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Follicular Lymphoma in a Young Male: A Case Report

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ABSTRACT

Follicular Lymphoma is an uncommon cancer that involves B-cells in germinal centres. Non-Hodgkin's lymphoma is also significantly represented by follicular lymphoma; different morbidity figures are observed in some countries. This case report describes the clinical journey of a 33-year-old man whose shortness of breath, worsening cough, along systemic symptoms culminated in a diagnosed case of follicular lymphoma. Hepatosplenomegaly was observed on clinical examination, and laboratory blood tests showed lymphocytosis and significant lymphadenopathy. Quick diagnostic imaging such as Ultrasound and X-rays/CT scans was instrumental in determining disease extent. Later, following further discussions between a haematologist-oncologists at the tertiary care centre and a definitive biopsy of lymph nodes,, the final diagnosis was affirmed as Follicular lymphoma, Grade 1A, accompanied by circulating lymphoma cells in the peripheral blood. This incident exemplifies the significance of identifying Follicular Lymphoma at an early stage, conducting a thorough evaluation, and involving many medical specialists in treating it. For optimal outcomes in patients with follicular lymphoma, timely interventions and tailored treatments may be necessary.

INTRODUCTION

FL is a relatively common systemic neoplasm characterised by the differentiation of B cells of the germinal centre (Carbone *et al*., 2019). This is about 5% of all blood cancers and approximately 20-25% of new cases of non-Hodgkin lymphomas in Western countries (Carbone *et al*., 2019). FL is the second most prevalent lymphoma in the United States, with an estimated annual diagnosis of approximately 14,000 patients(Batlevi *et al*., 2020). Fl exhibits variations in its prevalence across regions, with it being less common in Central and South America, accounting for 20% of all non-Hodgkin lymphomas(Carbone *et al*., 2019). FL does not display a strong prediction for either gender. However, its incidence tends to rise with advancing age, with a median age at diagnosis of 65 years, rarely manifesting in children and adolescents(Batlevi *et al*., 2020). Although there is a slightly increased risk of FL among individuals with affected relatives, the absolute risk remains relatively low(Carbone *et al*., 2019). FL's oncogenic journey begins in precursor B-cells and culminates in a fully developed tumour upon reaching the terminal centre maturation stage. The diagnosis of FL hinges upon histological analysis of a biopsy obtained from affected lymph nodes, with preference given to incisional biopsies to facilitate grading and transformation assessment(Freedman & Jacobsen, 2020). A defining genetic hallmark in the majority of FL cases is the t(14,18) translocation involving the igH/bcl-2 genes(Freedman & Jacobsen, 2020). Rituximab, often in combination with chemotherapy, is effective but not curative for treating FL(Cahill & Smith, 2022). Lenalidomide and rituximab provide a chemotherapy-free option for both initial and relapsed cases(Cahill & Smith, 2022). Replace patients may benefit from PI3 kinase inhibitors and anti-CD20 therapy, with stem cell transplantation rarely needed(Freedman & Jacobsen, 2020).

Our case report seeks to provide valuable insights into the challenges and multidisciplinary approaches involved in diagnosing and treating this haematological malignancy, ultimately contributing to medical knowledge and improving patient care in similar cases.

Case Presentation

A 33-year-old male presented on May 30th 2023 at Al Ain Hospital /Al Ain Region, Central District - Abu Dhabi - United Arab Emirates, with a chief complaint of worsening shortness of breath over the past four weeks. He also reported experiencing a cough that worsened when lying flat on the back. The patient reported that the shortness of breath had progressively worsened over the last month. Initially, he experienced it only with physical exertion, but it advanced to the point where he felt shortness of breath even during minimal activity like walking 10 meters. Notably, he observed that the cough became more pronounced when he lied down.

Additionally, he reported orthopnea, which was difficulty breathing when lying flat , and tachypnea. The patient was informed about the cervical lymphadenopathy in 2019 and was advised, as per the patient's statement, to consult a dentist. Remarkably, over 4.5 years, the patient did not seek any medical attention or consult with any physician regarding this issue, suggesting a prolonged period of unaddressed concern related to cervical lymphadenopathy.

