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Case Report

A Case of Spondyloarthritis with Deep Vein Thrombosis

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ABSTRACT

Spondyloarthritis (SpA) is an autoimmune disease that has several clinical manifestations with certain characteristics. In this report, we present the case of an immobilized 54-year-old female with SpA who complained of a painful swollen left leg. Laboratory workup and imaging study supported the diagnosis of SpA complicated with deep vein thrombosis (DVT). The patient was given glucocorticoid, an anticoagulant, and medical rehabilitation. Symptoms improved following treatment. SpA increases the inflammatory state, leading to the increased risk of DVT. Holistic and comprehensive treatment is required in SpA patients with DVT to prevent further exacerbation or poorer prognosis.

Keywords: Spondyloarthritis; Deep vein thrombosis, Treatment, Complication.

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INTRODUCTION

Spondyloarthritis (SpA) is an autoimmune disease with clinical manifestations involving axial and peripheral joints, enthesitis, dactylitis, and extraarticular manifestation, including inflammatory bowel disease. Axial Spondyloarthritis (AxSpA) is divided into 2 groups which are (i) radiographic AxSpA mainly involves the spine and sacroiliac joint, ankylosing spondylitis (AS), and (ii) non-radiographic AxSpA, which showed no clear sign of sacroiliitis on x-ray examination.[1] In a systematic meta-analysis, Stolwijk et al[2] reported that the global prevalence of AxSpA ranges from 20/10,000 in Southeast Asia to 161/10,000 in Northern Artic. AxSpA patients have an elevated risk of Deep Vein Thrombosis (DVT) as a complication that is related to a high inflammation burden.[3] Here, we report the case of SpA with DVT as a complication to understand the comprehensive treatment.

CASE REPORT

A 53-year-old housewife was admitted to the emergency department due to exacerbating pain and limited range of movement on the patient's swollen left leg, starting from the groin to the sole, 2 weeks before admission. The swelling had been evident for 1 month. The patient was bedridden for 6 months due to initial trauma on her sacrum area which led to chronic lower back pain that exacerbated at night since then. The patient also complained of hair fall and tarry stool since 2 months prior, which had been exacerbating for 2 weeks. She also had chronic on-off diarrhea for 3 months. No facial rash or oral or mucosal ulcers were evident. The patient admitted no prior medical history nor family medical history. The patient took antalgin and dexamethasone for the last 6 months.

The patient's vital signs were within normal range. Abnormal findings on physical examination were anemic conjunctiva and swollen left lower extremity. Well's score was 5: swelling on the tibia, swollen left lower extremity, pain, immobilization, and pitting edema. The patient had an initial blood test (Table 1), urinalysis, stool analysis, and x-ray. Stool analysis showed erythrocyte 4-6/field and leukocyte 6-8/ field. Urinalysis and x-ray indicated osteophytes visible in corpus VL 2-3.

The patient was suspected of left lower extremity DVT, lower back pain (LBP) due to SpA, microcytic hypochromic anemia, hypoalbuminemia, post melena due to suspected Nonsteroidal anti-inflammatory drug (NSAID) gastropathy. The patient was treated with a high protein diet (2,100 calories), intravenous fluid drip of NaCl 0.9% 1,000 cc/ 24 hours, 1 bag of Pack Red Cell (PRC) transfusion, intravenous omeprazole 2x40 mg, ceftriaxone 2x1gram, metronidazole 3x500 mg, oral paracetamol 3x500 mg, and codeine 3x10 mg. The patient was consulted by the rheumatology, hematooncology division, and cardiovascular department.

The patient was treated as an inpatient for 13 days. Serial blood analyses were taken as described in Table 1. During follow-up, low back pain, and peripheral edema slowly reduced. The patient reported infrequent loose stools without melena. Patient vital signs were stable throughout follow-ups. On the second day of admission, the D-dimer result was revealed supporting the diagnosis of DVT. The Thorax and lumbal x-ray showed osteophytes visible in corpus VL 2-3 and sacroiliitis on the sacroiliac joint. Hence, axial spondyloarthritis was confirmed. The patient received additional treatment: head elevation 30-45°, gradual sitting position, application of elastic bandage on the lower extremity, AROM exercise, ankle and wrist elevation, and isometric quadriceps strengthening exercise. Subcutaneous fondaparinux 1x2.5 mg and intravenous dexamethasone 1x62.5 mg were added.

