Case Series

The Variability in the Clinical Presentation of Acute Pulmonary Embolism: A Case Series

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Abstract

Introduction: Acute pulmonary embolism (PE) occurs when a thrombus dislodges from a peripheral part of the body to block any of the branches of the pulmonary artery. Its variable nature of presentation frequently leads to a missed diagnosis and increased morbidity or mortality from PE. This series aims to highlight some of the variable presentations of acute pulmonary embolism with the objective of stimulating a high index of suspicion, which can lead to early diagnosis and treatment.

Methods: The electronic medical records of 3 patients in a private hospital in Abuja were selected for the series, together with a review of the existing literature. Electrocardiographic tracings were also different in all 3 cases. Consent to use patient information was obtained from the patients, and the approval for the case series obtained from the head of the department of research of the hospital.

Results: The clinical presentation of acute PE was highly variable in all 3 cases, with the least symptomatic case having a saddle-embolus lodged at the bifurcation of the pulmonary artery.

Conclusion: The prognosis of PE depends on early diagnosis and treatment. Mortality and morbidity from this condition can be reduced with a background knowledge of its variable clinical presentation and a high-index of suspicion.

Keywords Deep venous thrombosis, D-dimer; multi-detector computed tomography pulmonary angiography, MD-CTPA; Pulmonary embolism, PE.

Introduction

Acute pulmonary embolism mostly occurs when a deep venous thrombus in the leg dislodges and travels to the lungs to block one of the pulmonary arteries. It is a medical emergency that requires prompt diagnosis and treatment to ensure the patient's survival[1].

After occlusion of the pulmonary artery branches, the embolus causes hemodynamic and gas exchange abnormalities[2]. The mechanical occlusion of the arteries reduces the cross-sectional area of the vessels thereby increasing pulmonary vascular resistance. There are also contributions from vasoconstriction caused by release of serotonin from the platelets, and hypoxemia from the ventilation-perfusion mismatch where blood flow from obstructed pulmonary arteries is redirected to other gas exchange units[2]. The increased right ventricular afterload can lead to right heart strain, reduced venous return to the left ventricle and then reduced cardiac output. This is usually the pathway for hemodynamic instability.

Acute pulmonary embolism is a major health problem, and the 3rd most common cause of death in hospitalized patients[3]. Autopsy studies have shown that approximately 60% of patients who have died in the hospital had pulmonary embolism, with the diagnosis having been missed in up to 70% of the cases[3]. Despite it being a frequent diagnosis, its actual incidence is still uncertain, with several studies reporting an annual incidence between 0.2-0.8/1000, where discrepancies lie with differences in the inclusion criteria[4]. It is a life-threatening condition with a wide spectrum of presentations ranging from being asymptomatic to presenting with right ventricular dysfunction, hemodynamic instability and sudden death. The overall mortality rates for massive, sub-massive and low-risk pulmonary embolism were found to be 71.4%, 44.5% and 28.1% respectively[5].

Risk factors for acute pulmonary embolism include obesity, cigarette use, trauma, surgery, pregnancy, immobilization, use of oral contraceptives or hormone replacement therapies and a prior history of pulmonary

embolism or a known hypercoagulable disorder. However, studies have shown that 30% of patients with pulmonary embolism have no detectable provoking factors[6]. Its clinical features are also non-specific and variable, and can mimic a couple of other medical conditions including acute exacerbation of asthma, left heart failure, right heart failure, community-acquired pneumonia, acute coronary syndrome, syncope etc. Data derived form a systematic review and meta-analysis involving a total of 5,997 patients with acute pulmonary embolism stated that the most useful features used to rule in acute pulmonary embolism include a history of syncope, thrombophlebitis, leg swelling, current deep vein thrombosis, sudden dyspnea, active cancer, recent surgery, hemoptysis and leg pain. While features used to rule out acute pulmonary embolism were absence of sudden dyspnea, any dyspnea and tachypnea[7]. Acting individually, these features can only increase or reduce the probability of a pulmonary embolism and have limited diagnostic value without further testing[7].

