

Deep vein thrombosis

H. Ouasif*, H. Yahyaoui, M. Aitameur and M. Chakour

Hematology Laboratory, Avicenne Military Hospital, FMPM, Marrakech, Morocco.

World Journal of Advanced Research and Reviews, 2023, 18(01), 294–298

Publication history: Received on 05 February 2023; revised on 05 April 2023; accepted on 08 April 2023

Article DOI: <https://doi.org/10.30574/wjarr.2023.18.1.03436>

Abstract

DVT is a serious condition that remains common despite advances in prophylaxis. It is a condition that poses a serious health problem due to its morbidity and mortality. The aim of our work was to analyse the epidemiological, clinical and biological characteristics of venous thrombosis at the Avicenne Marrakech military hospital.

This is a retrospective descriptive study, which focuses on patients with venous thromboembolic disease over a period of 6 years, extending between June 2013 and June 2019, collecting 64 observations. The average age was 50.5 years (extremes: 15-90 years) with a dominant age range (25%) between 40 and 49 years. We note a male predominance with a male/female sex ratio of 1.28. 88% of patients had at least one thromboembolic risk factor.

DVT of the lower limbs was the most frequent location (57.8%), with a predominant involvement of the left lower limb in 16 cases (43.2%),

The aetiological work-up showed a predominance of acquired thrombophilia, with a high frequency of neoplasia, cancer, and frequency of neoplasia, Behçet's disease and lupus + SAPL. The assessment of constitutional thrombophilia showed a combined deficiency of protein S and protein C in 1 case, elevation of factor VIII in 2 cases and hyperhomocysteinemia in 1 case.

VTE remains a serious condition and is often under-diagnosed, especially in atypical locations. Once the diagnosis has been made, an etiological assessment must be systematic to look for neoplasia in particular. It is only through preventive measures, early diagnosis and effective treatment will reduce the risks.

Keywords: Deep vein thrombosis; Thrombophilia; Neoplasia; Pulmonary embolism

1. Introduction

Despite advances in antithrombotic prophylaxis, deep vein thrombosis (DVT), due to its morbidity and mortality, still represents a public health problem. The diagnosis is systematically evoked by taking into account the clinical signs, the context and the presence of underlying risk factors.

Confirmation by additional examinations is essentially based on the triad: D-dimer - Doppler ultrasound - thoracic CT angiography. DVT of the lower limbs and pulmonary embolism are the most common clinical expression, but other rarer locations may also occur, usually in specific pathological contexts (cerebral veins, vena cava, veins of the upper limbs, portal vein, suprahepatic veins) [1].

* Corresponding author: H. Ouasif

It is a multifactorial pathology with interaction of acquired and constitutional FDR. The aim of this study was therefore to analyse the epidemiological, etiological, diagnostic and therapeutic characteristics of deep vein thrombosis in patients hospitalised at the Avicenne military hospital in Marrakech.

2. Material and methods

This is a retrospective descriptive study of patients with venous thromboembolic disease (VTE) in the Internal Medicine Department at the Military Hospital Avicenne Military Hospital in Marrakech (HMA) over a period of 6 years, from June 2013 to June 2019. Medical record of all patients hospitalized for a new or recurrent episode of deep vein thrombosis, confirmed by imaging, regardless of location, were included.

2.1. Exclusion criteria

Patients who were hospitalised for suspected but unconfirmed deep vein thrombosis, patients with superficial vein thrombosis without deep thrombosis and patients whose records did not contain sufficient information.

The data collection was done from the patients' files in the archives of the Internal Medicine Department of the Avicenne Military Hospital in Marrakech, while respecting the confidentiality of the data; using a pre-established exploitation form. Data entry and analysis were carried out using EXCEL software. For the realization of our study, a descriptive method using percentages and averages was used.

3. Results

3.1. Epidemiological data

In this study, we collected 64 cases of patients with venous thromboembolic disease. These were deep vein thrombosis in 58 cases and pulmonary embolism in 6 cases. The age of our patients at the time of hospitalisation ranged from 15 to 90 years, with an average of 50.5 years. The distribution of cases according to the main age categories showed a dominant age range (25%) between 40 and 49 years. Our study series included 64 patients, 28 of whom were women (43.7%) and 36 men (56.2%). The different risk factors for thrombosis found in our study series are Previous personal episode of VTE 21.8, Venous insufficiency 3.12, Bed rest 9.3%, Recent surgery 6.2%. Pregnancy 1.5%.

