Short Communication

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

Christian O Ramírez-Serrano Torres, Edgardo Román-Guzmán[1], Carlos-Manuel Ortiz-Mendoza[2]
Departments of General Surgery, [1]Vascular Surgery and [2]Surgical Oncology, ISSSTE Hospital General Tacuba, Mexico City, Mexico

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

How to cite this article: Ramirez-Serrano Torres CO, Román-Guzmán E, Ortiz-Mendoza CM. Occult cancer in patients with deep-vein thrombosis in a general hospital at Mexico City: A pilot study. J Res Med Sci 2017;22:63.

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.

Access this article online

Quick Response Code:

Website: www.jmsjournal.net

DOI: 10.4103/jrms.JRMS_559_16

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

Address for correspondence: Dr. Carlos-Manuel Ortiz-Mendoza, Department of Surgical Oncology, ISSSTE Hospital General Tacuba, Lago Ontario #119, Colonia, Tacuba, CP 11410, Delegación Miguel Hidalgo, Mexico City, Mexico. E-mail: cortizmendoza@yahoo.com.mx
Received: 26-06-2016; **Revised:** 22-01-2017; **Accepted:** 09-02-2017

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].[4,6] 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]

Table 1: Type and frequency of identified cancer

Cancer	Cancer stage	Males	Females
Endometrial	III C IV	-	2 moderately differentiated endometrioid adenocarcinoma 1 adeno-squamous cell carcinoma
Cervical	IV	-	1 squamous cell carcinoma 1 moderately differentiated adenocarcinoma
Ovary	III C	-	2 high grade papillary serous carcinoma
Breast	IV	-	1 lobular carcinoma 1 ductal carcinoma
Stomach	IV	1 moderately differentiated adenocarcinoma	4 moderately differentiated adenocarcinomas
Prostate	IV	2 poorly differentiated adenocarcinoma 2 moderately differentiated adenocarcinoma 1 no biopsy	-
Pancreas	IV	1 no biopsy	-
Colorectal	IV	1 moderately differentiated adenocarcinoma 1 poorly differentiated adenocarcinoma	1 poorly differentiated rectal adenocarcinoma
Lung	IV	1 squamous cell carcinoma	1 squamous cell carcinoma 1 no biopsy
Kidney	II	1 clear cell carcinoma	1 papillary cell carcinoma
Thyroid	IVA	1 papillary thyroid carcinoma	1 papillary thyroid carcinoma

Table 2: Studies regarding DVT and occult cancer

Author	Year	R/P	*n*	Frequency (%)	Common cancer	Gender (%)	Mean Age (years)
Piccioli[6]	2004	P	201	11.4	Urinary bladder, lung, C-R, prostate	♀ 52.7	66.4
White[7]	2005	R	528, 693	0.11	Prostate, lung, breast	♀ 51	66
Oktar[8]	2007	P	126	7.9	Lung, prostate	♀ 53.9	56
Chung[4]	2014	R	28, 243	6.9	Lung, liver, C-R	♀ 51.4	63.4
Semb[10]	2014	P	499	9.4	Lung	♀ 53	75
Carrier[9]	2015	P	854	3.9	C-R/Gyn	♀ 67.4	54
Ramírez	2015	P	182	16.5	Prostate, Gyn	♀ 56.6	61.3

DVT = Deep vein thrombosis; R = Retrospective; P = Prospective; C-R = Colorectal; Gyn = Gynecological cancers; ♀ = Females; ♂ = Males.

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.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

REFERENCES

1. Globocan 2012: Estimated Incidence, Mortality and Prevalence Worldwide in 2012. Available from: http://www.globocan.iarc.fr/Pages/fact_sheets_cancer.aspx. [Consulted on 2015 Sep 17].
2. Elyamany G, Alzahrani AM, Bukhary E. Cancer-associated thrombosis: An overview. Clin Med Insights Oncol 2014;8:129-37.
3. Marks MA, Engels EA. Venous thromboembolism and cancer risk among elderly adults in the United States. Cancer Epidemiol Biomarkers Prev 2014;23:774-83.
4. Chung WS, Lin CL, Hsu WH, Sung FC, Li RY, Kao CH. Idiopathic venous thromboembolism: A potential surrogate for occult cancer. QJM 2014;107:529-36.
5. Carrasco-González H, Rojas-Guevara PA, Serrano-Lozano JA, Sánchez-Nicolat NE, Rojas-Gómez C. Trousseau´s syndrome experience in the Hospital Lic. Adolfo Lopez Mateos. Rev Mex Angiol 2010;38:14-8. Available from: http://new.medigraphic.com/cgi-bin/resumen.cgi?IDARTICULO=42791. [Consulted on 2017, Mar 14].
6. Piccioli A, Lensing AW, Prins MH, Falanga A, Scannapieco GL, Ieran M, *et al.* Extensive screening for occult malignant disease in idiopathic venous thromboembolism: A prospective randomized clinical trial. J Thromb Haemost 2004;2:884-9.
7. White RH, Chew HK, Zhou H, Parikh-Patel A, Harris D, Harvey D,

et al. Incidence of venous thromboembolism in the year before the diagnosis of cancer in 528,693 adults. Arch Intern Med 2005;165:1782-7.
8. Oktar GL, Ergul EG, Kiziltepe U. Occult malignancy in patients with venous thromboembolism: Risk indicators and a diagnostic screening strategy. Phlebology 2007;22:75-9.
9. Carrier M, Lazo-Langner A, Shivakumar S, Tagalakis V, Zarychanski R, Solymoss S, *et al.* Screening for occult cancer in unprovoked venous thromboembolism. N Engl J Med 2015;373:697-704.
10. Semb VB, Tveit A. Limited malignancy screening of patients with idiopathic venous thromboembolism. Tidsskr Nor Laegeforen 2014;134:407-11.
11. Castillo-Costa YN, Gómez-Santa-María HR, Mauro VM, Blanco-Cerdeira P, Thierer J, Higa C. Argentine registry of venous thromboembolism. Rev Argent Cardiol 2013;81:233-8. Available from: http://www.scielo.org.ar/pdf/rac/v81n3/en_v81n3a08.pdf. [Consulted on 2017 Mar 14].