikuchi-Fujimoto Disease Coexistent with Papillary Thyroid Carcinoma: A Report of Two Cases

Ari M. Abdullah[1,2], Aras J. Qaradakhy[1,3], Yadgar A. Saeed[1], Aso S. Muhialdeen[1], Rebaz O. Mohammed[1], Hiwa O. Baba[1], Abdulwahid M. Salih[1], Abdullah A. Qadir[1], Rezheen J. Rashid[4], Fahmi H. Kakamand[5*]

1. *Scientific Affairs Department, Smart Health Tower, Madam Mitterrand Street, Sulaymaniyah, Iraq*
2. *Department of Pathology, Sulaymaniyah Teaching Hospital, Sulaymaniyah, Iraq*
3. *Department of Radiology, Shorsh Teaching Hospital, Sulaymaniyah, Iraq*
4. *Radiology Department, Hiwa Hospital, Sulaymaniyah, Iraq*
5. *College of Medicine, University of Sulaimani, Madam Mitterrand Street, Sulaymaniyah, Iraq*

[*] ***Corresponding author***: fahmi.hussein@univsul.ed.iq *(F.H. Kakamad) Doctor City, Building 11, Apartment 50, Zip code: 46001, Sulaymaniyah, Iraq*

Keywords:
Kikuchi-Fujimoto Disease
Papillary thyroid carcinoma
Co-occurrence
Thyroid cancer

Received: February 05, 2025
Revised: February 15, 2025
Accepted: February 26, 2025
First Published: March 10, 2025

Citation: Abdullah AM, Qaradakhy AJ, Saeed YA, Muhialdeen AS, Mohammed RO, Baba HO et al. Kikuchi-Fujimoto Disease Coexistent with Papillary Thyroid Carcinoma: A Report of Two Cases. Barw Medical Journal. 2025;3(2):65-69.
https://doi.org/10.58742/bmj.v3i2.167

Abstract

Introduction

Kikuchi-Fujimoto Disease (KFD), characterized by histiocytic necrotizing lymphadenitis, is a rare condition of unknown etiology. Diagnosis is dependent on lymph node biopsy. Despite its self-limiting nature, accurate identification is essential to exclude more serious conditions. This paper reports on two cases of KFD coexisting with papillary thyroid carcinoma (PTC).

Case presentation

Two cases of KFD related to papillary thyroid carcinoma (PTC) are described. In Case 1, a 25-year-old woman experienced submental swelling, fever, and exhaustion. Subsequent tests revealed a thyroid lesion and cervical lymphadenopathy, which were confirmed as PTC and KFD. In Case 2, a 39-year-old female patient had right neck swelling, prompting a complete thyroidectomy that revealed papillary thyroid cancer with KFD in cervical lymph nodes.

Conclusion

The conclusion emphasizes the importance of considering KFD while highlighting its masquerading nature and the unique scenario of its coexistence with PTC.

1. Introduction

Kikuchi-Fujimoto Disease (KFD), or histiocytic necrotizing lymphadenitis, is a relatively rare medical condition characterized by painful cervical lymphadenitis and fever. It was first identified in Japan in 1972 [1,2] and typically manifests as a benign and self-limiting disorder [3] with documented cases primarily in Asian countries [4]. Although both genders can be affected, there is a slight predilection towards females. The etiology of KFD remains unknown [3]. The disease exhibits a higher incidence in adults aged 20 to 35 [1]. Due to its rarity, KFD is often not considered in the initial differential diagnosis

and its diagnosis relies on histopathologic examination (HPE) of lymph node biopsies. Despite its benign nature, accurate diagnosis is crucial to exclude other causes of lymphadenopathy such as lymphoma, tuberculous adenitis, and systemic lupus erythematosus [5]. There is no specific treatment for KFD; however, supportive care with analgesics, antipyretics, and corticosteroids can alleviate symptoms. In refractory cases, treatment with immunoglobulins or hydroxychloroquine may be considered [3]. While PTC is the most common type of thyroid cancer, its association with KFD is seldom emphasized [6]. Although metastatic lymphadenopathy can occur in cancer patients, simultaneous occurrence with other conditions in the same lymph node is unusual [7]. The current study aims to present two cases of KFD associated with PTC.

