

CASE REPORT

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Lymphoma Mimicking Signs of Deep Vein Thrombosis

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ABSTRACT The patient complained of leg swelling and pain, venous thrombosis was reported on Doppler ultrasonography, D-dimer value was high, hormones test was positive and did not respond to anti-coagulant and elevation. The thrombosed pseudo aneurysm mass, which had previously undergone an interventional procedure in the same leg, was found to be enlarged on control magnetic resonance imaging. Operation was decided to reduce the increased congestion. The soft tissue mass causing congestion was excised along the vascular bed. No vascular pathology was observed in the superficial and deep venous bed. Pathology revealed diffuse large B-cell lymphoma. Although clinical findings and laboratory values were suggestive of deep vein thrombosis, we wanted to emphasise that malignant diseases should be suspected in cases not responding to treatment.

Keywords: Lymphoma; thrombus

Deep vein thrombosis (DVT) arising from femoral artery pseudo aneurysm is a complication that has been underreported in the literature.¹ Although elevated D-dimer initially suggests venous thromboembolism, it may also increase with sepsis and/or cancerous diseases.² However, there are publications showing that the diagnostic accuracy of D-dimer in detecting venous thromboembolism (VTE) in cancer patients varies significantly according to the type of cancer. D-dimer has been reported to perform poorly in diagnosing VTE in patients with lymphoma or leukaemia.^{3,4} Although we know that colour Doppler ultrasonography (CDU) is 90.5% sensitive in diagnosing venous thrombus, we should not ignore malignant pathologies causing leg swelling.

CASE REPORT

The patient was informed that the case data would be published and a consent form was obtained. A 64-

year-old woman underwent femoral artery access for coronary angiography through the right groin 8 months ago. She had pain and swelling in the right groin. The pain and swelling increased in the following days. One month ago, a 50×22 heterogeneous hypoechoic lesion was diagnosed as thrombosed pseudo aneurysm by CDU. When the complaints of pain and swelling increased, Doppler was requested again. CDU examination of the right main and superficial femoral veins showed no filling with colour and did not respond to compression, which was reported as DVT. She was admitted to the outpatient clinic with a prediagnosis of venous thrombus. 14 years ago, total thyroidectomy was performed due to Graves' disease. She has been using 125 mcg levothyroxine 1x1 for 10 years. Type 2 diabetes for 13 years; 5 mg dapagliflozin 1x1 (Forziga) for 5 years. 5 mg linagliptin (Trajenta) has been used for 1 year. Urea and creatine values were normal. D-dimer 1,500

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ng/ml, sedimentation 32ml/H, Procalcitonin 0.06µg/L, Hemoglobin A1c 7.5 mmol/L. C-reactive protein (CRP) was 35mg/L. Aspartat aminotransferaz, alanin aminotransferaz and lactate dehydrogenase values were within normal limits. Renal values were within normal limits. Piperacillin Tazobactam 3x4.5 gr anticoagulant (Enoxaparin Sodium 60 mg/0.6 ml (100mg/ml) 2x1 Warfarin 5 mg 1x1) was started. The leg was elevated. The patient with increased CRP (75 mg/L) was started on linezolid 600 mg 2x1. On the 3rd day, oedema increased and haematocrit values decreased and anticoagulant treatment was terminated. Firstly, iliac and femoral artery CT angiography was performed followed by thigh magnetic resonance imaging (MRI) with and without contrast. The image, which was thought to be a right thigh haematoma, showed an increase in haematoma compared to the previous MRI. In the anamnesis, the complaint of swelling in the leg after angiography increased our suspicion. The fact that our patient's pain complaint also increased: led us to make a surgical decision to reduce congestion. One unit of TDP was given and the or-

thopaedics and traumatology clinic was consulted. The right thigh was dissected along the Hunter's canal (subsartorial, adductor canal) under general anaesthesia. No haematoma was seen. Intra operative Doppler ultrasonography (USG) along the incision line showed congestion in the femoral vein. It did not coapt with compression. Mass excision was performed along the canal (Figure 1). Samples were sent to pathology. After excision of the mass, control Doppler USG showed that the congestion disappeared and the femoral vein was coaptated. The specimen was reported as "Diffuse Large B Cell" Lymphoma. Immunohistochemically, CD20 diffuse, CD45, PAX5, MUM1, BCL6 were positively labelled in atypical lymphoid cells. CD5, MYC, BCL-2, CD10, CD3, CD138, CD15, CD30, EMA, ALK and EBV were negative and Ki-67 proliferation index was reported above 95% (Figure 2). Edema and congestion in the vulvar region and leg decreased rapidly after surgery. Chemotherapy (Rituximab, Cyclophosphamide, Doxorubicin, Vincristin, Prednisolone) was started by the haematology clinic after the diagnosis.