3.2. Clinical and paraclinical manifestations

Thrombosis of the lower limbs was the most common location observed in our patients (37 cases), i.e. 57.8%, with a predominant involvement of the left lower limb in 16 cases (43.2%), the right lower limb in 14 cases (37.8%) and bilateral involvement in 7 cases (18.9%).

3.2.1. Venous Doppler ultrasound showed

37 cases of lower limb thrombosis and 6 cases of upper limb thrombosis The thoracic angioscanner showed: Thrombosis of the superior vena cava in 3 cases Abdominal angioscanner findings were: 5 cases of portal DVT 3 cases of inferior vena cava DVT and 1 case of renal vein thrombosis Abdominal ultrasound showed: 3 cases of portal thrombosis, 2 cases of inferior vena cava thrombosis Cerebral angio-MRI, performed in all patients with signs of HTIC, showed: Cerebral thrombophlebitis in 4 cases.

3.3. Biological examinations

The haemogram showed: anaemia (32.8%), hyperleukocytosis (20.3%), thrombocytosis (7.8%) and thrombocytosis (21.8%) The SV was accelerated in 9 patients. The renal assessment showed nephrotic syndrome in 1 patient and renal failure in 3 cases. Acquired thrombophilia work-up: included anti phospholipid antibodies, Behçet's disease, myeloproliferative syndromes and paroxysmal nocturnal haemoglobinuria. Anti-phospholipid antibodies (APL) came back positive in 4 cases Anti-nuclear antibodies and anti-native DNA antibodies were positive in 3 cases Flow cytometry revealed 1 case of paroxysmal nocturnal haematuria Hyperhomocysteinemia was found in only 1 patient Elevation of factor VIII was found in 2 cases The constitutional thrombophilia work-up included protein C, protein S, antithrombin, activated protein C resistance (APCR) +/- factor V mutation and factor II mutation: A combined protein C and S deficiency was found in 1 patient .No cases of activated protein C resistance, antithrombin deficiency or factor II mutation have been noted . The V617F mutation of the JAK2 gene in relation to polycythemia vaquez was not found in any patient.

3.4. Etiologies

The etiological investigation was based on the data of the interrogation, the clinical examination, complementary biological examinations, according to the context and the clinical signs of call. It mainly found: Neoplastic disease in 25 patients, Behçet's disease in 23 patients, associated with Crohn's disease in 1 patient, Lupus in 3 patients with secondary APS in 2 cases, SAPL in 4 patients, 2 of which were secondary to Lupus, Other aetiologies were found including: Hyperhomocysteinemia in 1 patient, Elevation of factor VIII in 2 patients, Paroxysmal nocturnal haematuria in 1 patient, Combined protein C and protein S deficiency in 1 patient, Nephrotic syndrome in 1 patient, Locoregional infectious origin: (hepatic micro-abscesses) in 1 patient. At the end of the etiological investigation, VTE remained idiopathic in 4 cases.

4. Discussion

As evidenced by epidemiological data, age is an important risk factor for VTE. The incidence of DVT increases with age, and after the age of 40 the risk doubles every 10 years. In the EPI-GETBO study, 75% of VTE cases were over 60 years of age, and 40% over 75 years (2). A study conducted in Tunisia by Boukhris, I et al found a mean age of 51 years with extremes ranging from 15 to 93 years (3). The distribution according to ten-year age brackets showed 2 peaks of frequency between 31 and 40 (21.3%) and between 41 and 50 (23%) (4). In our series, the age of diagnosis varied between 15 and 90 years with a mean age of 50.5 years. On the other hand, the distribution of cases according to ten-year age groups showed a peak in frequency between 40 and 49 years (25%). This is consistent with the literature. VTE is most often multifactorial, and most studies of DVT patients show the presence of many more DRFs than in the control population. In our study, at least one VTE DRF was found in 88% of cases, which is consistent with the study by Ben Salah (86.1%) (4). Strict bed rest is a recognised risk factor for venous thromboembolism and was by far the most frequent factor for transient stasis in our series, found in 9.3% of cases, which is in line with the studies conducted by Pottier (5) and Ben Salah (4).

Strict bed rest is a recognised risk factor for venous thromboembolism and was by far the most frequent factor for transient stasis in our series, found in 9.3% of cases, which is consistent with studies by Pottier (5) and Ben Salah (4). Neoplastic disease increases the risk of VTE by a factor of about eight (109), the risk being higher for certain types of cancer (pancreatic cancer, brain tumours, ovarian cancer, myeloproliferative syndromes) and in the presence of metastases.