2. Case Presentations

2.1. Case 1

2.1.1. Patient information

A 25-year-old female presented with a one-month history of submental swelling, accompanied by fever and fatigue. She had no significant past medical history except for a tonsillectomy and rhinoplasty.

2.1.2. Clinical findings

Thyroid examination revealed a palpable submental lymph node classified as Grade 0. Other systemic examinations were unremarkable.

2.1.3. Diagnostic assessment

Routine laboratory tests showed normal thyroid-stimulating hormone (TSH) levels at 2.083 mIU/L, and elevated free T4 (FT4) levels at 15.13 ng/dL, indicating hyperthyroidism rather than normal thyroid function. Neck ultrasound (U/S) revealed a well-defined, irregular surface and a solid hypoechoic nodule of 10*9*7.8 mm in the mid-upper third categorized as TIRAD 5.

Multiple bilateral cervical lymphadenopathies were noted with well-defined margins, round to oval shape, loss of hilar echogenicity, and mild vascularity. The largest lymph node, measuring 12x9x8mm, was located submentally, and another measuring 10x6 mm was found in the left level III group, suggesting potential pathological involvement. Fine needle aspiration (FNA) confirmed PTC VI.

2.1.4. Therapeutic intervention

Under general anesthesia, total thyroidectomy, left central and lateral lymph node dissection, and submental lymph node biopsy were performed via a collar incision. Preservation of both recurrent laryngeal nerves and parathyroid glands **was** ensured**.** Hemostasis was achieved, and the wound was closed in layers with a drain on the left side. A total of 37 lymph nodes were evaluated from the left central and lateral cervical groups during the procedure. Among these, three lymph nodes were involved by papillary thyroid carcinoma. The submental lymph node biopsy revealed histiocytic necrotizing lymphadenitis, confirmed by immunohistochemistry (Figure 1). Specific staining patterns were observed using antibodies sourced from monoclonal mouse for CD15 (pH 9), CD20 (pH 9), and CD30 (pH 6), and from rabbit for CD68 (pH 6). The CD68 exhibited predominant cytoplasmic positivity in histiocytes localized within the necrotic areas, while CD20, CD15, and CD30 demonstrated negative staining within the necrotic regions, indicative of the absence of B-cell lymphocytic infiltrates and granulocytes, respectively. Scattered positive cells for CD15 and CD30 were observed both within and outside the necrotic foci.

2.1.5. Follow-up and Outcome

Post-operatively, the patient received levothyroxine 100 mg daily for thyroid hormone replacement therapy and was placed on regular follow-up. Three months later, neck U/S showed no focal lesions or signs of recurrence, with recovery supported by symptomatic care.

2.2. Case 2

2.2.1. Patient information

A 39-year-old female presented with right-sided neck swelling and no prior medical or surgical history.

2.2.2. Clinical findings

Examination revealed cervical lymphadenopathy without additional clinical complaints.

2.2.3. Diagnostic assessment

Routine laboratory tests indicated normal thyroid function with thyroid-stimulating hormone (TSH) levels of 3.82 mIU/L and free T4 (FT4) levels of 12.6 ng/dL. Anti-thyroid peroxidase (ATPO) levels were elevated at 600 IU/ml. Neck U/S revealed multiple bilateral cervical lymphadenopathies, predominantly on the right side, characterized by well-defined hypoechoic, mildly vascular lymph nodes with loss of hilum echogenicity. The largest lymph node in the right group III measured 17×8mm and was pathologically significant. The thyroid gland appeared normal, with small nodules <3mm in the right lobe, and the largest measuring 13×12×10mm in the left lower third, classified as TR4 with solid isoechoic features and microcalcifications. The FNA confirmed PTC VI and benign lymphoid cells in the left lymph node.

