Occult cancer in patients with deep-vein thrombosis in a general hospital at Mexico City: A pilot study

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Background: We aimed to explore the frequency of occult cancer in patients with deep-vein thrombosis (DVT) at a general hospital in Mexico City. Materials and Methods: From March 2012 to February 2015, all patients with primary DVT of lower extremities attended in the emergency department of our hospital were studied. Initially, all patients were evaluated with clinical history, physical examination, basic laboratories, abdominal ultrasound, chest X-ray, and duplex venous ultrasonography. In a case-by-case approach, if necessary, computed tomography, endoscopy, colonoscopy, and tumor markers were done. Results: From 182 patients with primary DVT, 30 (16.5%) presented occult cancer: Thirteen males and 17 females, with an average age of 61 years. In males, prostate cancer prevailed (6/13, 46%); meanwhile, in females, pelvic gynecologic cancers predominated (7/17, 41%). Conclusion: Our results suggest that in Mexican patients with primary DVT, occult cancer is frequent.

Key words: Cancer, deep-vein thrombosis, thromboembolism/prevention and control, Trousseau’s syndrome, venous thrombosis/etiology

INTRODUCTION
Cancer is increasing worldwide, and residents of low- and middle-income countries present a greater morbidity and mortality.[1] Sometimes, cancer manifests as a paraneoplastic syndrome that challenges its correct diagnosis; this is the case of Trousseau’s syndrome (TSx): Deep-vein thrombosis (DVT) in patients with an underlying malignancy.[2,3] Furthermore, TSx may be the herald of occult cancer and it may be its first sign.[4]

Some studies have found that occult cancer occurs in nearly 10% of DVT cases.[4] In Mexico, there is only one retrospective study, in a service of oncology, about DVT in patients with a previous diagnosis of cancer.[5] Hence, in Mexico, there are no data available about the frequency of occult cancers in patients with primary DVT in general hospitals. Therefore, our aim was to explore, prospectively, the frequency of occult cancer in patients with primary DVT at a general hospital in Mexico City.

MATERIAL AND METHODS
Subjects and procedures
This was a pilot prospective study approved (#013-2012) by the Board of Ethics and Research of the “Hospital General Tacuba.”

Patients
From March 2012 to February 2015, all adult patients attended the “Hospital General Tacuba” emergency department with DVT diagnosis of lower extremities were studied. All cases were evaluated by the staff of vascular surgery.

Patients with secondary DVT due to cardiac diseases (cardiac failure, arrhythmias, etcetera); lower-extremity
trauma, pregnancy, coagulopathies (lupus, protein C or S deficiency); platelets disorders, long-lasting immobilization during the past 6 months, estrogen use, autoimmune diseases, and childbirth were excluded from the study.

**Procedures**

Initially, all cases with primary DVT were assessed with a full clinical history and a thorough physical examination. Their evaluation included D-dimer, complete blood count, creatinine, activated partial thromboplastin time, transaminases, gamma-glutamyl transpeptidase, and alkaline phosphatase. Besides, duplex venous ultrasonography of the affected extremity, abdominal-pelvic ultrasound, and chest X-rays were done.

According to individual clinical data, the evaluation was extended to thoracic-abdominopelvic computed tomography (CT scan), CT scan of head-neck-thorax, transabdominal prostate ultrasound, mammography, Pap smear, neck ultrasound, gastroscopy, colonoscopy or sigmoidoscopy, and biopsies whenever possible. Furthermore, tumor markers including carcinoembryonic antigen, α-fetoprotein, CA-125, CA-15.3, and total specific prostate antigen were obtained, if necessary. This approach was a modification to the SOMIT study.[6]

The Department of Vascular Surgery follows up the patients with DVT during 6 months after the diagnosis and no signs of cancer, according to standard protocols. With an objective diagnosis of cancer achieved, the treatment to patients with DVT was with low-molecular-weight heparin. Then, the patients were sent to the oncology department, and treatment was performed according to standard protocols.

**Statistical methods**

All values are expressed in absolute numbers and percentages; the descriptive statistic was used.