The left lower extremity venous ultrasound Doppler was completed on the 5th day and showed a thrombus on the left femoral and popliteal vein. Hence, left lower extremity DVT was confirmed. Additional treatment was oral sulfasalazine 2x500 mg and prebiotic lacto-b 3x1 sachet. The corticosteroid was tapered down and changed

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Table 1. Serial Laboratory Results on Admission to Discharge Day.

	Day-1	Day-2	Day-5	Day-9	Day-13
Hemoglobin	7.7		11.4	11.5	10.8
HCT	22.3		32.8	34.7	25.6
MCV	82.2		87.4	88.4	88.4
MCH	25.2		28.2	26.2	26.2
Leukocyte (/mm^3)	14,321		9,360	8,730	7,240
Neutrophil (%)	84%		77.5	70	77
Lymphocyte (%)	10.5%		14.5	19.7	16.7
Platelet (/mm^3)	178,000		279,000	263,000	263,000
Natrium (mEq/L)	137		135	139	134
Kalium (mEq/L)	3.9		3.4	3.7	4.0
Clorida (mEq/L)	102		105	102	104
Blood glucose (mg/dL)	148		142	162	132
Creatine (mg/dL)	0.7		0.6	0.5	0.8
BUN (mg/dL)	15		8	7	9
AST (U/L)	46		23	28	34
ALT (U/L)	52		25	15	21
Albumin	2.7		2.8	2.6	
PT	14.7		16.2		
aPTT	24.6		28.3		
HbsAg	Non-reactive				
HIV	Non-reactive				
Anti HCV	Non-reactive				
Blood gas analysis					
pH	7.42				
pCO_2 (mmHg)	31				
pO_2 (mmHg)	102				
HCO_3	24.5				
BE	-2.5				
SO_2 (%)	99				
D-dimer (ug/ml)		8,860	5,610	3,920	1,360
ANA		3.54			
C3 (mg/L)		51			
C4 (mg/L)		14.3			
CRP (mg/L)		29.8	35.6	15.6	10.2
ESR (mm/jam)		60			

Values are presented as number only. MCH: mean corpuscular hemoglobin; HIV: human immunodeficiency virus; BE: base excess; CRP: C-reactive protein; HbsAg: hepatitis B surface antigen; ALT: alanine aminotransferase; pO_2: partial pressure of oxygen; PT: prothrombin time; HCV: hepatitis C virus; SO_2: oxygen saturation; C3: complement 3; aPTT: activated partial thromboplastin time; HCO_3: bicarbonate; HCT: hematocrit; pCO_2: partial pressure of carbon dioxide; ANA: antinuclear antibody; ESR: erythrocyte sedimentation rate; AST: aspartate aminotransferase; C4: complement 4; MCV: mean corpuscular volume

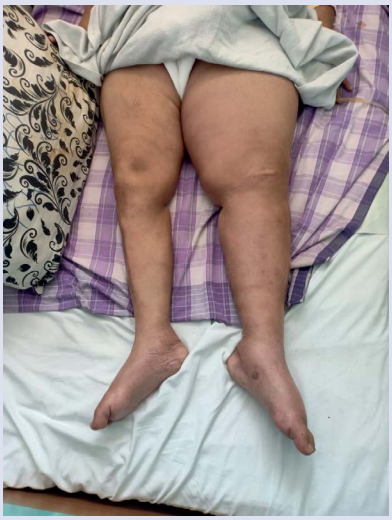

Figure 1. The Patient's Swollen Left Leg.

