JOURNAL OF FORENSIC SCIENCES

J Forensic Sci, May 2012, Vol. 57, No. 3
doi: 10.1111/j.1556-4029.2011.02042.x
Available online at: onlinelibrary.wiley.com

PAPER

PATHOLOGY/BIOLOGY

Hannah E. Rosenfeld,[1,2] *and Roger W. Byard,*[1,2] *M.D.*

Is There a Relationship Between Bladder Outlet Obstruction due to Benign Prostatic Hyperplasia and Pulmonary Thromboembolism?

ABSTRACT: Benign prostatic hyperplasia with chronic bladder outlet obstruction has been associated with deep venous thrombosis (DVT) and fatal pulmonary thromboembolism (PTE). To evaluate this further, 60 autopsy cases of men with PTE were compared with 60 age-matched controls. The criteria for outlet obstruction were macroscopic prostatic enlargement with bladder trabeculation and benign prostatic hyperplasia on microscopy. Ten of the 60 men (16.7%) with fatal PTE had evidence of bladder outlet obstruction (age 57–78 years; mean 71.4 years). Of the 60 controls, 12 had evidence of bladder outlet obstruction (20%) (age 67–86 years; mean 75.5 years). No significant relationship could be demonstrated between bladder outlet obstruction and fatal PTE cases ($p = 0.8$). Given reports of this association, however, it is possible that bladder distension with venous compression may act as a risk modifier in certain individuals in association with other significant comorbidities, but this risk appears low.

KEYWORDS: forensic science, pulmonary thromboembolism, deep venous thrombosis, benign prostatic hyperplasia, bladder outflow obstruction

Pulmonary thromboembolism (PTE) is an important cause of sudden death in Western countries, being responsible for *c.* 5% of deaths in hospitalized patients (1–3). Abnormalities in blood flow may lead to thrombosis, and it has been noted in the literature, and in a separate study that we have conducted (4), that bladder distension secondary to benign prostatic hyperplasia may be associated with lower limb venous stasis and deep venous thrombosis (DVT) with fatal PTE. This study was undertaken to determine whether there was an increased risk of DVT and fatal PTE in individuals with evidence of chronic bladder outlet obstruction secondary to benign prostatic hyperplasia compared with those without bladder outlet obstruction.

Materials and Methods

Sixty autopsy cases in men where sudden and unexpected death had been attributed to PTE were randomly selected from the case files of Forensic Science SA, Adelaide, South Australia, from January 2004 to December 2008. Sixty age- and gender-matched controls were also randomly selected from the same time period. Case files were reviewed, and those cases where chronic bladder outlet obstruction was identified were selected. The criteria used to define bladder outlet obstruction were macroscopic evidence of prostatic enlargement with urinary bladder surface trabeculation and benign prostatic hyperplasia on microscopy. Case details including age, underlying medical conditions, and other significant autopsy findings were summarized. Forensic Science SA is the South Australian state forensic facility where medico-legal autopsies are performed. The population served is *c.* 1.6 million. All of the cases had full autopsies with complete coronial and police investigations. Statistical analysis was performed using Pearson's chi-square test.

[1]The University of Adelaide Medical School, Frome Road, Adelaide, SA 5005, Australia.
[2]Forensic Science SA, 21 Divett Place, Adelaide, SA 5000, Australia.

Received 24 Feb. 2011; and in revised form 19 April 2011; accepted 23 April 2011.

Results

A total of 10 of the 60 men (16.7%) with fatal PTE had evidence of bladder outlet obstruction. The age range was 26–96 years; average = 62.5 years. Of the 60 men controls (age range = 26–96 years; average = 62.5 years), 12 had evidence of bladder outlet obstruction, representing 20% of cases. The age range of the 10 cases with PTE and bladder outlet obstruction was 57–78 years, mean = 71.4 years, compared with the age range of the 12 control cases with simple bladder outlet obstruction whose age range was 67–86 years, mean = 75.5 years. Statistical analysis revealed no significant difference in the proportion of men with evidence of bladder outlet obstruction between the fatal PTE cases and the controls ($p = 0.8$).

Discussion

DVT and PTE are significant causes of morbidity and mortality in Western countries (1,5). Proposed by Virchow in 1856, the triad of predisposing factors to thrombosis consists of blood stasis, hypercoagulability, and endothelial injury (6). Accordingly, risk factors for DVT and PTE include recent surgery, lower limb trauma, hospitalization, immobility, lower limb paralysis, malignancy, inherited thrombophilias, and acquired hypercoagulable states. The latter may be associated with oral contraceptive use, hormone replacement therapy, and pregnancy. In addition to these

predisposing factors, increasing age is also a well-recognized risk factor for venous thromboembolism (5–8). Occasionally, fatal PTE may arise from the periprostatic venous plexus (9).

As with venous thromboembolism, benign prostatic hyperplasia is an age-related condition (10–12). The histologic prevalence of benign prostatic hypertrophy is *c.* 10% among men in their 30s and rises progressively to a prevalence of 80–90% in those over 70 years of age (10,13,14). The etiology of benign prostatic hyperplasia is not well understood, but androgens are generally considered to play a pathogenic role. As such, risk factors for benign prostatic hypertrophy are thought to include advancing age and the presence of functional testes (10,11,14,15).