2.2.4. Therapeutic intervention

Under general anesthesia, total thyroidectomy with excision of left central and right posterior cervical lymph nodes was performed through a collar incision. Both recurrent laryngeal nerves and parathyroid glands were preserved. Hemostasis was achieved, and the wound was closed in layers with a drain on the left side. A total of five central lymph nodes were evaluated during the thyroidectomy, all of which were tumor-free. Additionally, two right posterior cervical lymph nodes were sampled, both showing histological features consistent with Kikuchi disease (Figure 2), confirmed by immunohistochemistry with CD68 positivity in histiocytic cells, CD20 negativity, CD15, CD30 negativity in the necrotic area, and sporadic CD15, CD30 positivity outside necrotic regions.

2.2.5. Follow-up and Outcome

Post-operatively, the patient was stable and started on levothyroxine 100 mg daily for thyroid hormone replacement therapy. Three months later, U/S showed no focal lesions, indicating recovery under supportive care.

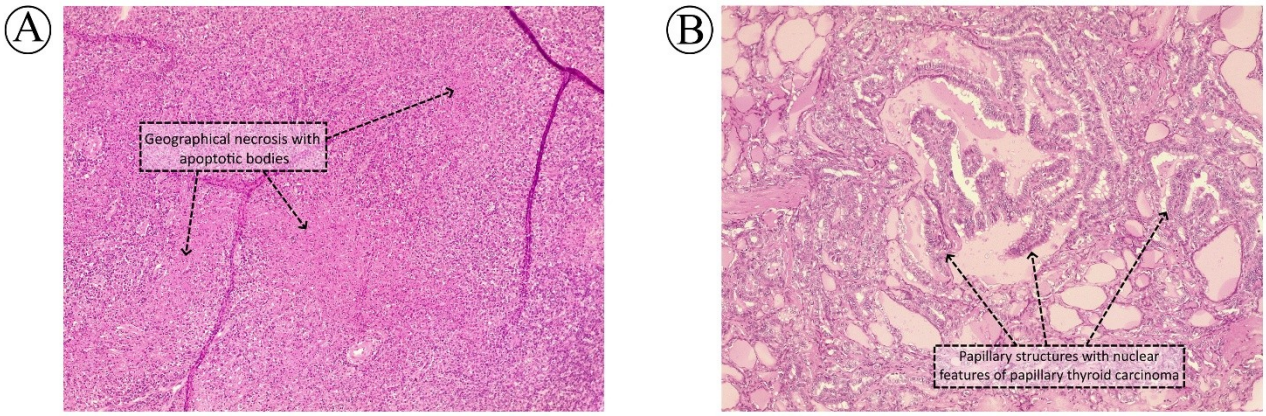

Figure 1. A) The lymph node from the first case shows pale areas of dendritic cells and histiocytes with geographic coagulative necrosis containing apoptotic debris but no neutrophilic activity. B) The thyroid tumor shows papillary formations lined by follicular cells that have elongated, overlapping nuclei with chromatin clearing, grooves, and pseudo-inclusions. [Hematoxylin and eosin; 40x (A), 100x (B)]

3. Discussion

The KFD is a rare, benign lymphadenopathy predominantly affecting cervical lymph nodes, although cases involving axillary and supraclavicular nodes have been documented [1]. Initially identified in Japan, KFD has been reported globally across Europe, America, Asia, and the Middle East [5], with a higher prevalence among women under 40 years of age [8]. The exact cause of KFD remains unclear, with theories suggesting infectious and autoimmune origins. Associations with herpes viruses and Epstein-Barr virus have been noted, although evidence remains inconclusive. Concurrent autoimmune diseases like systemic lupus erythematosus also suggest an autoimmune component [3]. While lymph nodes as large as 5 to 6 cm have been reported, typical KFD-associated lymphadenopathy is less than 3 cm. Fever episodes lasting from one to seven weeks with temperatures ranging from 38.6°C to 40.5°C are common, with variable tenderness on palpation. Additional symptoms may include chills, headaches, splenomegaly, arthralgia, vomiting, night sweats, fatigue, and malaise [1]. The disease onset is acute or subacute, progressing over 1-3 weeks and resolving spontaneously within 1-4 months