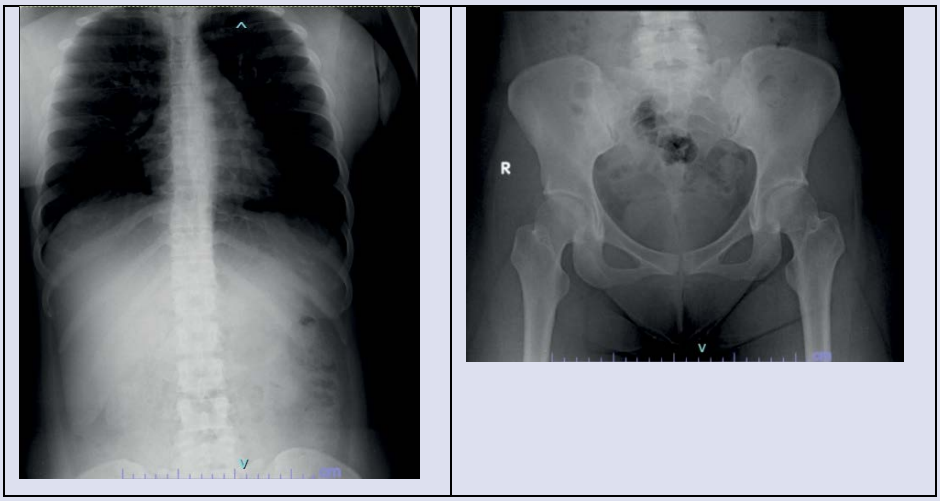

Figure 2. Osteophytes Visible in Corpus Vertebra Lumbalis 2-3.

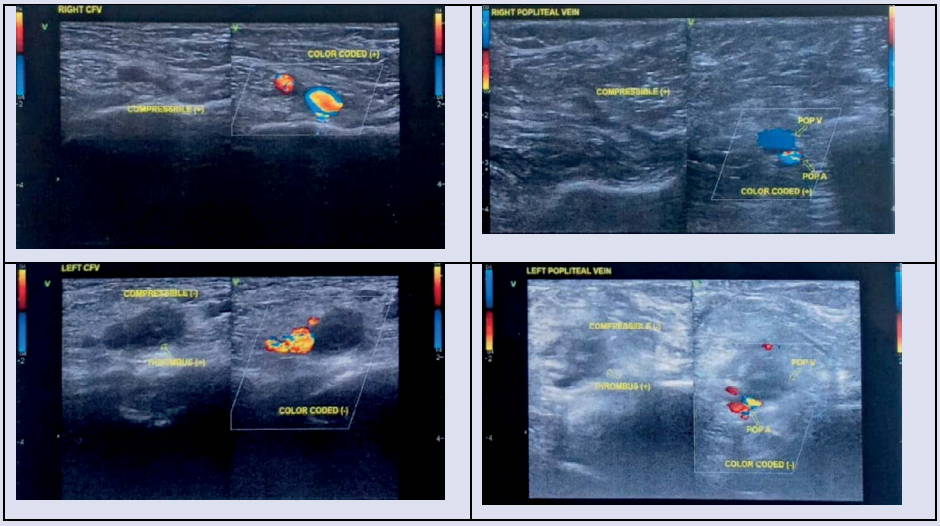

Figure 3. Lower Extremity Venous Ultrasound Doppler, Showed Thrombuses on The Left Femoral and Popliteal Vein.

into oral methylprednisolone 1x8 mg. The patient was suspected of ulcerative colitis, therefore, a colonoscopy was planned. On the 13th day of treatment, lower back pain had not been resolved completely. However, due to economic matters, the patient requested discharge against medical advice (DAMA). The patient was discharged with oral omeprazole 2x20 mg, Xarelto 1x10 mg, sulfasalazine 2x500 mg, lacto-b 3x1 sachet, and methylprednisolone 1x4 mg. She was planned for a colonoscopy following an outward visit.