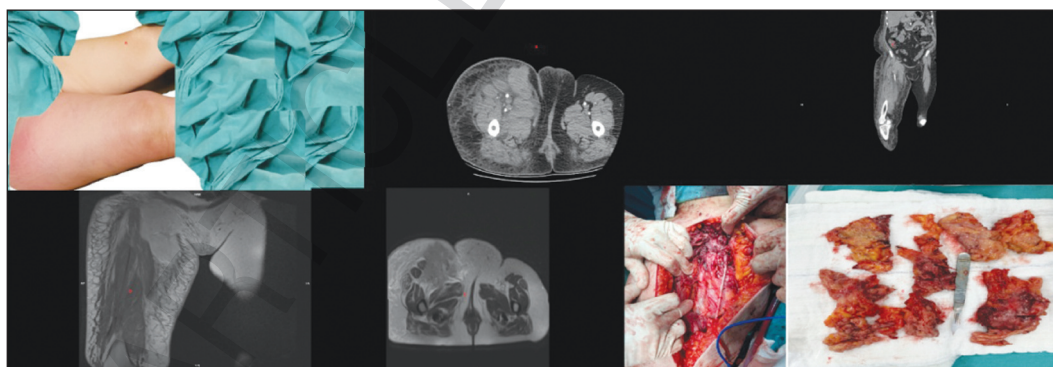


FIGURE 1: A) Patient's right leg oedema. **B)** CT angiography. **C)** Relationship of the mass with the vascular bed in the coronal plane. **D)** Coronal plane MRI soft tissue mass. **E)** Axial plane MRI soft tissue mass. **F)** Dissection along the Hunter canal. **G)** Specimens

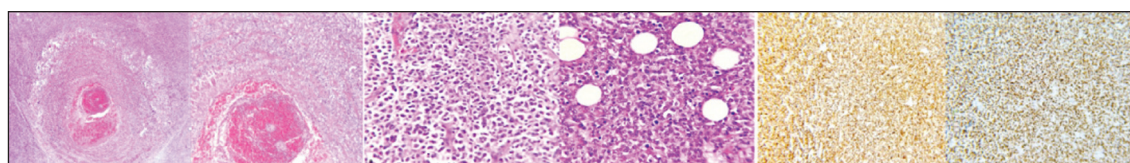


FIGURE 2: A) Presence of atypical B-cell lymphocyte infiltration within the vascular wall architecture (Hematoxylin and Eosin, x100, x400), **B)** Large, round atypical lymphocytes with prominent nucleoli and vesicular chromatin (Hematoxylin & Eosin, x400), **C)** Diffuse positive expression with CD20 (CD20, x200). The Ki-67 proliferation index shows nearly 100% positive expression (Ki-67, x200)

DISCUSSION

Non-Hodgkin Lymphoma (NHL) is the most common haematological malignancy. One of the subtypes of NHL is Diffuse Large B Cell Lymphoma (DLBCL). It is the most common histological subtype. It constitutes 30% of all NHLs in developed countries. Primary Skin Diffuse Large Cell Lymphoma, which involves one or both legs and is usually seen in women, has been reported to be one of the rare subtypes among all skin lymphomas (4%), with a 5-year survival rate of 40-60%.^{6,7} In 2018, the World Health Organization-European Organisation for Research and Treatment of Cancer classified skin-type lymphomas and categorized leg-Type B lymphomas.⁸ There are publications that detection of circulating tumour DNA (ctDNA) in blood samples (liquid biopsies), which is a minimally invasive method for disease follow-up in diffuse large B-cell lymphoma patients, is 100% sensitive.⁹ No such test was performed in our case. Another NHL subtype involving the leg has been reported as 0.1-1.4% among NHL involving skeletal muscles. The most common clinical finding is compartment syndrome and usually involves one leg.¹⁰ Intravascular large B-cell lymphoma is another pathology with a mortal course seen in one in a million people. It has been reported mostly in autopsy series.¹¹ Another Diffuse Large B cell lymphoma presenting with erythematous tumoural lesion in the leg has been reported.¹² Lymphomas with leg involvement with spontaneous remission have been reported in the literature.¹³ Another study reporting venous congestion with pseudo cellulitis finding is similar to our case. The distinguishing features of the above-mentioned Diffuse Large Cell B lymphomas causing swelling in the leg are presented as a list (Table 1).

