MASSIVE SADDLE PULMONARY EMBOLISM: A CASE REPORT IN A RESOURCE-POOR SETTING AND REVIEW OF LITERATURE

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CASE REPORT

A 45-year-old apparently healthy man presented to the Cardiology Clinic with a 6-month history of recurrent breathlessness and chest pain. Prior to referral, he had been treated for asthma and chronic obstructive pulmonary disease with no improvement. A cardiovascular cause of his recurrent breathlessness was queried and he was then sent to the cardiologist. An additional history of transient unilateral right leg pain and swelling 7 months earlier was obtained. This occurred following a long-haul flight from Nigeria to Zambia. He was not known to be hypertensive or diabetic.

On examination, he had a resting tachycardia which ranged between 114 and 140 beats per minute. Pulses were however not palpable on his left upper limb. Blood pressure was also not recordable on the same limb. Blood pressure measured over the brachial artery on the right was 118/78 mmHg. His neck veins were distended and the pulmonary component of his second heart sound was loud. Electrocardiography done showed sinus tachycardia with incomplete right bundle branch block. Chest x-ray showed multiple sites of sub-pleural infarction. Echocardiography showed mild systolic and diastolic dysfunction with an ejection fraction of 49%. Full blood count, fasting blood sugar, fasting serum lipids, electrolytes, urea, creatinine and uric acid were all normal. D-dimer was however elevated. Doppler ultrasound scan (USS) revealed a large deep vein thrombus (DVT) in the left femoral vein with associated non-compressibility of the vessel (Figure 1).

A chest computed tomographic angiography (CTA) was done which revealed a large saddle pulmonary embolus straddling the main pulmonary arterial trunk at its bifurcation and extending into the main right and left pulmonary arteries (Figure 2). He was commenced on subcutaneous low-molecular-weight heparin (LMWH) while delivery of tenectaplase was being awaited. He also received intravenous morphine for his chest pain. He subsequently received a single dose of intravenous tenectaplase and was continued on subcutaneous LMWH and oral warfarin with the LMWH withdrawn after a few days. He was anticoagulated to a target international normalized ratio (INR) of 2.5 – 3.

Within 24 hours of thrombolysis, pulses on the left upper extremity became palpable. Brachial blood pressure also became recordable. Oxygen saturation (by pulse oximetry) also increased in both upper extremities to 88% – 90%. Breathlessness and chest pain also diminished greatly and he no longer needed morphine. A repeat chest CTA scan showed a marked reduction in the size of the saddle embolus. He was subsequently discharged after a few more days on oral warfarin. However, few weeks after discharge, patient suddenly developed worsening breathlessness at home and was taken to a nearby hospital but all attempts are resuscitation were unsuccessful and the patient died.

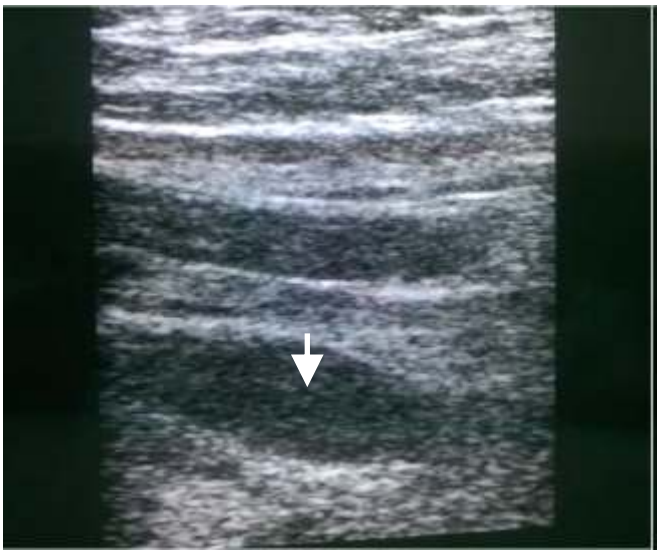

Figure 1: Doppler ultrasound scan (USS) of the left femoral vein showing dilatation and non-compressibility of the vessel (arrow).