There are many mechanisms that have been suggested as the cause of thrombosis in cancer, linked to the cancer itself (production of thrombogenic biological factors, venous compression) or linked to treatments (central venous catheters, chemotherapy, hormone therapy). Cancers represent 15 to 20% of VTE cases depending on the series. In our series, neoplastic disease was found in 39.06% of cases, which is consistent with the results of the literature. Approximately 20-30% of Behçet cases appear to be complicated by venous thrombosis according to Sağdıç (6). Venous involvement appears to be more frequent than arterial involvement in the various series in the literature. In our series, Behçet's disease was the second risk factor observed after neoplastic disease found in 35.9% of cases, this is explained by the frequency of this disease in our context.

The prevalence of antiphospholipid antibodies is 4-21% among patients with a thrombotic event versus less than 2% in the general population (7).

Many publications report a high frequency of thromboembolic complications, both arterial and venous, during the course of SLE (8,9). In our population, 4 patients (6.2%) were diagnosed with APS, 2 of them with lupus (4.6%) and 2 with primary APS. The coagulation inhibitor deficiencies were antithrombin, protein C and protein S deficiencies. Antithrombin is able to inhibit activated factors X and II, while proteins C and S inhibit activated factors V and VIII (10). Their diagnosis is based on weight assay and measurement of their activity as multiple genetic mutations may be responsible. These deficiencies are rare in the general population (less than 1%), and concern only 5% of patients who have had a thrombosis. In our study, these deficiencies were found in 1.5% of our patients with thrombosis. The coagulation factor abnormalities are represented by two genetic abnormalities that code for factors V and II, resulting in increased pro-coagulant activity of these two factors:

- The Leiden mutation of the factor V gene (RPCA) present in 20% of patients with a thromboembolic event (11).
- The prothrombin gene mutation is found in 10% of patients with a history of VTE.

These genetic abnormalities, unlike coagulation inhibitor deficiencies, are quite common in the general population (5%), but confer only a moderate risk of a first VTE event and are not known to be associated with a risk of VTE

recurrence. These abnormalities were absent in our series. Elevation of factor VIII is a new possible etiology of thrombophilia according to studies by the Leiden, Mitrio and Kraaijenhagen teams (12). The search for this anomaly in our series was positive in 2 cases.

In our series, the distribution of DVTs according to site shows that the location in the lower limbs was the most frequent (57.8%) (37 cases), which is in agreement with the literature (13). Several unusual locations of venous thrombosis were observed in our study series and are mainly represented by: upper limbs in 6 cases, portal system in 5 cases, cerebral veins in 4 cases, IVC in 3 cases, SVC in 3 cases, renal vein in 1 case. According to a study by Kefi. A et al (14), covering a period of 15 years and involving 268 patients, constitutional thrombophilia was found in 44 cases (16.5%). Hyperhomocysteinemia was found in 21 cases. DVT was related to Behçet's disease in 16 cases. Antiphospholipid syndrome was diagnosed in 11 cases and secondary to systemic lupus erythematosus in 6 cases. Neoplastic and infectious etiologies were observed in 46 and 8 cases respectively. Despite an exhaustive etiological investigation, DVT was considered idiopathic in 49 cases. A study by Sadki. I et al (15) in the internal medicine department of the Mohammed VI University Hospital in Oujda, over a period of about six years, collecting 195 observations, showed that an etiology was retained in 2/3 of the patients with a dominance of neoplastic origin (1/3 of the etiologies), Behçet's disease (n = 10). Seventy percent of the patients with cancer were under 65 years of age. In our series, neoplastic disease was the most frequent etiology found in 25 patients, followed by Behçet's disease (n = 10). In our series, neoplastic disease was the most frequent etiology found in 25 patients, followed by Behçet's disease in 23 patients, associated with Crohn's disease in 1 patient, lupus in 3 patients with secondary APS in 2 cases, APS in 4 patients, 2 of which were secondary to lupus, hyperhomocysteinemia in 1 patient, elevated factor VIII in 2 patients, paroxysmal nocturnal haematuria in 1 patient and combined protein C and protein S deficiency in 1 patient. At the end of the etiological investigation, VTE remained idiopathic in 4 cases.

5. Conclusion

Despite the progress in antithrombotic prophylaxis, venous thromboembolic disease, by its morbidity and mortality, still represents a public health problem. At the end of this retrospective study, we conclude that venous thromboembolic disease is a frequent condition of multifactorial origin that requires a precise diagnosis and codified management. When analysing the different locations, DVT of the lower limbs and pulmonary embolism are the most common clinical expression, but other rarer locations can also occur. These unusual locations should not be overlooked, given the delay in diagnosis that they pose, the seriousness of the location, the aetiology involved and the complications encountered. The diagnostic approach is based on clinical and imaging findings. The D-dimer test is considered to be a test of exclusion and not of diagnosis. Neoplastic disease, in addition to Behçet's disease, is the most frequent etiology of VTE in our series. We found a significant percentage of etiologies that are certainly underestimated.