There was no skin involvement in this patient. Positron emission tomography examination showed F-18 fluorodeoxyglucose uptake in the left cervical maximum standardized uptake value (SUV maximum=40.8), right pelvic inguinal mass lymph nodes (SUV maximum=43.5), left surrenal gland (SUV maximum=11.5) and bone (SUV maximum=6.2). Skeletal muscle uptake was not ob-

TABLE 1: Lymphomas causing leg swelling DVT, Lactate dehydrogenase, NHL

Lymphomas with leg swelling	Patient	Compartment syndrome/ venous congestion	DVT	Immunohistochemistry staining	Skin involvement	Muscle involvement	Liver Involvement	Secondary Malignancy	LDH
Primary skin diffuse large cell lymphoma (PCDBHL) ⁶	69 ♀	-	-	CD20, Bcl-2 (100%), C-Myc, Pax-5, Bcl-6(60%), CD3, CD4, CD8, CD43, CD2, CD7, MUM-1, Ki67 (90%)	+	-	+	+	1533 U/L
Recurrent lymphoma mimicking cellulitis ⁷	62 ♂	Venous congestion	-	CD20, CD45, PAX5, MUM1, Bcl-6	+	+	-	-	Unspecified
NHL involving skeletal muscles ¹⁰	62 ♀	Compartment	-	CD20, Bcl-2, C-Myc	-	+	-	+	19047 U/L
Intravascular diffuse large B-cell lymphoma ¹²	74 ♀	-	-	CD20, Bcl-2, Bcl6, MUM1, Pax5.	-	-	-	+	707 U/L
3Leg type diffuse large B-cell lymphoma ¹³	74 ♀	-	-	CD20, Bcl-2, Bcl-6, MUM-1, POX-P1, IGM, P63, Ki 67 (70%)	+	-	-	+	Unspecified
Diffuse large B cell lymphoma mimicking signs of DVT	64 ♀	Venous congestion	-	CD20, CD45, PAX5, MUM1, Bcl-6	+	-	-	-	236 U/L

PCDBHL: Primary skin diffuse large cell lymphoma; NHL: Non-Hodgkin lymphoma; DVT: Deep vein thrombosis

served. Intravascular uptake was not observed. There was an image mimicking cellulitis. Another detail is that the patient's use of sodium-glucose co-transporter 2 inhibitor (dapagliflozin) for 5 years and dipeptidyl peptidase-4 (linagliptin) for 1 year may have alleviated the progression of the disease. There are publications suggesting that these 2 groups of antidiabetic drugs act as anti-cancer agents and reduce tumour progression.^{14,15}

In conclusion, DLBCL may mimic DVT, lymphedema, thrombosed pseudo aneurysm, haematoma and cellulitis. Although RDUS is the gold standard in the diagnosis of DVT, femoral and iliac veins may not respond to compression. It may be interpreted as DVT. In patients presenting with pain and leg oedema without remission, CT angio/contrast-enhanced MRI examination should be performed and it should be considered that DLBCL may be present. Surgical intervention may be required to both relieve pain and reduce compression.

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: Osman Yaşar Işıklı, Ali Ateş, Burcu Yılmaz; **Design:** Osman Yaşar Işıklı; **Control/Supervision:** Osman Yaşar Işıklı, Ali Ateş, Burcu Yılmaz; **Data Collection and/or Processing:** Osman Yaşar Işıklı; **Analysis and/or Interpretation:** Osman Yaşar Işıklı; **Literature Review:** Osman Yaşar Işıklı, Ali Ateş, Burcu Yılmaz; **Writing the Article:** Osman Yaşar Işıklı; **Critical Review:** Osman Yaşar Işıklı, Ali Ateş, Burcu Yılmaz; **References and Fundings:** Ali Ateş, Burcu Yılmaz; **Materials:** Osman Yaşar Işıklı, Ali Ateş, Burcu Yılmaz.

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