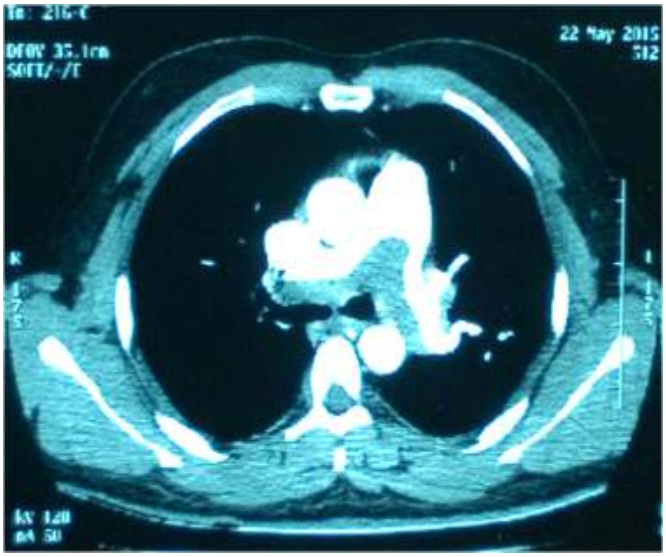

Figure 2: Chest computed tomographic angiography (CTA) scan showing a large saddle pulmonary embolus straddling the main pulmonary arterial trunk at its bifurcation and extending into the main right and left pulmonary arteries.

DISCUSSION

Venous thromboembolism (VTE) clinically manifested as deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common cause of increased morbidity and mortality. PE represents a spectrum of syndromes ranging from small peripheral emboli causing pleuritic pain to massive PE resulting in cardiogenic shock or cardiac arrest.

Saddle PE is a form of large pulmonary thromboembolism that straddles the main pulmonary arterial trunk at its bifurcation, usually extending into the main right and left pulmonary arteries. Its incidence among patients diagnosed with PE is approximately 2.6%. Such proximal thrombus may be regarded as an unstable, "in-transit" embolus, which can fragment spontaneously or secondary to treatment and obstruct multiple, distal pulmonary arteries. It remains unclear whether this may further increase haemodynamic compromise. Also, it is unknown whether saddle PE requires modification of clinical management.

Saddle PE frequently results in significant hemodynamic instability and signals the potential for imminent hemodynamic collapse. Unfortunately, the most common presenting symptoms of dyspnoea followed by syncope are relatively non-specific. Consequently, a high index of suspicion and emergent diagnosis and treatment are of critical importance.

There are well-known risk factors for development of PE, including venous stasis, obesity, trauma, advanced age, confirmed DVT and hypercoagulable states. However, a study of the International Cooperative Pulmonary Embolism Registry (ICOPER) found certain comorbidities to be specifically associated with massive PE, including congestive heart failure (CHF), renal dysfunction, decreased left ventricular systolic ejection fraction, cardiopulmonary disease and right ventricular thrombi.

Virchow's triad of local trauma to the vessel wall, hypercoagulability and stasis of blood leads to thrombus formation in the leg veins. As thrombi form in the deep veins of the legs, pelvis or arms, they may dislodge and embolize to the pulmonary arteries with potentially serious consequences. The most common sources of pulmonary emboli are the pelvic veins or deep veins of the thigh.

The incidence of mortality after PE has been reported to be as high as 300,000 per year, with a three-month mortality of 15% - 18%. While most patients with acute PE survive, possible long-term sequelae include chronic thromboembolic pulmonary hypertension and chronic leg pain and swelling. Right-sided heart failure is the usual cause of death from PE, and right ventricular dysfunction serves as a crucially important warning for a possible adverse outcome. The mortality rate at one year is three times higher in patients with right ventricular dysfunction compared to those with normal right ventricular function. Chronic pulmonary hypertension affects approximately 4% of patients within two years after a first episode of symptomatic PE.

A bedside transthoracic or transoesophageal echocardiogram can be used to demonstrate signs of right ventricular pressure overload and right ventricular hypokinesis and/or dilatation. The McConnell sign of PE is normal apical motion of the right ventricle despite hypokinesis of its free wall. Also, a bedside echocardiogram may eliminate other causes of shock, such as myocardial infarction, cardiac tamponade and aortic dissection.