On initial examination at the hospital, the patient was obese and had a pale complexion. He also experienced diaphoresis, characterised by excessive sweating. Clinical

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Test Item	Text Result	GrowthQualifier	Value	Pathogen Sub Type	Status	Units	Reference F
White Cell Count			27.3		Final	10^3/uL	3.6-10.2
Red Cell Count			3.71			10^6/uL	4.06-5.63
Haemoglobin			8.1			g/dL	12.5-16.3
HCT(PCV)			27.3			%	37-47
MCV			73.6			fL	73.0-96.2
MCH			21.8			pg	23.8-33.4
MCHC			29.7			g/dL	32.5-36.3
RDW			18.9			%	12.1-16.2
Platelet Count			223			10^3/uL	150-410
MPV			6.8			fL	7.4-11.4
Nucleated RBC			0.3			/100 WBC	0-0.6
Neutrophils			6.30			10^3/uL	1.70-7.60
Lymphocytes			19.40			10^3/uL	1-3.20
Monocytes			1.20			10^3/uL	0.3-1.10
Eosinophils			0.3			10^3/uL	0-0.5
Basophils			0.2			10^3/uL	0-0.1
Neutrophils %			23.1			%	43.5-73.5
Lymphocytes %			70.90			%	15.20-43.30
Monocytes %			4.30			%	5.50-13.70
Eosinophils %			0.9			%	0.8-8.10
Basophils %			0.8			%	0.2-1.5

Figure 1: Laboratory Results

examination revealed that the patient exhibited significant sinus tachycardia, with a heart rate exceeding 120 beats per minute. Upon auscultation of the posterior chest, bilateral crepitations was noted. The patient's oxygen saturation (SpO2) was measured at 94%. The patient presented with generalised lymphadenopathy, observed in both sides of the neck, axillae, and inguinal region. While the abdomen was soft to palpation, it appeared distended due to significant hepatosplenomegaly. An ECG confirmed sinus Tachycardia. Laboratory findings included high CRP, an ESr of 74, significant lymphocytosis, a white cell count of 27,000, and an HB level of 8.1 g/dl. Peripheral smear results raised concerns about haematological abnormalities (Figure 1).

The peripheral smear report reveals leukocytosis with a significant presence of mature lymphocytes characterised by cleaved nuclei and smudged cells, as shown in Figure 2 below. Platelet counts remain within adequate levels. These haematological findings are suggestive of a clinical condition associated with lymphoma.

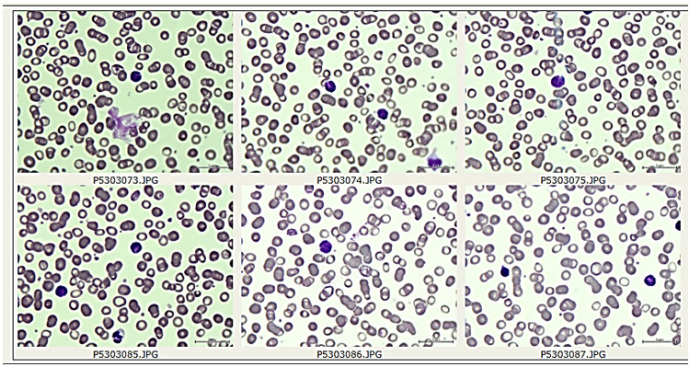

Figure 2: Peripheral Smear Report

Urgent diagnostic imaging was undertaken, including ultrasound and x-ray examinations, followed by subsequent CT scan of the neck/thorax, abdomen and chest. These diagnostic procedures were conducted promptly to assess the patient's medical condition and obtain detailed information about the relevant anatomical areas.

The ultrasound of the upper abdomen shown in Figure 3 reveals an enlarged cirrhotic liver measuring approximately xxx cm with a nodular echo pattern, suggestive of cirrhosis. The left portal vein is patent with normal diameter and the intrahepatic bile ducts and liver vasculature appear normal. The gallbladder is normal in size, configuration and contour with no gallstones seen. The pancreas is clearly visualized due to colonic gas and appears normal. The spleen is significantly enlarged, measuring approximately 22 cm. Both kidneys are of average size and normal sonographic structure with clear perinephric facial planes, no renal stones or cysts/masses seen, and no hydronephrosis. There is significant lymphadenopathy noted at the iliac chains bilaterally with compression of the bladder.

