A Male Case of Primary Antiphospholipid Syndrome and Recurrent Deep Venous Thrombosis

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Abstract

Antiphospholipid syndrome (APS) is an autoimmune disease with autoantibodies and hypercoagulability. Although APS has a variable clinical presentation, APS commonly presents vascular thrombosis and obstetrical complications, such as repeated miscarriages in women. Here, we report an elderly male with the clinical manifestations of APS and recurrent deep venous thrombosis (referred to as DVT) in Sudan. A 52-year-old male had a chief complaint of severe left leg pain and high-grade fever for 10 days, with no history of recent surgery, trauma or prolonged immobilization but with a previous history of DVT. Doppler ultrasonography revealed left lower limb DVT, and laboratory examinations detected autoantibodies without other causes. Accordingly, he was diagnosed with APS. He was treated with Cefuroxime, Flucloxacillin and subcutaneous enoxaparin. His clinical condition markedly improved and the swelling subsided. His blood international normalized ratio reached 2.5 and he was discharged.

Introduction

Antiphospholipid syndrome (APS) is a hypercoagulable state, characterized by the presence of vascular thrombosis and/or obstetrical events in addition to the presence of autoantibodies, including lupus anticoagulant, anticardiolipin antibodies and anti-β2-glycoprotein 1 antibodies. Most patients with APS are diagnosed between the ages of 15 and 50 years,1,2 and only less than 1% of APS patients are reported to be above the age of 50 years.3 APS prevalence was estimated to be 50 per 100,000, with 2 per 100,000 incidences (similar in both sexes).4 Factors related to gender have been suggested to affect the clinical course in patients with primary APS, with a significant prevalence of a central nervous system involvement in females in comparison with gastrointestinal involvement in males.5 The aim of this report was to describe the clinical manifestations of DVT in an elderly male with APS in Sudan.

Keywords: Antiphospholipid syndrome; Deep venous thrombosis; Male; Sudan.
Table 1. The laboratory test results for the patient

| Investigation                        | Results                        |
|--------------------------------------|--------------------------------|
| Hemoglobin                           | 11.8 g/dL                      |
| White blood cell                     | $5.3 \times 10^9$/L            |
| Erythrocyte sedimentation rate       | 90 mm/h                        |
| C-reactive protein                   | Negative (<0.6 mg/dL)          |
| Renal function test                  | All normal                     |
| Total protein                        | 9.4 g/dL                       |
| Total Bilirubin                      | 0.3 mg/dL                      |
| Direct Bilirubin                     | 0.1 mg/dL                      |
| Serum uric acid                      | 6.7 mg/dL                      |
| Prothrombin time                     | 27.5 sec                       |
| International normalized ratio       | 2.03                           |
| Vitamin D, total 25-hydroxy          | 42.1 ng/mL                     |
| Anti CCP                             | 0.3 U/mL                       |
| Rheumatoid factor                    | Negative (<8 IU/mL)            |
| total proteins                       | 9.4 g/dL (elevated)            |
| Protein C activity                   | 58%                            |
| Protein S                            | 55%                            |
| Antiphospholipid abs, IgG            | 0.9 GPL-U/mL (borderline)      |
| Antiphospholipid abs, IgM            | 0.3 MPL-U/mL                   |
| Anti-beta2 glycoprotein Immunoglobin G| 1.8 AU/mL (positive)            |
| Cardiolipin antibody IgM             | 0.3 MPL-U/mL                   |
| Cardiolipin antibody IgG             | 0.9 GPL-U/mL                   |
| Lupus anticoagulant                  | 40.8 (high)                    |
| Antithrombin III activity            | 90%                            |
| IgG                                  | 5.8 mg/dL                      |
| IgM                                  | 0.9 mg/dL                      |
| Antinuclear antibody profile         | All negative                   |
| Urine analysis                       | Normal                         |

Case Report

A 52 year-old male presented on 12 October, 2019 at Haj Alsafi Teaching Hospital, Bahri, Khartoum, Sudan, with severe pain below his left knee, associated with high-grade fever for the previous 10 days. His condition started 1 month earlier, with swelling in the left leg, which had been increasing gradually, followed by pain, fever, hotness and black discoloration of his left leg. There was no history of recent surgery, trauma, or prolonged immobilization. Moreover, the patient was a non-smoker. His family history was positive for diabetes mellitus and hypertension, while negative for any autoimmune disease. He had history of one previous hospitalization, due to DVT on the same leg in 2013. At that time his symptoms started (with pain in the thigh and leg, followed by hotness and gradually increasing swelling), he underwent Doppler ultrasound imaging to confirm the diagnosis.

The episode was not preceded by a period of prolonged immobilization or any of the risk factors, and the symptoms had started gradually, prompting him to seek medical advice and admission to a hospital in the west of Sudan. There, he received injectable low molecular-weight heparin for 5 days and oral warfarin for 1 month. The patient also had no history of arterial thrombosis and no other chronic illnesses, apart from the recently diagnosed hypertension, for which he took amlodipine (5 mg). He was also on aspirin (75 mg) since 2013 but with poor compliance. On examination, he looked well, was ambulant, and in no apparent stress, with stable vital signs. His left leg was swollen just below the knee, with black discoloration. Left-sided posterior tibial and popliteal pulses were weak in comparison to the right side.

