



Retroperitoneal Mass: Lymphoma as Differential Diagnosis to Retroperitoneal Fibrosis: Case Report

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Abstract

The etiology of solid retroperitoneal mass may be autoimmune or neoplastic and should be investigated by imaging and histology. The spectrum of differential diagnoses includes retroperitoneal fibrosis and retroperitoneal tumors. As treatment for these entities differs substantially, early and accurate diagnosis is essential. We present a case of a 54-year-old woman admitted to our hospital with stroke-like symptoms. Suspecting vasculitis, magnetic resonance imaging of the head and abdomen was performed, which revealed circular enhancement of the internal carotid artery as well as retroperitoneal and periaortic masses. In light of the radiographic findings, an autoimmune process, such as retroperitoneal fibrosis, was hypothesized. Steroid treatment was initiated but did not lead to significant remission. Re-evaluation of the mass with fine-needle aspiration did not show malignant cells while diagnostic surgery and histological assessment revealed neoplastic lymphoproliferation. The final diagnosis was a non-Hodgkin B-cell lymphoma. Chemo- and immunotherapy were initiated. Follow-up abdominal computed tomography revealed significant remission of the retroperitoneal mass. Initially, the retroperitoneal mass was highly suspicious for RF. While imaging can be useful, obtaining histology should always be considered when there is an uncertain clinical presentation. Without histology, we would have missed a non-Hodgkin B-cell lymphoma in this case. Minimally invasive techniques such as fine-needle aspiration may be practical but can give false-negative results.

Keywords Retroperitoneal mass · Retroperitoneal fibrosis · Lymphoma · Case report

Background

Retroperitoneal masses can present a diagnostic challenge to clinicians because radiological findings may suggest a number of possible diagnoses. The most likely diagnosis is retroperitoneal fibrosis (RF), characterized by chronic soft tissue fibrosis and often lead to compression of retroperitoneal

organs (e.g., obstructive mega-ureter/hydronephrosis and renal failure) and/or compression of veins, arteries, and lymphatic vessels leading to edema, thrombotic disease, hydrocele, and claudication [1]. In the retroperitoneum, lymphoma is the most frequent malignant tumor after retroperitoneal sarcoma [2, 3], but metastases originating from germ cell tumors or other epithelial tumors may also be seen in the retroperitoneal space [2]. However, the retroperitoneal space is uncommon as the primary site and exclusive manifestation of a malignant lymphoma [3–5]. Retroperitoneal lymphomatous involvement may be secondary to continuous spread from abdominal lymph nodes [5]. Radiological imaging may permit initial differential diagnostic triage, particularly with respect to RF [6], but this needs to be confirmed histologically [1].

We present a case of a 54-year-old female patient with an unclear retroperitoneal mass not responsive to steroid treatment.

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Case Presentation

A 54-year-old woman with a medical history of unprovoked lung and cerebral embolism presented with paresthesia and disabling weakness of the right hand that had persisted for 3 days. She also reported daily headache attacks for three weeks. At clinical presentation, the patient was afebrile and hypertensive (167/78 mmHg) with a normal pulse rate (HR 71 bpm). Her body weight was 90 kg (calculated BMI of 29.4 kg/m²) and she had normal oxygen saturation (95%) on ambient air. The heart and lung examinations were normal. Neurological findings showed paresis of the right finger movements (i.e., extension, flexion, spreading of the fingers, ab- and adduction, as well as opposition of the thumb). The remainder of the examination was normal.

Routine laboratory testing revealed normal C-reactive protein (CRP) levels and erythrocyte sedimentation rate (ESR). Creatinine was mildly elevated (111 µmol/L (normal value < 95 µmol/L); calculated GFR (Cockcroft-Gault) 73 mL/min, reference value > 70 mL/min). Liver enzymes, protein electrophoresis, blood count, and urinalysis were normal. Autoimmune serology did not show antinuclear antibodies (ANA) or antineutrophil cytoplasmic antibodies (ANCA), and there was no elevation of antiphospholipid antibodies. Testing for hereditary or acquired thrombophilia was negative. Magnetic resonance imaging (MRI) of the head showed multiple cerebral infarctions, but the most striking finding was an isolated circular enhancement of the left internal carotid artery (ICA), suggesting vasculitis. A 24-h ECG examination was normal. Abdominal sonography demonstrated a shrunken left kidney. Finally, MRI revealed extensive periaortic and left para-aortic soft tissue masses along the left internal iliac artery measuring 6.5 × 2.5 cm. Two computer tomography (CT)-guided fine needle aspirations (FNA) of the retroperitoneal mass were performed without any conclusive cytologic or molecular genetic results, neither for retroperitoneal fibrosis (Ormond's disease; CD 38 and IgG4 negative) nor for malignancy.