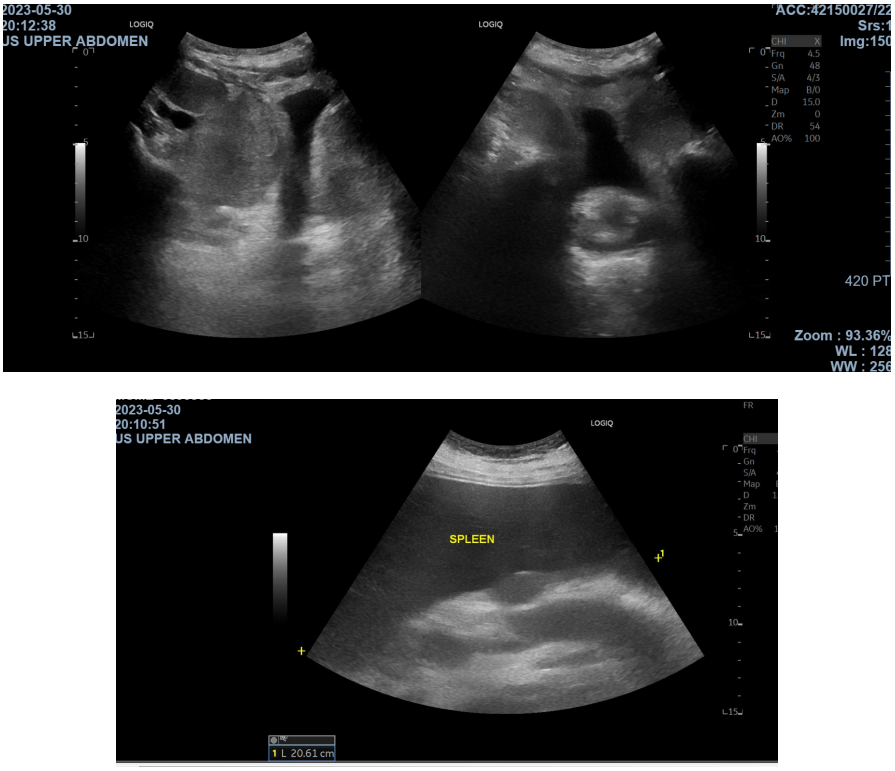

Figure 3: Ultrasound Upper Abdomen

The chest X-ray, as shown in Figure 4 below, showed marked enlargement of both hila in the lungs, primarily attributed to lymphadenopathy. Additionally, interstitial pulmonary infiltrates were identified in both lung fields, suggesting the presence of abnormal cells within the interstitial spaces of the lungs. Furthermore, extensive lymphadenopathy at the iliac chains bilaterally was observed, which was causing compression of the bladder and may lead to urinary symptoms. Moreover, hepatosplenomegaly was evident, with the liver displaying clear enlargement and a nodular echo pattern, particularly at the left lobe.

The neck ultrasound assessment (Figure 5) showed normal lymph nodes in the neck. The results indicated the presence of numerous enlarged lymph nodes on both sides of the neck. Additionally, there were hypoecholic lesions observed within the parotid glands on both sides. The preserved fatty hilum within the enlarged lymph nodes suggested characteristics typically associated with reactive lymph nodes.

The radiographic findings from the CT scan of the chest and thorax, shown in Figure 6 below, showed noticeable lymph node enlargement. The most significant enlargement was seen in the submandibular region, where the largest nodule measured 2.3cm in diameter. It was also noted that there were retrocrural lymph nodes, particularly on the left side. Additionally, it was discovered that the internal and pericardial mammary chains had lymphadenopathy. Interestingly, the intralobular septations in the lungs showed a noticeable