Compliance with ethical standards

Acknowledgments

We would like to thank the teams of Hematology laboratory. Military Hospital Avicenne.

Disclosure of conflict of interest

The authors declare no conflict of interests.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

- [1] Robert-Ebadi H, Sennouni FM, Righini M. Deep vein thrombosis of the lower limbs. *EMC - Cardiology* 2015, 10(1):1- 9 [Article 11-730-A10].
- [2] Oger E. Incidence of venous thromboembolism: a community-based study in Western France. *EPI-GETBP Study Group. Groupe d'Etude de la Thrombose de Bretagne Occidentale. Thromb Haemost.* May 2000, 83(5):657-60.
- [3] Boukhris I, Abdallah M, Bouslema K, Hamzaoui S, Larbi T, Harmel A, et al. Venous thromboembolic disease: what other risk factors in a North African population? A study of 276 cases. 4 Feb 2018

- [4] Ben Salah R, Frikha F, Kaddour N, Saidi N, Snoussi M, Marzouk S, et al. Etiological profile of deep vein thrombosis in internal medicine setting: a retrospective study of 318 cases. *Ann Cardiol Angéiologie*. Feb 1, 2014, 63(1):11-6.
- [5] Pottier P, Planchon B, Pistorius MA, Grolleau JY. Risk factors and incidence of venous thromboembolic disease in internal medicine: a prospective descriptive study of 947 hospitalized patients. *Rev Médecin Interne*. Apr 1, 2001, 22(4):348-59.
- [6] Sagdic K, Ozer ZG, Saba D, Ture M, Cengiz M. Venous lesions in Behçet's disease. *Eur J Vasc Endovasc Surg Off J Eur Soc Vasc Surg*. May 1996, 11(4):437-40. Ginsberg JS, Wells PS, Brill-Edwards P, Donovan D, Moffatt K, Johnston M, et al. Antiphospholipid antibodies and venous thromboembolism. *Blood*. 15 nov 1995, 86(10):3685-91.
- [7] Somers E, Magder LS, Petri M. Antiphospholipid antibodies and incidence of venous thrombosis in a cohort of patients with systemic lupus erythematosus. *J Rheumatol*. déc 2002, 29(12):2531-6.
- [8] Cervera R, Khamashta MA, Font J, Sebastiani GD, Gil A, Lavilla P, et al. Morbidity and mortality in systemic lupus erythematosus during a 5-year period. A multicenter prospective study of 1,000 patients. *European Working Party on Systemic Lupus Erythematosus. Medicine (Baltimore)*. mai 1999, 78(3):167-75.
- [9] Delluc A, Le Ven F, Mottier D, Gal G. Epidemiology and risk factors of venous thromboembolic disease. *Rev Mal Respir*. Feb 2012, 29(2):254-66.
- [10] Nicolaides, Cardiovascular Disease Educational and Research Trust, International Union of Angiology, Mediterranean League on Thromboembolism, A. N., Breddin HK, et al. Thrombophilia and venous thromboembolism. International consensus statement. Guidelines according to scientific evidence. *Int Angiol J Int Union Angiol*. mars 2005, 24(1):1-26.
- [11] Benjaber K, Constans J, Cougnard A, Salmi L-R. Elevation of coagulant factor VIIIc and risk of venous thrombosis: critical analysis of case-control studies. *Rev Médecine Interne*. 1 June 2003, 24(6):366-71.
- [12] Tagalakis V, Patenaude V, Kahn SR, Suissa S. Incidence of and Mortality from Venous Thromboembolism in a Real-world Population: The Q-VTE Study Cohort. *Am J Med*. 1 sept 2013, 126(9):832.e13-832.e21.
- [13] Kefi A, Daoud F, Toujani S, Hadj ali Z, Aydi Z, Baili L, et al. Deep vein thrombosis in internal medicine: a retrospective study of 268 cases. *J Mal Vasc*. 1 Sep 2015, 40(5):322.
- [14] Sadki I, Bachir H, Sabri S, Bouagaga R, Sandouno TM, Darine H, et al. Deep vein thrombosis: about 195 cases. *Rev Internal Medicine*. 1 Dec 2017, 38:A142.