**RESULTS**

There were totally 182 patients with primary DVT: 135 (74%) females and 47 (26%) males, with an average age of 63 years. Of these patients, 30 (16.5%) had occult cancer; 13 (43%) males and 17 (57%) females with an average age of 61 years.

In males, prostate cancer prevailed (6/13, 46%) followed by colorectal tumors. Meanwhile, in females, the pelvic gynecologic malignant neoplasms (cervix, uterus, and ovarian cancers, 7/17, 41%) predominated, tracked by stomach cancer (4/17, 23%) [Table 1].

**DISCUSSION**

This study establishes that occult cancer occurs in 16.5% of patients with primary DVT at a general hospital in Mexico City. There are no similar studies in Mexico and Latin America to compare. From seven studies of primary DVT and occult cancer found in different repositories (PubMed, Google academic, EBSCO, Scopus, and Lilacs), only two, one prospective and other retrospective, are in accordance with our findings of a major prevalence of women and mean age [Table 2].[6-8] Besides, three more studies agree with occult prostate cancer as a main associated malignant neoplasm with primary DVT.[6-8] And only one, with a greater frequency of gynecologic tumors, associated with DVT.[9]

| Cancer | Cancer stage | Males | Females |
|--------|--------------|-------|---------|
| Endometrial | III C | - | 2 moderately differentiated endometrioid adenocarcinoma |
| Cervical | IV | - | 1 adeno-squamous cell carcinoma |
| Ovary | III C | 1 squamous cell carcinoma | 1 moderately differentiated adenocarcinoma |
| Breast | IV | 2 high grade papillary serous carcinoma | 1 lobular carcinoma |
| Stomach | IV | 1 moderately differentiated adenocarcinoma | 1 ducal carcinoma |
| Prostate | IV | 1 moderately differentiated adenocarcinoma | 4 moderately differentiated adenocarcinomas |
| Pancreas | IV | 2 poorly differentiated adenocarcinoma | - |
| Colorectal | IV | 1 moderately differentiated adenocarcinoma | 1 poorly differentiated rectal adenocarcinoma |
| Lung | IV | 1 moderately differentiated adenocarcinoma | 1 squamous cell carcinoma |
| Kidney | II | 1 clear cell carcinoma | 1 no biopsy |
| Thyroid | IVA | 1 papillary thyroid carcinoma | 1 papillary thyroid carcinoma |
In a contrary sense to our information, five studies find that the DVT with occult cancer affected men more frequently than women [Table 2].[6‑10] Moreover, four investigations find different main cancers affecting its evaluated patients. These circumstances could be explained according to the well-known geographical differences in cancer risk factors.[1]

We are well aware of the limitations of our study. It was a study conducted only in one hospital, and it is reasonable that our circumstances are not applicable to other clinical settings; we only evaluated DVT in lower extremities; furthermore, we did not evaluate the impact of cancer stage on patients’ survival. However, our research has some advantages. The analysis of 182 patients with DVT, in a 3-year study of a single second-level hospital, is a good sample; only to have a perspective, in a 1-year multi-institutional study of all Argentina, 181 patients were found with venous thromboembolism.[11]

If our results are verified, it would determine to change how we should evaluate the patients with DVT in our country. Furthermore, there is a great need for further studies regarding how extensive the screening for occult cancer should be, and its costs. In addition, it is critical to establish the malignant neoplasm stage when it is noticed, and whether a prompt diagnosis could impact on patients’ survival, due to conflicting data in a recent bibliography.[6,9]

Our results drive us to some advices. Considering that one in six patients (16.5%) with primary DVT may have occult cancer in our country, it is rational to assess this option in all cases; in addition, in men, the digital prostatic rectal examination is essential; and in women, the pelvic gynecologic examination is crucial. In literature, there is no agreement as to how extensive screening for occult cancer should be in primary DVT patients with no apparent risk factors. In this sense, we recommend using a modification of SOMIT’s study protocol, to detect more patients affected with neck cancers. In addition, from an economic point of view, it is advisable first to use an elementary approach and, only if needed, later to employ complex and expensive studies.

**CONCLUSION**

Our results suggest that in Mexican patients with primary DVT, occult cancer is frequent. Our results warrant additional projects.

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**Conflicts of interest**
There are no conflicts of interest.

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