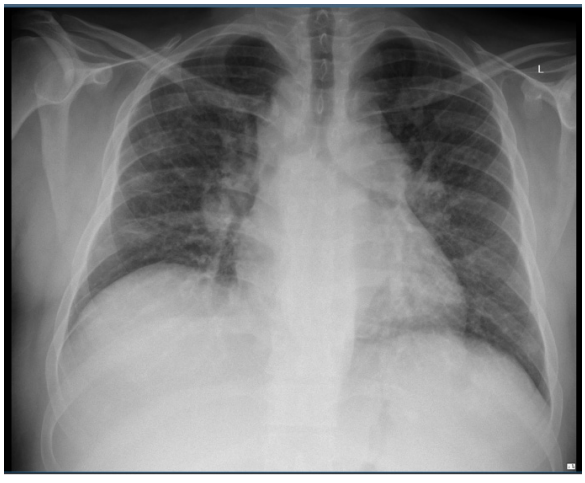

Figure 4: Chest X-Ray

US Neck Misc Final

NECK ULTRASOUND:CLINICAL HISTORY: Bilateral routine nodesFINDINGS:Multiple bilateral cervical enlarged lymph nodes are noted. The largest lymph node on the right side at level 2 measures about 5.5 x 1.8 cm, and the largest on the left side at level 2 measures about 3.5 x 1.8 cm in short axis.Bilateral intraparotid hypoechoic lesions most likely represent enlarged lymph nodes, it measures about 1.2 x 0.8 cm on the right parotid gland and 3.3 x 1.6 cm on the left parotid gland.The fatty hilum of most of the other mentioned enlarged lymph nodes is preserved, features most likely represent reactive lymph nodes. However, other possibility like neoplastic process, lymphoma cannot be excluded.Otherwise, no soft tissue mass lesion or fluid collection is seen.CONCLUSION:Multiple bilateral cervical lymphadenopathy. Bilateral intraparotid enlarged lymph nodes. Features most likely represent reactive lymphadenopathy and less likely neoplastic.Note: Findings are based on the images obtained by the sonographer.

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Figure 5: Neck Ultrasound Report

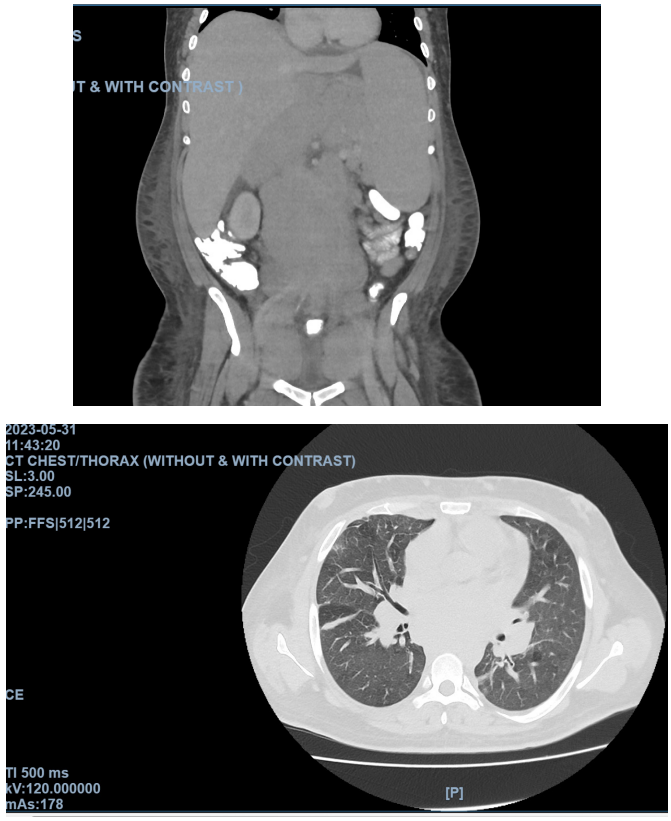

Figure 6: CT Chest/Thorax (Without and With Contrast)

thickening, which suggested lymphangitis carcinomatosis. Small pulmonary nodules were also present, which were most obvious in the midzone of the right lung. In both axillary regions, there was also significant lymph node enlargement, with some lymph nodes growing as large as 4 cm.

The CT scan of the abdomen and pelvis revealed important liver-related findings. Figure 7 illustrates these findings, which included liver enlargement and the presence of a nodular echo pattern, which was most obvious in the left lobe. The portal vein remained open, which was significant because it showed continuous blood flow. The intrahepatic bile ducts and liver vasculature also looked normal, and the portal vein's diameter and patency were within normal limits. There were no clearly visible gallstones inside the gall bladder, which had a typical size, shape, and contour. There were no notable abnormalities in the liver's surrounding region. The common bile ducts maintain a normal diameter and patency. Hepatic Segment Inferior Vena Cava demonstrates a typical diameter with unobstructed hepatic vein patency. Additionally, the spleen is notably enlarged, measuring 22cm. Lastly,

