Deep venous thrombosis caused by congenital inferior vena cava agenesis and heterozygous factor V Leiden mutation – a case report

Pablo Guisado Vasco MD PhD¹, Angel Ruedas López MD¹, María Laiño Piñeiro MD², José Ignacio Gallego Rivera MD³

P Guisado Vasco, A Ruedas López, M Laiño Piñeiro, JI Gallego Rivera. Deep venous thrombosis caused by congenital inferior vena cava agenesis and heterozygous factor V Leiden mutation – a case report. *Int J Angiol* 2009;18(3):147-149.

The unusual clinical presentation, importance of imaging techniques and role of low molecular weight heparin are described for an initial treatment of thrombosis in inferior vena cava agenesis associated with heterozygous factor V Leiden. The patient, a 36-year-old woman, presented to the emergency room with sudden onset of back pain, swelling of the legs and thighs, and claudication while walking. Abdominal ultrasonography was immediately ordered. Anomalies in vascular

blood flow were detected. Computed tomography was performed, and initially showed a complete absence of the infrarenal segment of inferior vena cava caudally to the origin of both renal veins. Treatment with enoxaparin (1 mg/kg twice per day) was started. The patient was discharged and returned to her activities of daily living two weeks after admission. This vascular abnormality is mostly incidentally diagnosed in adults and only a few cases are described as being associated with thrombophilia.

Key Words: Anticoagulation; Factor V Leiden; Inferior vena cava agenesis; Low molecular weight heparin

Anomalies in the development of the inferior vena cava (IVC) appear between the sixth and eighth weeks of gestation if improper development or regression of the following three paired embryonic veins occurs: the vitelline, subcardinal and embryonic cardinal veins. Absence of the IVC has been estimated in between 0.3% to 0.5% of the general population (1). However, its prevalence in the group of patients with deep venous thrombosis may reach up to 5% (2,3). The mean adult age of clinical onset is between the second and fourth decade of life (4,5). Two main events lead to discovery of such anomalies in adults – incidental medical diagnosis and thrombosis.

CASE PRESENTATION

A 36-year-old Caucasian woman presented to the emergency department complaining of swelling in both legs and nonradiating acute low back pain for less than 24 h. She experienced intense thigh tenderness on walking during the previous three days. The patient denied any abdominal pain, leg numbness or weakness, or standing for extended periods or physically exerting herself to exhaustion in the preceding days. She had no other systemic symptoms.

The patient had an active life, practicing climbing frequently. She smoked 20 cigarettes per day. She had no previous pregnancies. She was not taking oral contraceptives or any other medication. Her mother suffered from deep venous thrombosis.

On physical examination, she appeared healthy, and had an arterial blood pressure of 100/60 mmHg, a regular heart rate of

72 beats/min, a respiratory rate of 16 breaths/min and an axillary temperature of 35.5°C. She had no jugular venous distention. No skin lesions or enlarged lymph nodes were detected. Her chest was clear to auscultation on both sides and she had normal heart sounds. Her abdominal examination did not reveal any masses or vascular murmurs. Both legs presented tight nonfoveal edema down to her knees. The Hoffman sign was negative and her calves were pain free. The peripheral arterial pulses were symmetrical.

Abdominal duplex ultrasonography was performed in the emergency room. It showed abnormal filling of the hypogastric vessels. After this finding, contrast-enhanced computed tomography (CT) was performed. CT showed a complete absence of the infrarenal segment of IVC caudally to the origin of both renal veins. The suprarenal section was preserved. Thrombi were observed inside both common iliac veins. The ascending lumbar and venous plexus, azygos and hemiazygos veins, and anterior paravertebral collateral veins were enlarged (Figure 1).

Laboratory investigations did not reveal any abnormalities of renal and hepatic functions. The hemogram was normal. The erythrocyte sedimentation rate was 30 mm/h and the C-reactive protein reached 14.4 mg/L. Antinuclear antibodies, immunoglobulins, cryoglobulins and tumoral markers were within the normal ranges. The thrombophilia study revealed heterozygous factor V Leiden mutation.

Anticoagulation with low molecular weight heparin (LMWH) (enoxaparin) was started at a dose of 1 mg/kg twice per day. Thigh tenderness and leg swelling improved over the

¹Departments of Internal Medicine; ²Rheumatology; and ³Radiology, University Hospital Ramon y Cajal, Madrid, Spain

Correspondence: Dr Pablo Guisado Vasco, Department of Internal Medicine, University Hospital Ramon y Cajal, Bordadores street number 9.

Bis. 3ºD. Madrid (Madrid), Spain 28013. Telephone 003-491-336-8402, e-mail pg_vasco@yahoo.es

Figure 1) **A** Coronal contrast-enhanced computed tomography (CT) image. The inferior vena cava could not be visualized inferior to the liver (arrow). **B** Coronal contrast-enhanced CT slice. The left iliac vein appears thrombosed (arrow). **C** Axial contrast-enhanced CT image (thorax section) showing a hypertrophied azygos vein system. The dilated dorsal paravertebral anterior vein and epidural plexus (arrow) can also be seen. **D** Axial gadolinium-enhanced magnetic resonance imaging showing huge retroperitoneal vein collateralization system (arrows)

following week. The patient was discharged and returned to her activities of daily living two weeks after admission.