DISCUSSION

SpA is a systemic disease that includes the inflammation of the axial skeleton, extra-axial, and extraarticular.[4] SpA encompasses a group of diseases that, despite their diverse manifestations, share common characteristics. These include a negative rheumatoid factor, anterior uveitis, sacroiliitis, a positive family history, peripheral arthritis, and often, a positive HLA-B27 marker. HLA-B27 is an allele of the HLA-B locus that encoded the MCH class I. HLA-B27 is postulated to have molecular mimicry with the SpA trigger microorganism.[5] SpA is often found in a middle-aged woman based on a previous study in one of the Indonesian Tertiary Hospitals.[6]

AxSpA diagnosis criteria based on ASAS 2016[7]: back pain ≥ 3 months with or without peripheral manifestation and the onset at age <45 years old, with 86.2% of predictive positive value (PPV) if sacroiliitis is found in imaging study with ≥ 1 SpA clinical manifestation. The PPV is 88 % if positive HLA-B27 with ≥ 2 clinical manifestations is evident. Clinical manifestations of SpA include dactylitis, arthritis, increased CRP, uveitis, family history of SpA, IBP, enthesitis, psoriasis, and Crohn's/ ulcerative colitis. Peripheral SpA criteria are limited to peripheral manifestation: arthritis/enthesitis/ dactylitis with ≥ 1 symptom of SpA (uveitis, psoriasis, Cron's/ ulcerative disease, prior infection, sacroiliitis based on imaging) or ≥ 2 symptoms of SpA (arthritis, enthesitis, dactylitis, IBP, family history of SpA). The patient in this case fulfilled ASAS-EULAR 2016 criteria including AxSpA with spine and sacroiliac manifestation based on imaging study, The HLA-B27 examination had not been done and a colonoscopy was planned in the outward visit.

AxSpA patients are at higher risk of venous thrombi emboli, related to increased inflammation. Previous studies have indicated that the absolute risk of recurrent VTE ranges from 30% to 40%.[8] This increased risk of venous thromboembolism may stem from various underlying factors across different autoimmune diseases, potentially

signifying more severe manifestations of these disorders.[9] Venous thromboembolism is understood as a complex condition influenced by interactions among multiple triggering factors, which can act additively or synergistically.[10] Inflammatory cytokine, including IL-6, IL-8, and TNF-α, was found to increase the coagulation cascade, inhibit the anticoagulation pathway, and disarrange the fibrinolytic process that led to a thrombophilic state. In addition to endothelial cell dysfunction due to oxidative stress, this condition becomes the fundamental pathophysiology of increased coagulation. AS might elevate the risk of venous stasis. Previous studies showed that AS was related to the risk of stroke, myocardial infarction, venous thromboembolism.[11] This SpA patient had left lower extremity DVT proven by the evidence of pain and swelling on her lower limbs with immobilization history, increased D-dimer, and USG Doppler findings. A previous retrospective study evaluated in the current analysis indicates that patients exhibited elevated rates of various types of thromboembolic events.[12] DVT is often found in the age group of 41-55 years old, similar to the current patient age.[13] As SpA increases the risk of venous thromboembolism, awareness of SpA might be considered as part of DVT prevention in the mentioned patient. Unfortunately, Indonesian public awareness of SpA is still low.[14] Despite patients with AS showing a higher prevalence of known risk factors for VTE, this association remained statistically significant even after adjusting for these baseline factors.[15]

Based on ASAS-EULAR 2016, SpA management is divided into 3 phases. The first phase includes NSAID, physical therapy, routine exercise, and smoking cessation. The second phase comprises glucocorticoid injection, sulfasalazine, or bDMARD. The third step includes TNF inhibitor or IL-17 inhibitor. Each phase will be evaluated in a few weeks based on ASDAI and BASDAI score and rheumatology assessment.[7] This Patient had been given an NSAID that did not resolve her complaint completely. Therefore, she was given intravenous dexamethasone continued with oral methylprednisolone, and sulfasalazine.