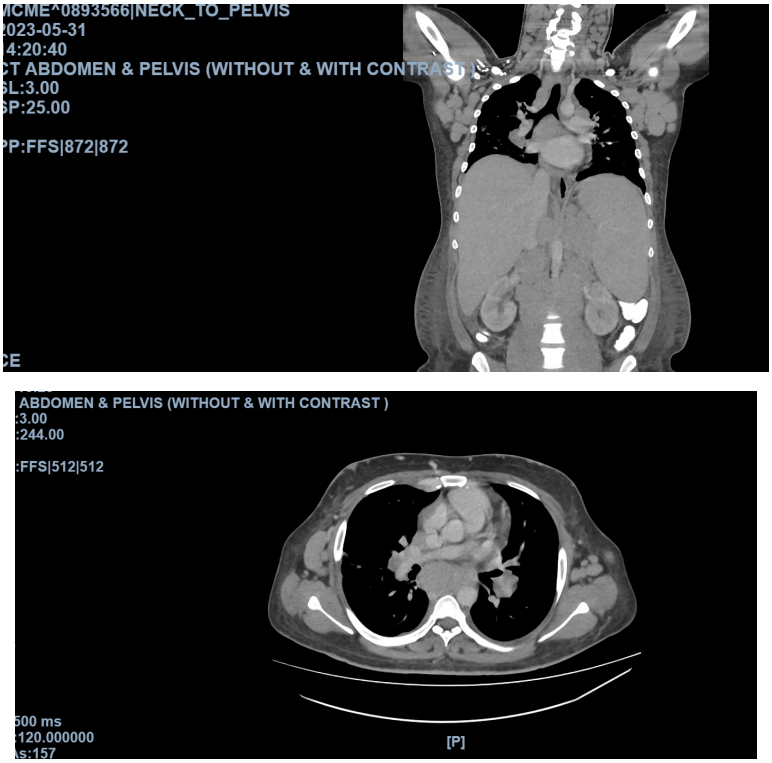

Figure 7: CT Abdomen and Pelvis (Without and With Contrast)

significant lymphadenopathy was observed at the iliac chains, resulting in compression of the bladder.

The images show significantly enlarged lymphadenopathy in the neck, abdomen, pelvis, axillary, and inguinal regions, among other body parts. Hepatosplenomegaly was also seen, which points to lymphoma. Excisional lymph node biopsy was highly advised in order to confirm the diagnosis and carry out a thorough assessment.

The case was discussed with a haemato-oncologist at Tawam Hospital, a tertiary hospital in the Emirate of Abu Dhabi. The haemato-oncologist recommended performing a lymph node biopsy to definitively confirm the diagnosis, a crucial step for acceptance into their department. Simultaneously, the patient was advised to initiate treatment with dexamethasone and allopurinol, medications that were prescribed to manage the condition. Following the referral for a lymph node biopsy, the patient was initially scheduled to undergo the procedure at the facility hospital; however, the patient did not attend. Subsequently, the patient sought care at Tawam Hospital. There, the lymph node biopsy was successfully performed on July 12th 2023, and the results confirmed the final diagnosis of Follicular Lymphoma, specifically Grade 1A. Notably, circulating lymphoma cells were detected in the patient's peripheral blood. Fortunately, the absence of B symptoms in the clinical presentation indicated a relatively less aggressive form of the disease. This multidisciplinary approach underscores the importance of accurate diagnosis and the immediate initiation of appropriate treatment in managing the patient's medical condition. These findings were pivotal for guiding the subsequent management and treatment plan for the patient's condition.

Impression and Plan

Diagnosis

Follicular lymphoma grade I (ICD10-CM C82.00, Working, Medical).
Follicular lymphoma grade I (ICD10-CM C82.00, Working, Medical).
Anemia in neoplastic disease (ICD10-CM D63.0, Working, Medical).

Course: Worsening.

Figure 8: Final Diagnosis

In the tertiary hospital, a thorough workup was conducted for the patient diagnosed with FL to precisely determine the extent of the disease and devise an optimal treatment approach. This evaluation included a thorough physical examination with an emphasis on the size of the liver, spleen, and areas that contained lymph nodes. The clinical performance status and the presence of B symptoms were evaluated to assess general health and symptomatic presentation. A full metabolic panel was used in the laboratory tests to assess metabolic parameters, as well as a complete blood count with differential and LDH measurements to track blood cell levels and disease activity.

A treatment plan of bendamustine and rituximab/obintuzumab was discussed with the patient. This will be followed by maintenance therapy with rituximab or obintuzumab. An alternative of CHOP-R (cyclophosphamide, doxorubicin, vincristine, prednisone plus rituximab) chemotherapy followed by rituximab maintenance was also recommended, if the patient's disease is limited to follicular lymphoma. Due to the patient's age and fertility concerns with chemotherapy, fertility issues were discussed in detail. The patient was counselled on the potential risks to fertility from chemotherapy and the recommendation was made for him to pursue sperm banking prior to starting treatment.

All treatment options, potential side effects, risks and benefits were properly explained to the patient and an informed consent was obtained.