Treatment of saddle PE includes anticoagulants, thrombolytics and catheter-based or surgical embolectomy. In the absence of any large scale data, treatment should be individualized

according to clinical status, evidence of right ventricular dysfunction and risk of bleeding. Anticoagulants (heparin and warfarin) remain an integral part of all treatment plans.

It has been suggested that saddle PE should be urgently treated surgically. However, other authors have reported successful recovery following less aggressive treatment comprising intravenous thrombolysis or even routine anticoagulation. It was even suggested that capture of a large thromboembolus at the level of bifurcation of the main pulmonary artery might provide protection from complete obstruction of the pulmonary arteries and therefore prevent sudden death.

Whether or not patients undergo primary therapy (fibrinolysis or embolectomy), anticoagulation is a critical component of the management of PE. Parenteral anticoagulation with either low molecular weight heparin or unfractionated heparin should be administered, unless contraindicated. Heparin accelerates the action of antithrombin III, thereby preventing additional thrombus formation and permitting endogenous fibrinolysis to dissolve some of the clot. Unfractionated heparin, which can be rapidly reversed, is preferred in patients undergoing fibrinolysis or embolectomy. Low-molecular-weight heparins (LMWHs) such as enoxaparin have been shown to be as safe and effective as intravenous unfractionated heparin.

Fondaparinux is a synthetic pentasaccharide with anti-Xa activity approved by the Food and Drug Administration (FDA) for the initial treatment of VTE including PE. In haemodynamically stable patients with acute symptomatic PE, fondaparinux is as safe and effective as intravenous unfractionated heparin. Unlike intravenous unfractionated heparin, fondaparinux is administered in a fixed dose and does not require dose adjustment with laboratory coagulation tests.

Oral vitamin K antagonists such as warfarin have remained the mainstay of outpatient anticoagulation for VTE. Oral anticoagulation is usually initiated simultaneously with heparin, LMWH or fondaparinux and overlapped for at least 5 days until full therapeutic efficacy has been achieved. The target international normalized ratio (INR) is between 2.0 and 3.0 for the majority of patients with PE. The optimal duration of anticoagulation depends on the risk of recurrent VTE. In patients without reversible causes for DVT or PE, VTE represents a chronic illness with a high risk of recurrence after completion of standard anticoagulation.

Thrombolysis can be lifesaving in patients with massive PE, cardiogenic shock or overt hemodynamic instability. Thrombolytic agents accelerate the lysis of the PE. Currently, the Food and Drug Administration (FDA) recommends thrombolysis for the treatment of “massive PE.” “Massive” universally indicates cardiogenic shock secondary to PE, but also can suggest profound hypoxaemia (like in the index case) or impending respiratory failure. Patients treated with thrombolytic therapy show rapid improvement of right ventricular function and pulmonary perfusion which may lead to a lower rate of early recurrent PE and a decrease the late sequela of chronic pulmonary hypertension.

Several studies have shown the physiological benefits of thrombolytics in cases of PE such as improvement in haemodynamics, oxygenation and a lower incidence of early PE recurrence, but they have not shown a clear long-term mortality benefit. According to the results of Phase 1 of the Urokinase Pulmonary Embolism Trial, haemodynamically stable patients treated with anticoagulation alone have similar outcomes as those treated with thrombolytics. Importantly, the difference in the degree of clot resolution between the two groups progressively decreases after 24 hours, such that both treatment groups have no difference in clot burden at five or 14 days or even several months. Other thrombolytics like alteplase and tenectaplase are also in use.

Surgical embolectomy may be considered for patients in whom fibrinolysis is contraindicated. Additional indications include paradoxical embolism, persistent right heart thrombi and haemodynamic or respiratory compromise requiring cardiopulmonary resuscitation. In specialized centres caring for patients with massive PE, surgical embolectomy has been demonstrated to be a safe and effective treatment technique. Catheter-based pulmonary embolectomy is an emerging modality for the primary therapy of acute PE. Catheter-based strategies are considered when fibrinolysis and open surgical embolectomy are contraindicated. In general, catheter-based

embolectomy is most successful when applied to fresh thrombus within the first 5 days of symptoms of PE.