In the management of AxSpA with DVT, the key objectives are to prevent pulmonary embolism, decrease morbidity, and mitigate the risk of post-thrombotic syndrome. Anticoagulation therapy, including options such as Low Molecular Weight Heparin (LMWH), fondaparinux, and Vitamin K analogs, is employed for treating DVT. Before initiating treatment, it is essential to thoroughly assess the risks and benefits associated with anticoagulation.[16] Thrombolitic may induce intracranial hemorrhage. Besides medication, endovascular intervention and compression stocking are other DVT treatments .[17] The patient in this case was administered subcutaneous fondaparinux and continued with Xarelto alongside routine medical rehabilitation.

Patients with Chronic Inflamatory disease have an increased risk of post-thrombotic syndrome and included their risk of recurrent VTE as secondary outcome.[17] The systematic review and meta-analysis underscore the heightened prevalence of various cardiovascular diseases among individuals with gout.[18] Although DVT has a high recurrence risk (up to 25%) and a mortality rate (6%), DVT may resolve without complication. Post-thrombotic syndrome manifests in 43% of cases within 2 years following DVT (comprising 30% mild, 10% moderate, and 3% severe cases), with DVT mortality associated with cancer, advanced age, pulmonary embolism, and underlying cardiovascular disease. The current patient prognosis was poor and, therefore, required further evaluation of colitis and the possibility of venous thromboembolism recurrence. Improvement of spine function should be completed simultaneously to reduce the morbidity risk. The application of a diagnostic marker, for instance, dickkopf-related protein 1, for early SpA might be useful to delay disease progression or complication.[19] These findings, along with those from other studies, can enhance awareness among healthcare providers, patients, and the public that individuals with autoimmune diseases may face an elevated risk of developing VTE.[20] Further studies on disease prevention should be completed in the near future.

CONCLUSION

This report presents a case of SpA with DVT as a complication. SpA increases the risk of DVT due to the increase in inflammation state. A comprehensive and holistic approach to management is essential to enhance patient quality of life and minimize the risks associated with disease progression, complications, and mortality.

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CONFLICTS OF INTEREST

No conflicts of interest pertinent to this article were disclosed by the authors.

AUTHORS' CONTRIBUTION

All authors participated in drafting and revising the article, and jointly take responsibility for all aspects of this study.

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REFERENCES

1. Poddubnyy D. Axial spondyloarthritis: is there a treatment of choice? Ther Adv Musculoskelet Dis. 2013;5(1):45–54.
2. Stolwijk C, van Onna M, Boonen A, van Tubergen A. Global Prevalence of Spondyloarthritis: A Systematic Review and Meta-Regression Analysis. Arthritis Care Res (Hoboken). 2016 Sep;68(9):1320–31.
3. Ungprasert P, Srivali N, Kittanamongkolchai W. Ankylosing spondylitis and risk of venous thromboembolism: A systematic review and meta-analysis. Lung India. 2016;33(6):642–5.
4. Molto A, Gossec L, Lefèvre-Colau MM, Foltz V, Beaufort R, Laredo JD, et al. Evaluation of the performances of "typical" imaging abnormalities of axial spondyloarthritis: results of the cross-sectional ILOS-DESIR study. RMD open. 2019;5(1):e000918.
5. Manica SR, Sepriano A, Pimentel-Santos F, Gouveia N, Barcelos A, Branco JC, et al. Effectiveness of switching between TNF inhibitors in patients with axial spondyloarthritis: is the reason to switch relevant? Arthritis Res Ther. 2020 Aug;22(1):195.
6. Yudha C, Rahmawati L, Indrasari Y, Yuliasih. Clinical and Demographic Profiling of Patients with Spondyloarthritis and Its Association with Disease Activity in a Tertiary Hospital in Surabaya, Indonesia. Curr Intern Med Res Pract Surabaya J. 2024 Jan 31;5.
7. van der Heijde D, Ramiro S, Landewé R, Baraliakos X, Van den Bosch F, Sepriano A, et al. 2016 update of the ASAS-EULAR management recommendations for axial spondyloarthritis. Ann Rheum Dis. 2017 Jun;76(6):978–91.
8. Leeuw, K., Rutgers, A., Meijer, K., Tichelaar, V., & Borjas-Howard, J. (2018). *Risk of Recurrent Venous Thromboembolism in Autoimmune Diseases: A Systematic Review of the Literature. Seminars in Thrombosis and Hemostasis.* doi:10.1055/s-0038-1661387
9. Zöller, B., Li, X., Sundquist, J., & Sundquist, K. (2012). *Risk of pulmonary embolism in patients with autoimmune disorders: a nationwide follow-up study from Sweden. The Lancet, 379(9812), 244–249.* doi:10.1016/s0140-6736(11)61306-8

