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EARLY DETECTION OF THORACIC VESSELS INVOLVEMENT IN PATIENTS WITH BEHDzT'S DISEASE HAVING ONE EPISODE OF LOWER EXTREMITY DEEP VEIN THROMBOSIS

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- **ABSTRACT**

Objective: To determine the risk of thoracic vessels involvement in patients with Beh 祇's disease (BD) presenting with lower extremity deep vein thrombosis (DVT).
Methods: The study was performed from August 1997 to April 1998, on 10 patients with BD, who had at least one episode of DVT in the lower extremities in their past or present illness. The diagnosis of DVT was based on physical examination and sonography and/or Doppler sonography. Medical history taking regarding pulmonary symptoms such as: cough, with or without sputum production, dyspnea, chest pain, and hemoptysis as well as physical examination, including vascular examination, was performed in all the cases. A new chest x-ray was taken from all 10 cases and following an informed consent, 7 patients had a high resolution CT scan (HRCT) of the chest. All of the 10 studied cases underwent thoracic vessels angiography using the intra-venous digital subtraction angiography (IVDSA) method. The analysis of data was done using Fisher's exact test and student T-Test.
Results: Out of the 10 studied cases, seven were male and three were female. Three patients had only one episode, while the other 7 had more than one episode of DVT in the lower extremities. The time interval from diagnosis of BD to the emergence of vascular lesions was 7.8 years. Regarding respiratory manifestations, 5 out of 10 cases were symptomatic and the rest were asymptomatic. Chest x-rays of 9 out of 10 cases were normal, while in one case changes in favor of pulmonary artery aneurysm (PAA), were observed. HRCT scans from the thoracic cage were done in 7 out of 10 cases, with 3 positive findings, [2 with pulmonary artery thrombosis (PAT) and 1 with superior vena cava obstruction (SVCO)]. On thoracic vessel IVDSA 6 cases with positive findings were detected (3 with PAA, 3 with SVCO, and 2 with pulmonary artery thrombosis), in both symptomatic and asymptomatic cases. (Fisher exact =0.4850)(p value=0.05%, t (9) = 1.97, risk = 30%). Gender and pulmonary symptomatology had no significant effect with respect to the results.
Conclusion: Patients with (BD) with at least one episode of DVT in the lower extremities have a 30% risk of thoracic vessels involvement by non-invasive angiography using the IVDSA method. Hemoptysis is a late heralding sign for thoracic vessels involvement in BD patients with thrombophelebitis of the lower extremities. Therefore, we recommend radiological screening of thoracic vessels by IVDSA method in this group of BD patients, especially in areas with an increased prevalence of BD. Chest x-ray is not a good screening method for detection of thoracic vessels involvement although HRCT scan can be a helpful procedure for detection of thrombosis in thoracic vessels.

Irn J Med Sci 2000; 25(1&2):15-20

Key Words • Beh 祇's disease • deep vein thrombosis • thoracic-vessel • IVDSA

Introduction

Beh 祇's disease (BD) is a multi-systemic disease of unknown etiology, classified in rheumatology in the category of vasculitis. BD has a worldwide distribution, but is more prevalent in Japan, Korea, China, Turkey and Iran.[1-3] Davatchi et al, give a prevalence of 1 patient in 6000 for the Iranian population.[4] BD was first described in 1937 by Hulusi Beh 祇, a Turkish dermatologist. In the classic form, it comprises recurrent oral ulcer, genital lesions and eye involvement in the form of uveitis. Later on, other organ systems are also involved. These include skin, joints, pulmonary, gastro-intestinal and cardio-vascular systems, with small and large vessel involvement. The latter may lead to thrombosis, arterial aneurysm or occlusion.[1]

Pulmonary arterial aneurysms (PAA) in BD, carry a high short-term mortality despite treatment. BD patients with PAA are reported to have a higher prevalence of deep vein thrombosis (DVT) in the lower extremities.[1]

In this study, we have shown that BD patients with at least one episode of DVT in the lower extremities carry a higher risk of thoracic vessels involvement. Hence, early diagnosis is essential in these patients,[5] given that anticoagulant therapy may adversely affect an occult PAA.