Inferior vena cava (IVC) filters are indicated for patients in whom anticoagulation is contraindicated, those who experience recurrent PE despite adequate anticoagulation and those undergoing open surgical embolectomy. IVC filters are associated with an increased incidence of DVT. Although further studies are required, a recent analysis from ICOPER demonstrated a significant reduction in 90-day mortality associated with IVC filters. Retrievable IVC filters should be considered for patients with transient contraindications to anticoagulation.

Rapid recognition and treatment are very important to prevent severe morbidity and mortality after PE. Current methods used to prevent DVT and PE have significantly reduced the incidence of fatal PE. Treatments that combine mechanical prophylaxis such as, sequential compression devices or IVC filters, with LMWH appear to be most effective. However, even patients on appropriate prophylaxis are still developing DVT and PE. Future research will hopefully help with better prevention and treatment of PE.

REFERENCES

1. Lee A, Ortiz J. Management of a patient with perioperative saddle embolus. World Journal of Anesthesiology 2013; 2(1): 11-3.
2. Piazza G, Goldhaber SZ. Acute pulmonary embolism: part II: treatment and prophylaxis. Circulation 2006; 114(3): e42- 7.
3. Rya J, Pellikka P, Froehling D, Peters S, Aughenbaugh G. Saddle pulmonary embolism diagnosed by CT angiography: frequency, clinical features and outcome. Respiratory Medicine 2007; 101: 1537-42.
4. Pruszczyk P, Pacho R, Ciurzynski M, et al. Short term clinical outcome of acute saddle pulmonary embolism. Heart 2003; 89(3): 335-6.
5. Satya R, Bagherpour A, Christofferson M, Satya RJ. Large saddle pulmonary embolism in patient with previously placed IVC filter: A case report of successful Angiojet thrombectomy. Respiratory Medicine CME 2011; 4: 133-5.
6. Uflacker R. Interventional therapy for pulmonary embolism. Journal of Vascular and Interventional Radiology : JVIR 2001; 12(2): 147-64.
7. Kucher N, Rossi E, De Rosa M, Goldhaber SZ. Massive pulmonary embolism. Circulation 2006; 113(4): 577-82.
8. Jarreau T, Hanna E, Rodriguez F, 3rd, Romero J, Martinez J, Lopez FA. Clinical case of the month. Massive pulmonary embolism: a case report and review of literature. Pulmonary embolism. The Journal of the Louisiana State Medical Society : Official Organ of the Louisiana State Medical Society 2008; 160(4): 189-94; quiz 94, 233.
9. Goldhaber SZ. Pulmonary embolism. The New England Journal of Medicine 1998; 339(2): 93-104.
10. Dieck JA, Ferguson JJ, 3rd. Indications for thrombolytic therapy in acute pulmonary embolism. Texas Heart Institute Journal 1989; 16(1): 19-26.
11. MacDougall DA, Feliu AL, Boccuzzi SJ, Lin J. Economic burden of deep-vein thrombosis, pulmonary embolism, and post-thrombotic syndrome. American Journal of Health-System Pharmacy (AJHP): Official Journal of the American Society of Health-System Pharmacists 2006; 63(20 Suppl 6): S5-15.
12. Goldhaber SZ. Thrombolysis for pulmonary embolism. The New England Journal of Medicine 2002; 347(15): 1131-2.
13. Pengo V, Lensing AW, Prins MH, et al. Incidence of chronic thromboembolic pulmonary hypertension after pulmonary embolism. The New England Journal of Medicine 2004; 350(22): 2257-64.
14. McConnell MV, Solomon SD, Rayan ME, Come PC, Goldhaber SZ, Lee RT. Regional right ventricular dysfunction detected by echocardiography in acute pulmonary embolism. The American Journal of Cardiology 1996; 78(4): 469-73.
15. Zalpour A, Hanzelka K, Patlan JT, Rozner MA, Yusuf SW. Saddle pulmonary embolism in a cancer patient with thrombocytopenia: a treatment dilemma. Cardiology Research and Practice 2010; 2011: 835750.
16. Shih WJ, Robinson MC, Huber C, Pulmano C. Tc-99m MAA lung perfusion scintigraphy performed before and after