Initially assuming idiopathic retroperitoneal fibrosis, prednisone treatment was commenced but proved ineffective. Follow-up cranial CT 6 months after presentation showed a decline in ICA vessel caliber and wall enhancement compared to initial findings, while CT follow-up of the abdomen at month 5 demonstrated progression of the retroperitoneal mass. As the mass extended from the renal hilus deep into the pelvis and was intimately associated with vessels and the ureter, complete resection without a firm diagnosis was rejected. A diagnostic, robot-assisted laparoscopy was performed with the goal of obtaining as much tissue as possible for examination in a minimally invasive way.

Tissue samples from the left iliac region obtained by diagnostic robotic laparoscopy were compatible with

malignant B-cell lymphoma, both morphologically and immunohistochemically. This was verified with immunoglobulin heavy chain gene rearrangement by polymerase chain reaction (PCR) that yielded clonality in frameworks 2 and 3 (Fig. 3). Six months of chemo- and immunotherapy with R-bendamustine was administered. Eight months after diagnosis, partial remission was observed, with a reduction in the size of the retroperitoneal mass in response to chemotherapy. Therapy was well tolerated by the patient who remained in good condition and regularly attended the planned follow-up visits. Currently, maintenance therapy with rituximab is planned for two additional years to optimize progression-free survival. NHL has a good prognosis with contemporary treatment, with 5-year survival rates of over 80% [7].

Discussion and Conclusion

This case report illustrates the challenges associated with the diagnosis of a retroperitoneal mass. Initially, we diagnosed the mass as RF, but subsequent histologic work-up confirmed the presence of B-cell lymphoma. Initial neurological presentation with stroke due to multiple cerebral vascular irregularities led to the assumption of vasculitis. Further diagnostic steps to confirm vasculitis consisted of angio-MRI of the entire aorta and proximal vessels, which revealed an unexpected retroperitoneal mass interpreted as RF. Clinical onset of RF may be asymptomatic or may mimic lymphoproliferative diseases [8]. The main symptoms of RF arise from the compression of retroperitoneal organs. Additional symptoms include non-specific constitutional symptoms such as fatigue, anorexia, and weight loss [1].

In our case, FNA failed to achieve a conclusive diagnosis, although the MRI appearance was characteristic of RF. In line with other cases described in the literature, we noted a periaortic mass (Figures 1 and 2) with pelvic extension and associated ureteric encasing [9]. Glucocorticoid treatment was ineffective. CT follow-up of the abdomen 5 months later showed progression of the mass with no systemic inflammatory signs, which made us reconsider the diagnosis.

Inflammatory markers such as ESR and CRP are elevated in more than 50% of RF patients [10]. In approximately one-third of cases, RF is secondary to other causes (i.e., infection, autoimmune disease, medications, radiotherapy, surgery, malignant lymphoma, or other cancers found in about 8% of cases). Two-thirds of RF cases is considered to be idiopathic [6]. IgG4-related disease (IgG4-RD) leading to RF is a fibro-inflammatory condition characterized by a dense lymphoplasmacytic infiltrate rich in IgG4-positive plasma cells and involving sclerosis including lymph nodes [6]. In their case report, Sato et al. postulated neoplastic potential of IgG4-producing cells leading to lymphoma [11],

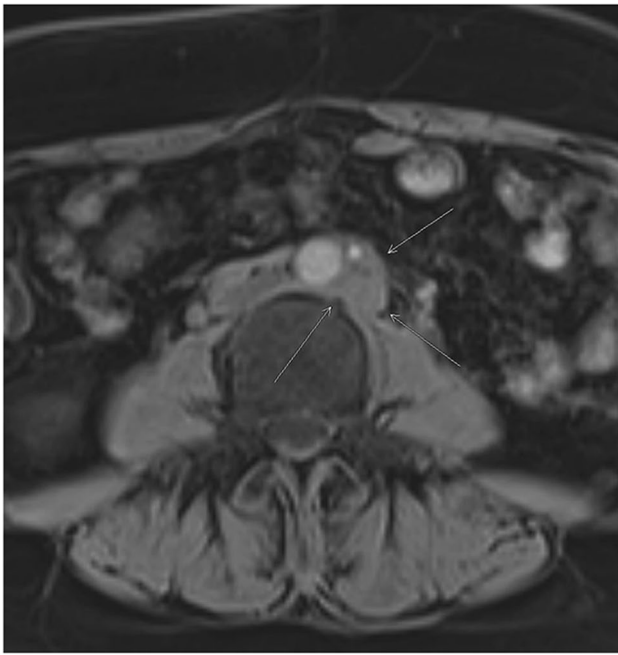


Fig. 1 Unenhanced, axial T1-weighted fat-suppressed magnetic resonance image of the abdominal aorta showing a retroperitoneal left-sided periaortic mass (indicated by arrows)