Initial investigations were done as shown in Table 1. Doppler ultrasonography revealed left lower limb DVT with mild cellulitis (Fig. 1). At that point, a diagnosis of primary APS was suspected. Anticardiolipin, anti-beta2 glycoprotein 1 and antiphospholipid antibodies were positive (Table 1). Investigations confirmed the diagnosis of primary APS and excluded other causes of hypercoagulability. On 14 October, 2019 the patient received Cefuroxime.
Discussion

APS is an autoimmune disease that is more common among females than males; however, there is no significant difference between males and females in terms of arterial and venous thrombosis as a clinical presentation. The diagnosis of APS depends on clinical and laboratory findings. The disease is characterized by recurrent venous and arterial thrombosis, as well as pregnancy loss among females. Presence of anticardiolipin, anti-beta2 glycoprotein I and antiphospholipid antibodies are essential for the diagnosis. These tests should be repeated after at least 12 weeks for confirmation of persistent antibodies, although some cases are seronegative.

Our patient had positivity for lupus anticoagulant, anti-beta2 glycoprotein Immunoglobulin G and borderline antiphospholipid antibodies (IgG). Lupus anticoagulant is known to be associated with a higher risk for thrombotic events. Several reports have also indicated that Antiphospholipid syndrome may be strongly linked to the development of thrombotic events within the usual sites, although a few studies have also reported a relation to other unusual sites, such as splanchnic vein thrombosis. Splanchnic vein thrombosis consists of Budd-Chiari syndrome and portal venous system thrombosis. Some APAs have been found in splanchnic vein thrombosis patients, such as IgG aCL, which is itself observed to be more frequent than in healthy controls patients; other APAs, like IgM aCL, Las, ab2GPI and ab2GPI-oxidized low-density lipoprotein antibody were not evaluated in BCS, in contrast to portal venous system thrombosis, in which they have been shown to be unassociated.

The patients classified as primary APS have had other autoimmune diseases excluded, depending on negative rheumatoid factor, anticyclic-citrullinated-peptide (anti CCP) antibodies, and antinuclear antibody profile with positive anti-beta 2 glycoprotein IgG and high-level lupus anticoagulant. In addition to the absence of symptoms, other connective tissue diseases are excluded. The patient in our case report was diagnosed based on one clinical criterion (vascular thrombosis, such as DVT, confirmed by Doppler ultrasound imaging) and two laboratory criteria (positive anti-beta2 glycoprotein IgG and high-level lupus anticoagulant). Clinical manifestation of APS varies, but DVT is found in about one-third of patients with APS; other patients also show thrombocytopenia, livedo reticularis, Pulmonary Embolism (PE), stroke and other conditions.

Andreoli et al. found that the frequency of antiphospholipid antibodies among DVT patients was 9.5%. The patient described herein experienced recurrent left lower limb DVT. The differential diagnosis of APS depends on the clinical presentation. For presentation of recurrent DVT, both inherited and acquired causes for thrombosis should be considered, such as protein S and protein C deficiency. For this patient, bleeding profile, protein c level and antithrombin III activity were tested to exclude thrombophilia. Skin infection can also be a consequence of cellulitis, and the cellulitis itself can occur due to its association with DVT, as reported in this patient; such an association has been widely documented in many reports. Additionally, a coexisting condition that can add synergistic effect to the presentation, such as systemic lupus erythematosus (SLE), should be considered. Research studies have shown that about 40% of SLE patients test positive for antiphospholipid antibodies. There is an important clinical difference to remember between male patients who suffer from APS and those with SLE, as the former usually present with vascular thrombosis rather than joint, skin and renal manifestations, as in the latter.

Our patient presented with venous thrombosis and had a negative antinuclear antibody profile. APS can present with a wide spectrum of clinical manifestations involving many organs and systems. The most important is the occurrence of venous and/or arterial thrombosis, as in the current reported case, in which the patient presented with DVT in the left leg and past history of the same condition. Besides, it may present with other forms of thromboembolic events in different sites; for instance, cerebral venous thrombosis and pulmonary embolism with subsequent DVT occurred in both reported cases. Hypercoagulability may represent the initial presentation in most cases, while in some reported cases it was preceded by other symp-
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toms, e.g., generalized joint pain and body swelling with perior-
bial edema. In contrast, patients can present with different systems
involvement, such as the central nervous system, genitourinary,
endocrinological and cardiac.

It is recommended to use antithrombotic medications for treat-
ment rather than immunosuppression, unless the patient has an
underlying condition such as SLE or a severe life threatening con-
dition such as catastrophic APS. Current therapies for an acute
thrombotic event include heparin and warfarin. Prevention of
further thrombosis in patients who develop a thrombotic event is
essential, due to the high risk of recurrence in the first 6 months
following treatment discontinuation. Several studies have
suggested aspirin for patients who have a thrombotic event or are
asymptomatic but positive for antiphospholipid antibodies and
who are suffering from either SLE or other related autoimmune
diseases. Our patient received anticoagulant for treatment.

Conclusion

A Sudanese elderly male presented with severe leg pain and swell-
ing that had lasted for 10 days. Doppler ultrasound revealed the
presence of DVT complicated by cellulitis, and additional clinical
and lab results confirmed a diagnosis of APS. The patient received
Cefuroxime, Fluclouxacinilin and subcutaneous enoxaparin, and was
discharged with no complaints and 2.5 INR.

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The case was diagnosed and treated by a rheumatologist and inter-
nal medicine specialist: Dr. Ziryab Imad Taha.

Ethical approval and Patient consent

This study obtained ethical approval from the Federal Ministry of
Health, Khartoum, Sudan, and written consent was obtained from
the patient to publish this case report.

Data sharing statement

All the data used in the study are available from the first and cor-
responding authors, upon reasonable request.

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Conflict of interest

None.

Author contributions

Study design (ZIT, MEAE, SNE, ATIA), analysis and interpreta-
tion of data (MDYH, MMAH, ASSM, AMAA), manuscript writ-
ing (MEAE, SNE, ATIA, SKAM, SHE), collection of data (LME),
critical revision (ZIT, AAA).

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