DISCUSSION

In normal adults, the IVC has four main segments – prerenal, renal, hepatic and posthepatic (6). The absence of IVC inferior segments in slices of magnetic resonance and CT angiography suggests a congenital anomaly (7,8). A multiple cavocaval anastomosis procedure has been developed, switching the IVC and superior vena cava through the azygos and hemiazygos vein system, and the iliac, lumbosacral and vertebral vein plexus. If the collateral circulation is developed well enough, symptoms are likely to be prevented in adults, even in the presence of prothrombotic factors such as hyperhomocysteinemia (2), protein S deficiency (4) and factor V Leiden mutation (1,5). The absence of clinical symptoms in our patient may be justified by this consideration. It is hard to say how long both common

iliac veins were thrombosed. A possible hypothesis is that she had been experiencing several thrombotic events due to her thrombophilia (factor V Leiden carrier). Therefore, she was asymptomatic until the collateral vein system was suddenly blocked, possibly because of a new clot formation. This point could explain the patient's lumbar pain (8) given that possible clots were not seen on imaging, neither in the ascending collateral lumbar vein plexus nor another collateral small-sized vein.

Initial treatment with LMWH (2) is an alternative in patients who have contraindications or refuse oral administration of vitamin K inhibitors. Our patient refused initial anticoagulation with acenocoumarol during the first six months. The treatment with LMWH (1 mg/kg twice per day) was performed as maintenance until oral anticoagulation was finally started. After 24 months follow-up, no new symptoms were detected.

The role of the duplex ultrasonography in this pathology is not well studied. Most studies used CT angiography to show these anomalies. In our case, abdominal ultrasonography was used as a screening technique in the emergency room, helping lead us to the correct diagnosis. It is not known whether ultrasonography could be useful in the follow-up of these patients. We believe further studies should be performed to investigate this point.

Abdominal vascular pathology should be strongly considered in young women or men who complain of sudden swelling or weakness of both legs, regardless of whether it is associated with low abdominal or recent back pain (9). Other IVC malformation should be considered in young patients with idiopathic deep venous thrombosis (10-13).

The most appropriate treatment approach is long-term oral anticoagulation in those patients with thrombophilia and IVC abnormalities (9). Treatment with LMWH is a good and safe alternative for patients with any contraindication for oral anticoagulation. We also recommend avoiding additional thrombosis risk factors such as smoking, hormonal contraceptives, immobilization or unusual physical activity.

DISCLOSURE: All authors have read the manuscript and have participated in the writing and preparation of the present work. They also all had complete access to the data presented in this article. We have no potential conflict of interest arising from associations with commercial or corporate interest in connection with the work submitted.

REFERENCES

- Schneider JG, Eynatten MV, Dugi KA, Duex M, Nawroth PP. Recurrent deep venous thrombosis of the inferior vena cava and heterozygous factor V Leiden mutation. *J Intern Med* 2002;252:276-80.
- Yun SS, Kim JI, Kim KH, et al. Deep venous thrombosis caused by congenital absence of inferior vena cava, combined with hyperhomocysteinemia. *Ann Vasc Surg* 2004;18:124-9.
- Ruggeri M, Tosoletto A, Castaman G, Rodeghiero F. Congenital absence of the inferior vena cava: A rare risk factor for idiopathic deep-vein thrombosis. *Lancet* 2001;357:441.
- Obernoester A, Aschauer M, Schnedl W, Lipp RW. Anomalies of the inferior vena cava with iliac venous thrombosis. *Ann Intern Med* 2002;136:37-41.
- Chee YL, Cullighan DJ, Watson HG. Inferior cava malformation as risk factor for deep venous thrombosis in the young. *Br J Haematology* 2001;114:878-80.
- Körber T, Petzsch M, Placke J, Ismer B, Schulze C. Acute thrombosis of the deep leg and pelvic veins in agenesis of the renal inferior vena cava. *Z Kardiol* 2001;90:52-7.
- Bass JE, Redwine MD, Kramer LA, Huynh PT, Harris JH Jr. Spectrum of congenital anomalies of the inferior vena cava: Cross-sectional imaging findings. *Radiographics* 2000;20:639-52.
- Clayburgh DR, Yoon JD, Cipriani NA, Ricketts PA, Arora VM. Clinical problem-solving. Collateral damage. *N Engl J Med* 2008;359:1048-54.