pulmonary embolectomy for saddle-type pulmonary embolism. Clinical Nuclear Medicine 1995; 20(2): 128-31.
17. Torbicki A, Perrier A, Konstantinides S, et al. Guidelines on the diagnosis and management of acute pulmonary embolism: the Task Force for the Diagnosis and Management of Acute Pulmonary Embolism of the European Society of Cardiology (ESC). European Heart Journal 2008; 29(18): 2276-315.
18. Prandoni P. Anticoagulant treatment of pulmonary embolism: impact and implications of the EINSTEIN PE study. European Journal of Haematology 2012; 89(4): 281-7.
19. Barritt DW, Jordan SC. Anticoagulant drugs in the treatment of pulmonary embolism. A controlled trial. Lancet 1960; 1(7138): 1309-12.
20. Simonneau G, Sors H, Charbonnier B, et al. A comparison of low-molecular-weight heparin with unfractionated heparin for acute pulmonary embolism. The THESEE Study Group. Tinzaparine ou Heparine Standard: Evaluations dans l'Embolie Pulmonaire. The New England Journal of Medicine 1997; 337(10): 663-9.
21. Low-molecular-weight heparin in the treatment of patients with venous thromboembolism. The Columbus Investigators. The New England Journal of Medicine 1997; 337(10): 657-62.
22. Buller HR, Davidson BL, Decousus H, et al. Subcutaneous fondaparinux versus intravenous unfractionated heparin in the initial treatment of pulmonary embolism. The New England Journal of Medicine 2003; 349(18): 1695-702.
23. Jerjes-Sanchez C, Ramirez-Rivera A, de Lourdes Garcia M, et al. Streptokinase and Heparin versus Heparin Alone in Massive Pulmonary Embolism: A Randomized Controlled Trial. Journal of Thrombosis and Thrombolysis 1995; 2(3): 227-9.
24. Thabut G, Thabut D, Myers RP, et al. Thrombolytic therapy of pulmonary embolism: a meta-analysis. Journal of the American College of Cardiology 2002; 40(9): 1660-7.
25. Goldhaber SZ, Haire WD, Feldstein ML, et al. Alteplase versus heparin in acute pulmonary embolism: randomised trial assessing right-ventricular function and pulmonary perfusion. Lancet 1993; 341(8844): 507-11.
26. Urokinase pulmonary embolism trial. Phase 1 results: a cooperative study. JAMA 1970; 214(12): 2163-72.
27. Leacche M, Unic D, Goldhaber SZ, et al. Modern surgical treatment of massive pulmonary embolism: results in 47 consecutive patients after rapid diagnosis and aggressive surgical approach. The Journal of Thoracic and Cardiovascular Surgery 2005; 129(5): 1018-23.
28. Aklog L, Williams CS, Byrne JG, Goldhaber SZ. Acute pulmonary embolectomy: a contemporary approach. Circulation 2002; 105(12): 1416-9.
29. Kucher N, Windecker S, Banz Y, et al. Percutaneous catheter thrombectomy device for acute pulmonary embolism: in vitro and in vivo testing. Radiology 2005; 236(3): 852-8.
30. Decousus H, Leizorovicz A, Parent F, et al. A clinical trial of vena caval filters in the prevention of pulmonary embolism in patients with proximal deep-vein thrombosis. Prevention du Risque d'Embolie Pulmonaire par Interruption Cave Study Group. The New England Journal of Medicine 1998; 338(7): 409-15.
31. Millward SF, Oliva VL, Bell SD, et al. Gunther Tulip Retrievable Vena Cava Filter: results from the Registry of the Canadian Interventional Radiology Association. Journal of Vascular and Interventional Radiology (JVIR) 2001; 12(9): 1053-8.
32. Agudelo JF, Morgan SJ, Smith WR. Venous thromboembolism in orthopedic trauma patients. Orthopedics 2005; 28(10): 1164-71; quiz 72-3.