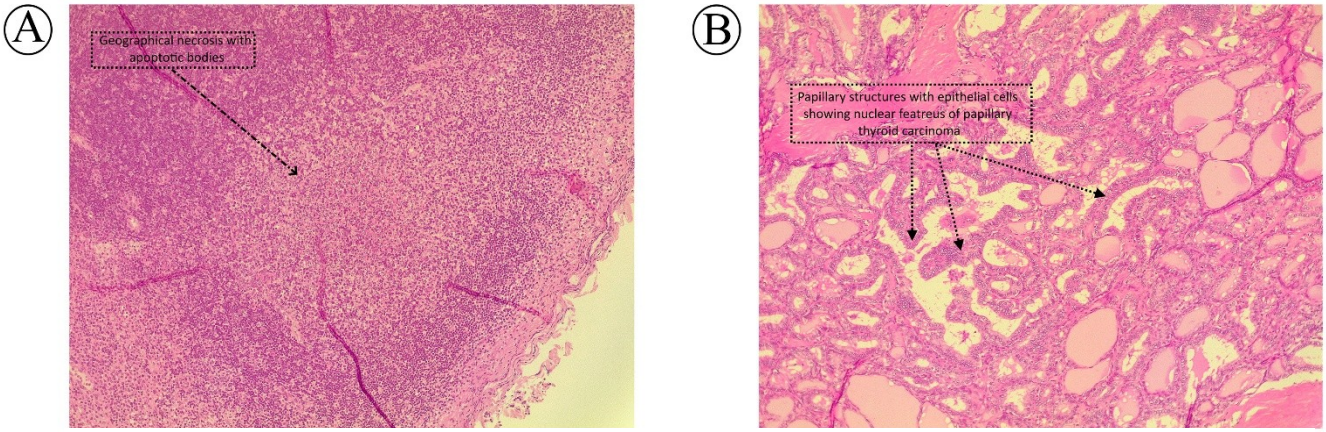

Figure 2. A) The lymph node from the second case shows partial involvement by pale areas composed of dendritic cells, histiocytes, and activated lymphocytes, associated with small areas of coagulative necrosis that contains apoptotic bodies but no neutrophilic infiltration. Reactive lymph node parenchyma is present at the top left. B) The thyroid from the second case shows papillary and follicular structures lined by low columnar cells that have elongated, enlarged, and overlapping nuclei with clearing, grooves, and pseudo-inclusions. [Hematoxylin and eosin; 40x (A), 100x (B)]

[3]. In the present study, two females (25 and 39 years old) presented with submental and anterior neck swelling, respectively.

In a study conducted by MD et al., an 11-year-old female presented with three weeks of multiple lymph node enlargement and one week of fever without systemic or oropharyngeal infection [8]. Maruyama et al., reported a case of a 48-year-old man who initially presented with a tongue lesion. Despite initial negative findings on examination and imaging for lymphadenopathy, subsequent biopsy revealed squamous cell carcinoma. Following tumor reduction surgery, lymphadenopathy developed [9]. In the current study, the first case presented with submental swelling and fever, while the second case presented with right-sided neck swelling without fever.