Materials and Methods

This study was performed from August 1997 to April 1998 at the Beh 祒 Research Clinic of Namazee Hospital, Shiraz, Iran on 10 patients who suffered from at least one episode of DVT of the lower extremities in their past or present illness. DVT was diagnosed by physical examination, sonography and/or doppler sonography. The diagnosis of chest involvement was based on the history of pulmonary symptoms including cough, with or without sputum production, dyspnea, chest pain, and presence of hemoptysis. Initially, a new chest x-ray was taken in all cases. Following an informed consent 7 patients had an HRCT of the chest and all 10 studied cases underwent thoracic vessels angiography by the intra-venous digital subtraction angiography IVDSA) method.[6,7]

Statistical analysis was done using Fisher's exact test and student T-Test.

Results

Out of 300 patients with BD, 44 cases suffered from vascular problems (14.66%). Out of these, ten patients with lower extremity thrombophlebitis were enrolled in this study. There were seven males and 3 females, (median of age = 34.4 ? 7.14 years). Three patients had only one episode, and the other 7 had more than one episode of DVT in the lower extremities.

The mean time interval from diagnosis of BD to emergence of thrombophlebitis was 93.5 months (7.8 years). The mean time interval between onset of DVT and initiation of this study was 72.8 months (6 years) (Table1).

Chest x-ray was taken in 10/10 patients. One chest x-ray showed a round left hilar mass that was diagnosed as an aneurysm using IVDSA (Fig.1). The other 9 chest x-rays were normal.

In 4/7 patients, HRCT scans were positive for vascular lesion (Table2). HRCT scans from the thoracic cage were performed in 7 out of 10 cases, with 3 positive findings, [2 with pulmonary artery thrombosis (PAT) and 1 with superior vena cava obstruction (SVCO)] (Table 2). On HRCT scan, PAA was characterized by a focal bulging in the main part of pulmonary artery or in its tributaries. Such bulging when reaching larger dimensions must be differentiated from hilar lymphadenopathy or pulmonary arterial hypertension.

Conventional pulmonary artery catheterization can show the pulmonary vascularities with a better resolution. However, due to the susceptibility of vessels of

Beh 祒's patients in developing thrombosis or aneurysmal lesions at the site of needle trauma during catheterization, conventional angiography is not warranted.[8] In

angiography of pulmonary and thoracic vessels by IVDSA, the vessels can be visualized without catheterization.[6,7]

In the cases that underwent IVDSA, six (3 females and 3 males) out of ten cases (60%), had thoracic vessel involvement in addition to

the thrombotic lesions in their lower extremities. Thus 60% of the patients with at least one episode of thrombophlebitis in the lower extremities had a positive vascular lesion in thoracic vessels, detected by IVDSA. Hence, the risk of thoracic vessels involvement in vasculo-BD was calculated to be 30% (T9=1.96, p=0.05%). This risk is without significant statistical association with pulmonary symptomatology such as hemoptysis, cough, chest pain and dyspnea (Fisher=1) (Table 2.) (Figs. 2,3).

Therefore, plain chest x-ray in the studied BD patients did not exclude the possibility of thoracic vessel involvement (Fisher=1). Out of 5 patients in the asymptomatic group, 3 patients had positive vascular findings in IVDSA (Table 2) (Fig. 3).

Absence of symptoms such as cough, sputum, dyspnea, hemoptysis and chest pain, does not rule out the possibility of thoracic vessel involvement. In this study, 3 out of 4 patients with a normal chest x-ray, had vascular involvement in the thorax, as shown by IVDSA. In patients with more than one episode of DVT (Fisher = 0.2), the risk of thoracic vessel involvement was the same as in those patients with one episode of DVT of the lower extremities.