Here we attempt to highlight the variability in the clinical presentation of acute pulmonary embolism and also to emphasize the presence and absence of the significant features mentioned earlier that can be used to increase or reduce the probability of acute pulmonary embolism. The aim is to increase the chances of a timely diagnosis of pulmonary embolism which is crucial because of the high associated mortality and morbidity which may be prevented with early diagnosis and treatment. It is worthy of note that 30% of untreated patients with pulmonary embolism die, while only 8% die after timely therapy[8].

Case Summary

Case 1

A case of a 56-year-old female who presented on the 12th of June 2019 with a 3-day history of sudden onset breathlessness, right-sided chest pain and fever. There was also some abdominal pain with 2 episodes of diarrhea. She was acutely ill-looking with a temperature of 39.6 c, there was also tachycardia (120 beats/min), tachypnea (40 cycles/min) and an oxygen saturation of 89% in room air. Her chest was clear to auscultation, but she had right upper quadrant and suprapubic abdominal tenderness. She has a background medical history of essential hypertension, diabetes mellitus and bilateral osteoarthritis of both knees, and there was a past medical history of unilateral left leg swelling that occurred about 5 years earlier.

Significant laboratory results were urine microscopy 0-6 pus cells/hpf, dipstick, protein ++, blood +. D-dimer 2,410 ng/ml (Ref: 0-500 ng/ml). Imaging studies, chest x-ray (PA view) reported cardiomegaly and electrocardiography showed sinus tachycardia (**figure 1**). Abdominopelvic ultrasound scan reported multiple calculi, > 10 in the neck and body of the gallbladder with hepatomegaly, and a lower limb doppler scan reported an extensive clot in the left tibio-peroneal veins with no compressibility or significant flow. There was also reduced compressibility of the proximal veins with echogenic stranding suggestive of recanalization of previous clot with some narrowing of the lumen seen.

She was admitted into the ward and commenced intranasal oxygen supplementation at a flow rate of 3L/min. Other treatments included subcutaneous enoxaparin 60 mg twice daily, intravenous antibiotics (amoxicillin/clavulanic acid) and use of anti-embolism compression stockings. On the 3rd day of admission, her vital signs trend showed an intermittent quotidian fever pattern with persistent tachycardia. She became lethargic and delirious with cold extremities; her blood pressure was found to be 76/50 mmHg and she developed crackles in the lower zones of her right lung. She was immediately transferred to the ICU, connected to the cardiac monitor, and commenced on continuous dopamine infusion at a dose rate of 10 mcg/kg/min with an infusion pump.

About 2 hours later, 100 mg of intramuscular hydrocortisone was given, and the dopamine infusion dose rate was gradually titrated upwards, but her systolic blood pressure persistently remained below 90 mmHg. At approximately 16 hours after admission into the ICU an acute massive pulmonary edema was suspected, but she was considered too unstable to be taken outside the hospital facility for a confirmatory CT pulmonary angiography. A collective decision was eventually made to administer a fibrinolytic agent. Streptokinase was procured, and after passing a hospital-made fibrinolytic checklist she was given 250,000 IU as an intravenous bolus slowly over 15-20 minutes, then 1,250,000 IU was diluted in 100 mls of 0.9% normal saline solution and set to run over 12 hours with a soluset. By the next day her blood pressure began to be stable with a systolic blood pressure well above 90 mmHg and mean arterial pressure above 60 mmHg. The dopamine infusion was gradually titrated downwards and eventually stopped.

On day 5 of her admission her urine culture grew streptococcus spp sensitive to the fluoroquinolones which prompted a change in her antibiotics. Other significant laboratory results at that point were a PCV of 25% and a platelet count of 84,000 cells/mm3. By the 6th day on admission, she was then transfused with 1 unit of grouped and cross-matched blood after adequate viral screening and oxygen supplementation was discontinued.