No specific laboratory tests are pathognomonic for the diagnosis KFD. Reported findings include variable results such as increased lactate dehydrogenase (LDH), leukopenia or leukocytosis, anemia, elevated erythrocyte sedimentation rate, raised C-reactive protein levels, and elevated transaminases. Leukopenia is observed in 25% to 58% of cases, while leukocytosis occurs in approximately 2% to 5% [1]. Diagnostic workup typically includes imaging with US and/or CT scans. Definitive diagnosis is established through excisional biopsy and HPE [1]. Radiologically, KFD lacks a distinct appearance and can resemble various nodal conditions with necrosis, including lymphoma, metastases, and tuberculosis. A retrospective CT study by Kwon et al. identified predominantly homogeneous lymphadenopathies involving levels II to V, with most nodes measuring less than 2.5 cm, distinguishing them from lymphoma which often presents with fewer but larger nodes, perinodal infiltration, and necrosis [8]. Garg et al. reported cases of females presenting with neck swelling, undergoing ultrasound and FNA revealing PTC [8]. Similarly, in the current study, both patients exhibited normal lab tests. Ultrasound revealed cervical lymphadenopathy and a thyroid nodule. FNA of the first patient's TR5 nodule confirmed PTC VI, while FNA of the second patient's LN and TR4 nodule suggested Kikuchi disease and PTC.

Three histological types were proposed: proliferative, necrotizing, and xanthomatous types. Notably, the absence of granulocytes distinguishes the xanthomatous variant, although differentiation from conditions like SLE, lymphoma, drug-induced lymphadenopathy, or Kawasaki disease poses challenges [10]. Immunohistochemistry plays a crucial role in resolving overlaps in histopathological findings [11]. Typically self-limiting, KFD resolves within one to four months without specific therapy, although recurrent cases, seen in 3–4% of patients, necessitate monitoring. No hereditary predisposition has been reported. Supportive care includes analgesics, NSAIDs, and antipyretics for symptom relief. Corticosteroids are beneficial for neurological involvement, while hydroxychloroquine, immunoglobulins, and minocycline have shown efficacy in selected cases [12]. In the context of the current study, patients with papillary thyroid carcinoma (PTC) and suspicious lymph nodes underwent total thyroidectomy and neck dissection, with subsequent HPE revealing concurrent PTC and KFD in the submental lymph node of the first case and the right cervical lymph node of the second. Both patients recovered with resolution of lymphadenopathy, highlighting the rarity of synchronous PTC with KFD, as documented minimally in the genuine literature by Park et al. and emphasized by Garg et al. [7,8,13]. In the current study, HPE of thyroid tumors revealed papillary structures with fibrovascular cores and nuclear features consistent with PTC VI classification based on the Bethesda system, without necrosis—a hallmark of well-differentiated papillary carcinomas. Conversely, non-tumoral tissues, particularly lymph nodes affected by KFD, exhibited histiocytic necrotizing lymphadenitis with necrotic foci surrounded by CD68-positive histiocytes, distinguishing it from PTC and emphasizing the diagnostic role of HPE in distinguishing these conditions.

The clinical diagnosis of KFD and PTC presents several limitations and challenges. Accurate diagnosis is crucial yet often hindered by the overlapping clinical and histopathological features of KFD and other conditions. To improve diagnostic precision, it is essential to utilize more detailed histopathologic images at both low and high magnifications. These enhanced imaging techniques can provide clearer insights into the cellular and structural characteristics of the lesions, thereby facilitating more accurate differentiation between KFD and other lymphadenopathies or neoplastic condition.

4. Conclusion

The simultaneous presence KFD and PTC highlights complex diagnostic challenges. Surgical intervention underscores the crucial role of detailed histopathological examination in achieving accurate diagnosis and tailored treatment strategies for these rare concurrent conditions.

Declarations

Conflicts of interest: The author(s) have no conflicts of interest to disclose.

Ethical approval: Not applicable.

Patient consent (participation and publication)**:** Written informed consent was obtained from the parent of the patient for publication.

Funding: The present study received no financial support.

Acknowledgements: None to be declared.

Authors' contributions: AMA and FHK were significant contributors to the conception of the study and the literature search for related studies. YAS, ASM, ROM, HOB and AMS were involved in the literature review, the study's design, and the critical revision of the manuscript, and they participated in data collection. AAQ and FHK were involved in the literature review, study design, and manuscript writing. AJQ and RJR were the radiologists who performed the assessment of the case. AAQ and AMS confirm the authenticity of all the raw data. All authors approved the final version of the manuscript.