10. Khan, F., Tritschler, T., Kahn, S. R., & Rodger, M. A. (2021). Venous thromboembolism. The Lancet, 398(10294), 64–77. doi:10.1016/s0140-6736(20)32658-1

11. Bengtsson K, Forsblad-d'Elia H, Lie E, Klingberg E, Dehlin M, Exarchou S, et al. Are ankylosing spondylitis, psoriatic arthritis and undifferentiated spondyloarthritis associated with an increased risk of cardiovascular events? A prospective nationwide population-based cohort study. Arthritis Res Ther. 2017 May;19(1):102.

12. Setyawan, J., Mu, F., Yarur, A., Zichlin, M. L., Yang, H., Fernan, C., … Strand, V. (2021). *Risk of thromboembolic events and associated risk factors, including treatments, in patients with immune-mediated diseases. Clinical Therapeutics.* doi:10.1016/j.clinthera.2021.06.008

13. Hanindito E, Airlangga P, Sulistiawan SS, Semedi B, Andriyanto L, Utariani A, et al. Comparison of Length of Stay and Deep Vein Thrombosis (DVT) Incidents in Dr. Soetomo Hospital. Folia Medica Indones. 2018 Dec 11;54:278.

14. Wahono CS, Pratama MZ, Rahman PA, Halim EN, Pranawa FJ, Aditya J, et al. Assessment of the public knowledge, perception and attitude in Indonesia toward spondyloarthritis: a national survey. Int J Heal Promot Educ [Internet]. :1–13. Available from: https://doi.org/10.1080/14635240.2024.2337733

15. Aviña-Zubieta, J. A., Chan, J., De Vera, M., Sayre, E. C., Choi, H., & Esdaile, J. (2019). *Risk of venous thromboembolism in ankylosing spondylitis: a general population-based study. Annals of the Rheumatic Diseases, annrheumdis–2018–214388.* doi:10.1136/annrheumdis-2018-214388

16. Faqah A, Sheikh H, Bakar MA, Tayyaab F, Khawaja S. Comparative analysis of enoxaparin versus rivaroxaban in the treatment of cancer associated venous thromboembolism: experience from a tertiary care cancer centre. Thromb J [Internet]. 2020;18(1):8. Available from: https://doi.org/10.1186/s12959-020-00221-2

17. Iding AFJ, Ten Cate-Hoek AJ. How to optimize the prevention of post-thrombotic syndrome: recent advances. Pol Arch Intern Med 2022;132. https://doi.org/ 10.20452/pamw.16288.

18. Cox, P., Gupta, S., Zhao, S. S., & Hughes, D. M. (2021). The incidence and prevalence of cardiovascular diseases in gout: a systematic review and meta-analysis. Rheumatology International, 41(7), 1209–1219. doi:10.1007/s00296-021-04876-6

19. Yuliasih Y, Permatasari A, Rahmawati LD, Wahyudi MI, Nisa' N. The Increasing Level of DKK-1 as a New Bone Formation Factor in Patients with Early Spondyloarthritis. Autoimmune Dis. 2023;2023:5543234.

20. Yusuf, H. R., Hooper, W. C., Grosse, S. D., Parker, C. S., Boulet, S. L., & Ortel, T. L. (2015). *Risk of venous thromboembolism occurrence among adults with selected autoimmune diseases: A study among a U.S. cohort of commercial insurance enrollees. Thrombosis Research, 135(1), 50–57.* doi:10.1016/j.thromres.2014.10.01

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