In a recent study conducted by the authors, a diverse range of pelvic space-occupying lesions were identified that could potentially play a causal role in lower limb venous stasis (4). The mechanism thought to explain this association was extrinsic compression of pelvic veins leading to obstruction of venous flow. Venous stasis has various clinical manifestations including lower limb edema, DVT, and PTE, although fatal PTE is rarely observed. Examples of pelvic masses that may be associated with lower limb venous stasis include uterine leiomyoma, a distended urinary bladder, extraperitoneal endometriosis, synovial cyst, gravid uterus, penile prosthesis reservoir, psoas abscess, and various other benign uterine and ovarian tumors (4).

In the literature, there have been cases of bladders distended with urine (>300 ml) causing compression of the iliac veins leading to lower limb venous stasis (16–20). This phenomenon raises the possibility that there could be an increased incidence of venous thromboembolism owing to this venous stasis.

Although the current study has shown that there was no demonstrable increase in the risk of PTE in men with bladder outlet obstruction, this does not explain isolated cases where DVT and PTE are found with benign prostatic hyperplasia. While it is possible that the two entities may have a purely coincidental relationship associated with increasing age, it also may be possible that bladder distension with venous compression acts as a risk modifier, increasing the risk of DVT in individuals who have other significant comorbidities or conditions predisposing to thrombosis (21). Certainly in the previous study, the two individuals with outflow obstruction DVT and PTE also had significant cardiovascular disease (4). It is possible that a study with larger numbers of cases may have greater power to detect any subtle additive effects that prostatic hypertrophy may have on the formation of DVT.

References

1. Park B, Messina L, Dargon P, Huang W, Ciocca R, Anderson FA. Recent trends in clinical outcomes and resource utilization for pulmonary embolism in the United States: findings from the nationwide inpatient sample. Chest 2009;136:983–90.
2. Baglin TP, White K, Charles A. Fatal pulmonary embolism in hospitalised medical patients. J Clin Pathol 1997;50:609–18.
3. Alikhan R, Peters F, Wilmott R, Cohen AT. Fatal pulmonary embolism in hospitalised patients: a necropsy review. J Clin Pathol 2004;57:1254–7.
4. Rosenfeld H, Byard RW. Lower extremity deep venous thrombosis with fatal pulmonary thromboembolism caused by benign pelvic space occupying lesions—an overview. J Forensic Sci 2012; e-pub ahead of print. DOI: 10.1111/j.1556-4029.2011.02047.x
5. Heit JA. The epidemiology of venous thromboembolism in the community. Arterioscler Thromb Vasc Biol 2008;28:370–2.
6. Esmon CT. Basic mechanisms and pathogenesis of venous thrombosis. Blood Rev 2009;23:225–9.
7. Lowe GDO. Common risk factors for both arterial and venous thrombosis. Br J Haematol 2008;140:488–95.
8. Thomas RH. Hypercoagulability syndromes. Arch Intern Med 2001;161:2433–10.
9. Reddy PV, Solomon D. Pulmonary emboli from massive thrombosis of the periprostatic venous plexus mimicking acute respiratory distress syndrome. Chest 2003;124:251S.
10. Bushman W. Etiology, epidemiology and natural history. Urol Clin North Am 2009;36:403–15.
11. Lepor H. Pathophysiology, epidemiology, and natural history of benign prostatic hyperplasia. Rev Urol 2004;6(Suppl. 9):S3–10.
12. Byard RW, Cutz E. Sudden and unexpected death in infancy and childhood due to pulmonary thromboembolism. Arch Pathol Lab Med 1990;114:142–4.
13. Paolone DR. Benign prostatic hyperplasia. Clin Geriatr Med 2010;26:223–39.
14. Tang J, Yang J-C. Etiopathogenesis of benign prostatic hyperplasia. Indian J Urol 2009;25:312–7.
15. Jacobsen SJ. Risk factors for benign prostatic hyperplasia. Curr Urol Rep 2007;8:281–8.
16. Meinardi JR, Kremer J, van der Meer J. Deep vein thrombosis associated with distension of the urinary bladder due to benign prostatic hypertrophy—a case report. Neth J Med 2004;62:137–8.
17. Karanth NS, Crausman RS, De Palo VA. Deep venous thrombosis as a consequence of benign prostatic hypertrophy. Med Health R I 2005; 88:18–9.
18. Palma L, Peterson MC, Ingebretsen R. Iliac vein compression syndrome from urinary bladder distension due to prostatism. South Med J 1995; 88:959–60.
19. Evans JM, Owens TP Jr, Zerbe DM, Rohren CH. Venous obstruction due to a distended urinary bladder. Mayo Clin Proc 1995;70:1077–9.
20. Andrew WK. An unusual cause of deep venous thrombosis of the lower limb. S Afr Med J 2000;90:42.
21. Nicklin A, Byard RW. Lethal manifestations of systemic lupus erythematosus in a forensic context. J Forensic Sci 2011;56:423–8.

Additional information and reprint requests:
Roger W. Byard, M.D.
Professor
Discipline of Anatomy and Pathology
Level 3 Medical School North Building
The University of Adelaide
Frome Road
Adelaide
SA 5005
Australia
E-mail: roger.byard@sa.gov.au