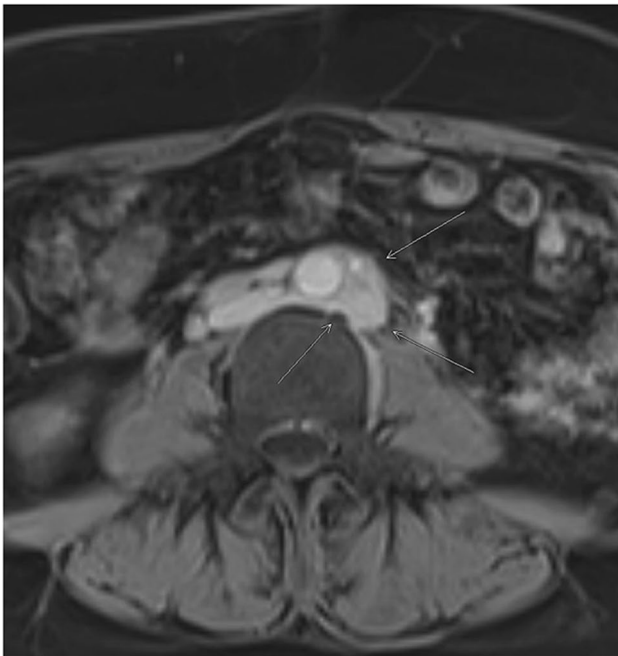


Fig. 2 Gadolinium-enhanced, axial T1-weighted fat-suppressed magnetic resonance image revealing enhancement of the periaortic mass (indicated by arrows)

but our patient had no serological elevation of IgG4. Histologic findings in biopsies obtained laparoscopically demonstrated clonal rearrangement of immunoglobulin heavy

chain genes (Figure 3: frameworks 2 and 3), thus confirming B-cell lymphoma.

Retrospectively, embolism could have been interpreted as part of a paraneoplastic syndrome, and vasculitis could have been understood as a secondary manifestation of extra-nodal lymphoma. Lymphoma predominantly occurs in suprarenal locations with perirenal extension and tends to be associated with retroperitoneal lymph node enlargement, resulting in larger contrast-enhanced areas [9]. These typical findings were not present in our patient. Further anterior displacement of the aorta and lateral displacement of the ureter seem to occur more often in malignancy than (idiopathic) RF [9].

Early in our diagnostic workup, FNA failed to rule out malignancy or RF. FNA has a limited role in the diagnosis of lymphoma because samples obtained by FNA do not provide the anatomic details derived from larger, intact nodal specimens [3]. Guo et al. compared 68 samples obtained by radiologically guided FNA with 36 biopsies of pelvic and retroperitoneal masses. The authors calculated a sensitivity of 90.2% and specificity of 100% for FNA [12]. Another study in 167 FNA samples obtained by ultrasonic guidance found a sensitivity of 86% and specificity of 100% in terms of differentiating between malignant and benign lesions of the retroperitoneum [13].