9. Salgado Ordoñez F, Gavilan Carrasco JC, Bermudez Recio FJ, et al. Absence of the inferior vena cava causing repeated venous thrombosis in an adult. *Angiology* 1998;49:951-6.
 10. Garcia-Fuster MJ, Forner MJ, Flor-Lorente B, Soler J, Campos S. Inferior cava malformations and deep venous thrombosis. *Rev Esp Cardiol* 2006;59:171-5.
 11. Simon RW, Amann-Vesti BR, Pfammatter T, Koppensteiner R. Congenital absence of the inferior vena cava: A rare risk factor for idiopathic deep-vein thrombosis. *J Vasc Surg* 2006;44:416.
 12. Takehara N, Hasebe N, Enomoto S, et al. Multiple and recurrent systemic thrombotic events associated with congenital anomaly of inferior vena cava. *J Thromb Thrombolysis* 2005;19:101-3.
 13. Jimenez Gil R, Miñano Pérez A, Bercial Arias J, Berbaneu Pascual F, Sansegundo Romero E. Agenesis of inferior vena cava associated with lower extremities and pelvic venous thrombosis. *J Vasc Surg* 2006;44:1114-6.
-

INSTRUCTIONS TO AUTHORS

Continued from page 118

REFERENCES: Identify references in the text by arabic numerals in parentheses on the line. Type the reference list double-spaced, on pages separate from the text, **with each reference numbered consecutively in the order in which it is mentioned in the text.** (References cited in figures and tables, but not in the text, should also be numbered following the text references). Personal communications, manuscripts in preparation and other unpublished data should not be cited in the reference list but may be mentioned in the text in parentheses. Identify abstracts with the abbreviation 'Abst' and letters to the editor by 'Lett' in parentheses; in general, abstracts should not be cited if more than two years old.

The style of references is that of Index Medicus. Journal references should contain inclusive page numbers; book references specific page numbers; and website references the date of last update, if available, and date of access (references to other types of electronic documents should include format of the document). Abbreviations of journals should conform to those used in Index Medicus, National Library of Medicine. The style and punctuation of references are as follows:

Periodicals

List all authors if six or less; otherwise list first three and add 'et al'. Do not use periods after authors' initials.

Kohl P, Day K, Noble D. Cellular mechanisms of cardiac mechano-electric feedback in a mathematical model. *Can J Cardiol* 1998;14:111-9.

Books

Svensson LG, Crawford ES. Cardiovascular and Vascular Disease of the Aorta. Toronto: WB Saunders Company, 1997:184-5.

Chapter in book

Trehan S, Anderson JL. Thrombolytic therapy. In: Yusuf S, Cairns JA, Camm AJ, Fallen EL, Gersh BJ, eds. Evidence Based Cardiology. London: BMJ Books, 1998:419-44.

Web site

National Library of Medicine. Images from the History of Medicine. <<http://www.nlm.nih.gov/>> (Version current at January 5, 1999).

FIGURE LEGENDS: Type double-spaced, separate from the text, with figure numbers corresponding to the order in which figures are presented in the text. Identify all abbreviations appearing on figures in alphabetical order at the end of each legend. Enough information should be given to allow interpretation of the figure without reference to the text. Written permission must be obtained from the publisher to reproduce any previously published figures. Cite the source of the figure in the legend. Figure legends should not appear on the actual figures.

TABLES: Tables must be created using Microsoft Word (.doc) or Excel (.xls). Type double-spaced on separate sheets with the table number above the table and explanatory notes below. Table numbers should appear in arabic numerals and should correspond to the order of the tables in the text. Footnote each table with an alphabetical listing of all abbreviations used. Written permission must be obtained from the publisher to reproduce any previously published figures.

FIGURES: All figures have to be submitted in their original formats. The lettering, decimals, lines and other details on the figures should be sufficiently large to withstand reduction and reproduction. Graphs must be created using Microsoft Word (.doc), Microsoft Power Point (.ppt), Microsoft Excel (.xls), Corel Draw (.cdr) or Adobe Illustrator (.ai or .eps). Any photographs or graphics imported into your figure must also be submitted separately. Photographs and graphics must be scanned at a resolution of no less than 300 dpi and saved as a .tiff file. Place crop marks on photomicrographs to show the essential field and designate special features with arrows (which must contrast with the background). The first author's last name, the figure number and the location of the 'top' must be indicated on the back of each proof. Figures are published in black and white. Photographs and graphics will not be returned.

POLICY ISSUES: All statements and opinions are the responsibility of the authors. With submission of the manuscript, a letter of transmittal must indicate that all authors have participated in the research, and have reviewed and agree with the content of the article. The publisher reserves copyright on all published material, which then may not be reproduced without the written permission of the publisher.

Conflict of interest

All authors must disclose any commercial associations or other arrangements (eg, financial compensation received, patient-licensing arrangements, potential to profit, consultancy, stock ownership, etc) that may pose a conflict of interest in connection with the article. This information will be made available to the editor and reviewers, and may be included as a footnote at the editor's discretion.

Proofs

Authors should keep a copy of their original manuscripts because page proofs will be sent to them without the manuscript. In order to avoid delays in publication, authors are required to return proofs within 48 hours by fax.

Potential authors who have further questions about these issues should contact the Editor-in-Chief at 516-484-3430.