A high-quality PET-CT scan was essential in identifying nodal and extranodal disease involvement during imaging studies. To assess cytopenias and record the disease stage, a bone marrow biopsy and aspirate were carried out. The patient had stage 4 FLIPI risk 4 and a Grade 1a FL, with an estimated 10-year survival rate of 35% and a leukemic phase. The importance of a multidisciplinary approach to FL management is highlighted by the fact that this thorough workup served as the basis for creating a treatment plan that took into account the disease stage, risk factors, and the patient's general health and fertility-related needs.

DISCUSSION

FL is characterised by its indolent nature, slow progression, and favourable outcomes, with an annual incidence of approximately 3.18 cases per 100,000 individuals. This incidence, while stable over time, exhibits variations with ethnicity, with the highest occurrence among white individuals. Fl accounts for a significant portion of non-Hodgkins lymphoma cases.

FL typically presents in older individuals, with a median age of >60 years at diagnosis (Freedman, 2018; Freedman & Jacobsen, 2020). However, our patient's relatively young age at presentation highlights that FL can occur in younger adults, although it remains less common in this age group. This observation aligns with the rarity of FL in pediatric and adolescent populations. FL presents insidiously with lymphadenopathy, often involving cervical, axillary, or inguinal lymph nodes. Patients may also experience systemic symptoms such as fever, night sweats and unintentional weight loss, referred to as B symptoms (Alnoor, Gandhi, Stein, & Gradowski, 2020; Dada, 2019). The diagnosis of FL relies on histological examination of a biopsy to assess grade and transformation potential accurately(Dada, 2019). Immunohistochemical staining is essential for confirming FL, with characteristic markers CD19, CD 20, CD10 monoclonal immunoglobulin and cytoplasmic expression of bcl-2 protein (Agostinelli *et al.*, 2019; Alnoor *et al.*, 2020). A case report by Tomohiko Tanigawa *et al.* (2019) illustrates the occurrence of histological transformation from Grade 1 FL to Diffuse large B cell Lymphoma. Despite initial observation, the FL eventually transformed, leading to widespread involvement and resistance to standard chemotherapy (Tanigawa *et al.*, 2019). In another case study by Sarah Péricart *et al.* (2019), a 65-year-old man presented with a large abdominal mass and lymphadenopathy, raising suspicion of lymphoma(Péricart *et al.*, 2020). Biopsy revealed large tumour cells expressing histiocytic markers but lacking lymphoid markers. The diagnosis was histiocytic sarcoma (HS). Due to clinical and histological discordance, further lymph node biopsy was performed to confirm the diagnosis(Péricart *et al.*, 2020). The literature revealed that both FL and HS tumours exhibited the t(14,18) translocation and shared clonal rearrangement, suggesting a clonal relationship between the two malignancies (Péricart *et al.*, 2020). Furthermore, the patient's leukocytosis with mature lymphocytes and smudged cells on the peripheral smear is consistent with haematological abnormalities often observed in lymphomas(Chabot-Richards & George, 2014). This reinforces the significance of haematological assessments in the diagnostic workup of lymphoma patients.

The treatment approach for FL depends significantly on the disease stage at the time of diagnosis (Lu, 2005). Patients with stage I disease, where the lymphoma is localised to one lymph node region or organ, often undergo radiation therapy (Los-de Vries *et al.*, 2022). In contrast, patients diagnosed with stage III or IV disease, collectively termed "advanced stage," are not typically curable with conventional therapies(Attarbaschi *et al.*, 2020). Instead, the focus shifts towards managing FL as a chronic condition with an emphasis on symptom control and improving the patient's quality of life(Lu, 2005). Many individuals with stage III or IV FL receive a combination of various treatment modalities over time, including immunotherapy, chemoimmunotherapy, and radiation therapy, often administered in different sequences with periods of active therapy followed by observation and surveillance(Attarbaschi *et al.*, 2020; Los-de Vries *et al.*, 2022).

Ultimately, the choice of treatment is tailored to the individual patient's specific clinical presentation and needs, with the goal of optimising outcomes and minimising the impact of FL on their daily life.

CONCLUSION

The case reports underscore the significance of early diagnosis, thorough evaluation, and a multidisciplinary approach in managing FL Grade 1A. Despite its indolent nature, FL can manifest in individuals of varying ages. The absence of B symptoms indicated a relatively less aggressive form of FL, offering a more favourable prognosis. This case emphasises the importance of tailored treatment strategies to optimise outcomes in FL and highlights the ongoing need for research and clinical experience to enhance FL management.

LIMITATIONS

The report can not be generalised as it focuses on a single case. Another limitation of the case is the missing long-term follow-up and management of the case, which could have given more information about the case.

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