Use of AI: AI was not used in the drafting of the manuscript, the production of graphical elements, or the collection and analysis of data.

Data availability statement: Not applicable.

References

1. Singh JM, Shermetaro CB. Kikuchi-Fujimoto disease in Michigan: a rare case report and review of the literature. Clinical Medicine Insights: Ear, Nose and Throat. 2019;12:1179550619828680. doi:10.1177/1179550619828680
2. Abdullah AS, Ahmed AG, Mohammed SN, Qadir AA, Bapir NM, Fatah GMet al. Benign Tumor Publication in One Year (2022): A Cross-Sectional Study. Barw Medical Journal. 2023; 1(4):20-25. doi:10.58742/wefvkv74
3. Tarabichi S, Nicola AA, Radu L, Enache S, Busuioc CI, Moldovianu AM, Nitu AF, Predeteanu D, Sarafoleanu C. Kikuchi-Fujimoto disease and systemic lupus erythematosus–an enigmatic association for clinicians and pathologists: Case report and short literature review. Romanian Journal of Rhinology. 2022;12(45):11-21. doi:10.2478/rjr-2022-0003
4. Santana A, Lessa B, Galrão L, Lima I, Santiago M. Kikuchi-Fujimoto's disease associated with systemic lupus erythematosus: case report and review of the literature. Clinical Rheumatology. 2005; 24:60-3. doi:10.1007/s10067-004-0923-6
5. Al Soub H, Ibrahim W, Al Maslamani M, Ali GA, Ummer W. Kikuchi-Fujimoto disease following SARS CoV2 vaccination: Case report. IDCases. 2021;25: e01253. doi:10.1016/j.idcr.2021.e01253
6. Mingomataj E, Krasniqi M, Dedushi K, Sergeevich KA, Kust D, Qadir AA. Cancer Publications in One Year (2023): A Cross-Sectional Study. Barw Medical Journal.2024;2(1):3-11. doi:10.58742/g9q9t715
7. Park JJ, Seo YB, Choi HC, Kim JW, Shin MK, Lee DJ, Lee J. Kikuchi-Fujimoto disease coexistent with papillary thyroid carcinoma in a single lymph node. Soonchunhyang Medical Science. 2015;21(1):10-4. doi:N/A
8. Garg S, Villa M, Asirvatham JR, Mathew T, Auguste LJ. Kikuchi-Fujimoto disease masquerading as metastatic papillary carcinoma of the thyroid. International Journal of Angiology. 2015:145-50. doi:10.1055/s-0033-1358784
9. Maruyama T, Nishihara K, Saio M, Nakasone T, Nimura F, Matayoshi A, Goto T, Yoshimi N, Arasaki A. Kikuchi-Fujimoto disease in the regional lymph nodes with node metastasis in a patient with tongue cancer: A case report and literature review. Oncology Letters. 2017;14(1):257-63. doi:10.3892/ol.2017.6139
10. Dalugama C, Gawarammana IB. Fever with lymphadenopathy–Kikuchi Fujimoto disease, a great masquerader: a case report. Journal of medical case reports. 2017;11(1):1-4. doi:10.1186/s13256-017-1521-y
11. Hassan M, Anees A, Zaheer S. Kikuchi-Fujimoto disease: diagnostic dilemma and the role of immunohistochemistry. Journal of Clinical Medicine Research. 2009 ;1(4):244. doi:10.4021/jocmr2009.09.1258
12. Tariq H, Gaduputi V, Rafiq A, Shenoy R. The enigmatic kikuchi-fujimoto disease: a case report and review. Case Reports in Hematology. 2014 ;2014. doi:10.1155/2014/648136
13. Kakamad FH, Abdalla BA, Abdullah HO, Omar SS, Mohammed SH, Ahmed SM, et al. Lists of predatory journals and publishers: a review for future refinement. European Science Editing. 2024;50:e118119. doi:10.3897/ese.2024.e118119