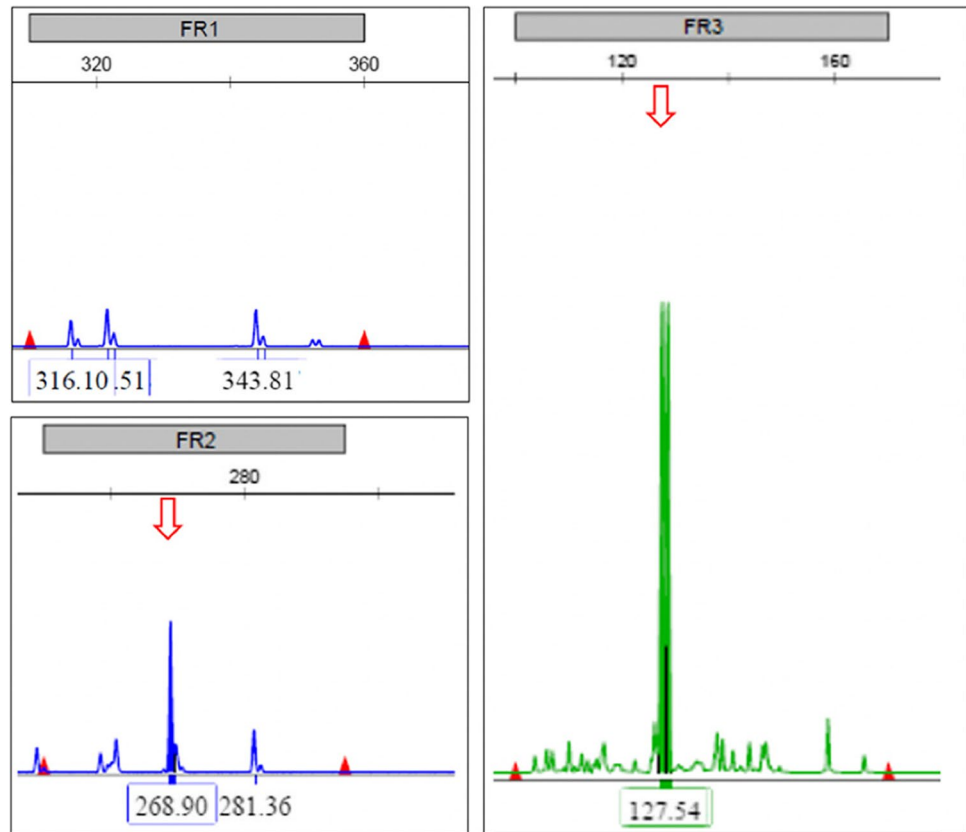
Although core biopsy allows larger specimens and a better evaluation of the tissue architecture, minimally invasive surgical tissue preservation was preferred due to the anatomical conditions and proximity to vessels with a correspondingly high risk of bleeding and injury to structures as well as unclear diagnostic significance after two negative FNAs.

After establishing the diagnosis of malignant B-cell lymphoma, therapy consisted of 6 cycles of R-bendamustine to prevent compression of the ureter as well as further retroperitoneal spread. The patient has been receiving rituximab maintenance therapy for 2 years. Interestingly, the cerebral vascular lesions had normalized 6 months after the start of prednisone treatment as seen in the follow-up MRI of the head. This may have been due to glucocorticoid treatment.

In conclusion, lymphoma mimicked RF in terms of imaging characteristics and vasculitis in our patient. Retrospectively, we should have aimed to obtain a histological diagnosis at the index presentation and not in the context of refractory disease. Diagnostic, minimally invasive procedures to obtain biopsies of deep masses can play a useful role in such cases, as the volume of tissue extracted by FNA tends to be insufficient for further investigations (i.e., microscopic examination, flow cytometry, immunophenotyping, and molecular analysis) [3].

Abbreviations ANA: antinuclear antibody; ANCA: antinuclear cytoplasmic antibody; bpm: beats per minute; BMI: body mass index; CRP: C-reactive protein; CT: computed tomography; CD: cluster of differentiation or cluster of designation; ECG: electrocardiogram; ESR: erythrocyte sedimentation rate; FNA: fine needle aspiration;

Fig. 3 Clonal rearrangement of the immunoglobulin heavy chain gene locus (IGH) in frameworks II (FR2) and III (FR 3) next to a polyclonal rearrangement pattern in the framework I (FR 1) revealed by Multiplex-PCR (IdentiClone IGH Gene Clonality Assay) and fragment analysis



GFR: glomerular filtration rate; HR: heart rate; ICA: internal carotid artery; IgG: immunoglobulin G; IgG4: immunoglobulin G4; IgG4-RD: immunoglobulin G4-related disease; kg: kilogram; RF: retroperitoneal fibrosis; mmHg: millimeters of mercury; MRI: magnetic resonance imaging; NHL: non-Hodgkin lymphoma; PCR: polymerase chain reaction; R-bendamustin: rituximab-bendamustine

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Author Contributions M.N. wrote and reviewed the manuscript. O.K. and S.G. contributed radiological and histological images and interpretation. G.M. contributed to manuscript revisions. T.N. wrote and reviewed the manuscript. All authors read and approved the final manuscript.

Data Availability The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval and Consent to Participate Ethical approval was not required for this single case report.

Consent for Publication Written, informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor of this journal.

Competing Interests The authors declare no competing interests.

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