Overall, the detected thrombotic and aneurysmal lesions in thoracic vessels of the studied BD patients were: 3 cases of PAT, 2 cases of SVC (superior vena cava thrombotic lesion), and 2 with PAA, diagnosed by both IVDSA and HRCT scan (Table 2).

Discussion

BD is a multi-system inflammatory disorder, which may involve the vascular system. It involves arteries and veins of all sizes. BD may run a very benign course although at times it may show a very aggressive behavior with poor prognosis. Vascular lesions include superficial thrombophlebitis, large vein thrombosis, arterial aneurysms and arterial occlusions.

Great vessel involvement in the thorax comprises aortic aneurysms, PAA, and/or pulmonary vessel thrombosis, SVCO and/or IVCO.[2] Arterial manifestations of BD carry a particularly poor prognosis. The incidence of arterial involvement in BD is reported to be 2.2%- 2.5%, however the incidence of arterial lesions seems to be underestimated; in one study it was as high as 34% at autopsy.[1,5] Great vessel involvement may progress to death. Patients with PAA, either due to dissection and rupture or hemoptysis due to broncho-arterial fistula, carry a high short-term mortality despite treatment.[3] Fatal rupture of aneurysms remains a major cause of death in Beh 祂's disease although spontaneous remission has also been reported.[5] The most common symptom is hemoptysis with pulmonary opacities on chest radiography. Of 4 cases with normal chest x-ray, 3 patients had vascular involvement in the thorax, as disclosed by IVDSA. (Fisher=1) (Table 2) (Figs.2,3).

Our study reconfirmed previous studies in the medical literature which stated that chest x-ray is not a good screening tool for the specific diagnosis of vascular involvement of the chest in vasculo-Beh 祴.[5] We feel that IVDSA is the procedure of choice for the documentation of pulmonary arterial involvement in BD. Magnetic resonance imaging is also helpful in the presumptive diagnosis of occluded aneurysms.[9]

The prevalence of thrombophlebitis in BD is around 25%, however in patients with PAA the prevalence is higher. In a report by Hamuryudan et al, this association was seen in 88% of BD cases.[5] Propagation of peripheral venous thrombosis may lead to serious vascular complications, such as caval, hepatic, or portal system occlusions.[1,3] The incidence of pulmonary emboli due to lower extremity thrombosis in BD is much lower than what is expected.[2] Hemoptysis in vasculo-Beh 祴, may be due to PAA, PAT, vasculitis in parenchymal tissue or less likely due to pulmonary thromboemboli and infarction. Hemoptysis is a late sign for heralding thoracic vessels involvement in BD with thrombophelebitis in lower extremities.

In this study, we reconfirmed that hemoptysis in BD patients with DVT in lower extremities, in the presence of a normal chest x-ray, is a sign which warrants more appropriate non-invasive radiological investigations of thoracic vessels in order to detect aneurysms or thrombosis in this particular group of patients, especially in areas with a higher prevalence of BD.

It should be emphasized, hemoptysis in BD with DVT of the lower extremity in the presence of normal chest x-ray may be misinterpreted as having pulmonary thromboemboli, and hazardous anticoagulation may be started for the patients.[1-3]

Although superficial thrombophlebitis is a relatively common presenting symptom, SVC thrombosis is rare and usually occurs several years after onset of the disease. Thrombosis of SVC may be life threatening owing to complications such as pulmonary embolism, and chylothorax.[5,9-12]

In the literature the mean time interval from the early diagnosis of BD to the emergence of vascular lesions is about three years,[5,9] however, our study revealed mean time interval of 7.8 years (93.5 months) (Table 2). Also a mean time of 72.8 months (6 years) was observed from the onset of DVT before the time of starting this study (Table 1).

Regarding pulmonary symptomatology, 3 out of 5 asymtomatic patients were found to have positive vascular involvement in the thoracic cage (Fisher=1) (Table 2).

Thus, the absence of symptoms such as: cough, sputum, dyspnea, hemoptysis and chest pain, does not rule out the possibility of thoracic vessels involvement in BD patients with DVT in the lower extremities. In our cases, with at least one episode of DVT, there was 30% chance of thoracic vessels involvement.

We have found a combination of thrombotic and aneurysmal vascular lesions in pulmonary and/or thoracic cage associated with lower extremity deep vein thrombosis (DVT), (simultaneously in the same patient) in 3 different cases (Table 2. Cases numbered 4,6,7).

The medical treatment in our patients consisted mainly of monthly pulse or daily oral Cyclophosphamide alone or with corticosteroids.[1,6,8] Warfarin was used for anticoagulation therapy of thrombosed vessels. In vasculo-Beh 祴 patients, the development of hemoptysis is a late sign of thoracic vessels involvement and initiating radiological investigations for diagnosis of PAA at that time may be too late and this delay in diagnosis may lead to an increase in the mortality rate of BD due to vascular problems, especially in regions with a high prevalence of the disease.

Conclusion

In this study BD patients with at least one episode of deep vein thrombosis in the lower extremities had a 30% risk of having another vascular lesion in thoracic vessels.

Normal chest x-ray in this group of BD patients does not exclude the possibility of thoracic vessel involvement.

The risk of thoracic vessel involvement was equal in patients with one episode of deep vein thrombosis and those with more than one episode.

Our suggestion for those countries in which BD is a health problem, is to screen the thoracic vessels in patients who have suffered from at least one episode of deep vein thrombophlebitis in the lower extremities, using angiography with a non-invasive method such as IVDSA for the possibility of other life threatening vascular involvements, regardless of the presence or absence of pulmonary symptomatology.

Acknowledgements

The authors would like to thank Prof. K. Vessal and Dr. F. Handjani for their assistance in reviewing the manuscript and their invaluable guidance.

References

1. Yazici H, Ozdogan H, Hamur Yudan V: Other forms of vasculitis and pseudovasculitis .*Baillier's Clinical Rheumatology* **1997:** 335-41.
2. Valnete RM, Hall S, O'Duffy JD: Beh 祴's disease. In: *Textbook of Rheumatology Kelley* 5th ed. Philadelphia: W.B. Saunders Co.**1997**.
3. Erkan F, Cavdar T: Pulmonary vasculitis in Beh 祴's Disease. *Am Rev Respir Dis 1992;***146:**232-9.
4. Davatchi F, Shahram F, Gharibdoost F, et al: Beh 祴's disease: Analysis of 3,443 cases. *APLAR J Rheumatol 1997;***1:**2-5.
5. Hamuryuan S. Yurdakul F, Moral F, et al: Pulmonary arterial aneurysms in Beh 祴's syndrome: a report of 24 cases. *Br J.Rheumatol 1994;***33;**48-51.
6. Tunaci A, Bertemen YM, Golemen E: Thoracic involvement in Beh 祴's disease: Pathologic, clinical and imaging features. *AJR 1995;***164:**51-6.
7. Ouitt TW, Newell JD: Digital subtraction angiography. *Radiol Clin North Am. 1985;***23:**177-209.
8. Numan F, Islak C, Berkmen T, et al: Beh 祴's disease: pulmonary arterial involvement in 15 cases. *Radiology 1994;***192:**465-8.
9. Hashimoto T, Haraoka H: Vasculo-Beh 祴's disease *Nipon Rinsho 1994;***52(8):**2138-42.
10. Mehmet A, Kzu MA, Ozasalan C, et al: Vascular involvement in Beh 祴's disease: 8-year audit. *World J Surg 1994;***18(6):** 948-54.
11. Roguin A, Edelstein S, Edoute Y: Superior vena cava syndrome as a primary manifestation of Beh 祴's disease. *Angiology 1997;***48(4):** 365-8.
12. Efthimiou J, Johnston C, Spiro SG, Turner-warwick M: Pulmonary disease in Beh 祴's syndrome. *Q J Med 1986;***227:**259-80.