By the 7th day, there was significant improvement in her clinical state, and anticoagulation was continued with 150 mg of Dabigatran twice daily. She was eventually discharged after 48 hours of further monitoring and her

post-discharge follow-up visit was scheduled for a week later.

During her first post-discharge visit she was diagnosed with community-acquired bronchopneumonia after presenting with low-grade fever, dyspnea at rest and chest x-ray features of pulmonary edema with bilateral pleural effusion. She was recommended antibiotics, while continuing her anticoagulation. By the next follow-up visit a week later, pneumonia had completely resolved. A repeat D-dimer was 520 ng/ml (0-500 ng/ml) and a repeat lower limb doppler showed left leg cellulitis with no evidence of deep venous thrombosis. She had stopped using her compression stockings due to superficial skin bruises.

By her 6-month follow up she had stopped using her anticoagulants and had not done any of the thrombophilia screening tests as advised. During her 12-month follow up visit, she gave a history of short-term use of Dabigatran when she experienced an acute onset of swelling of her left leg. She used the medication for a period of 2 weeks by which time the swelling had subsided. She has not used anticoagulants since then and still did not have plans of doing a thrombophilia screening.

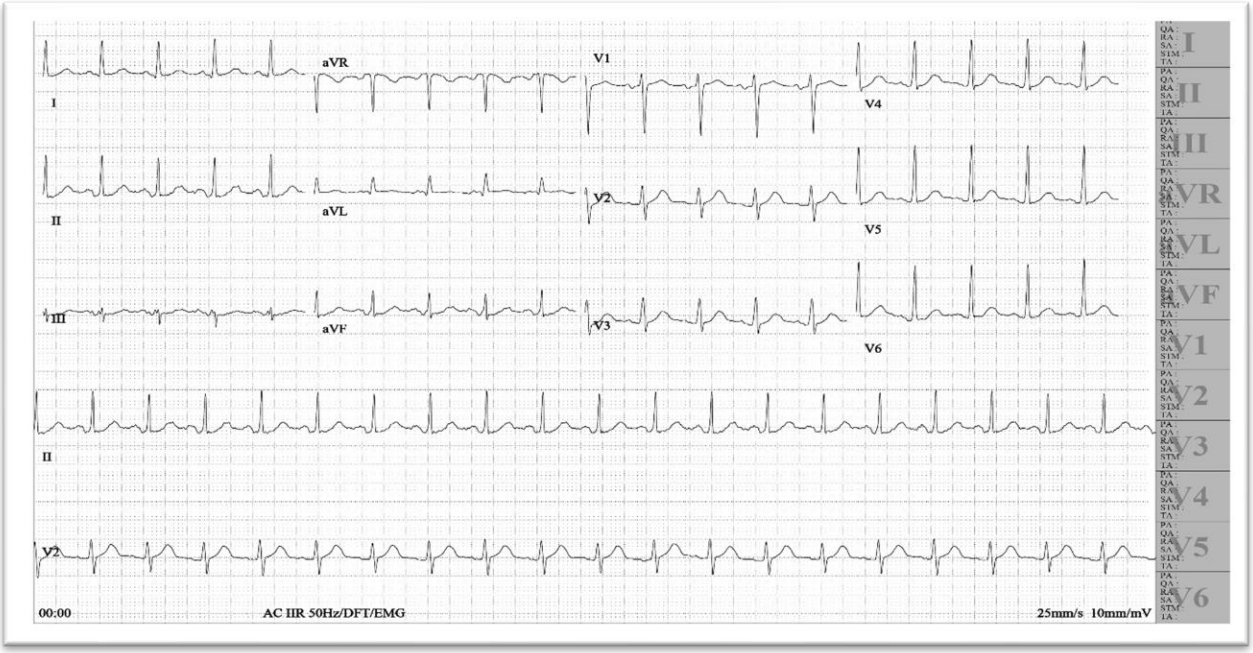

Figure 1: Electrocardiography showing Sinus tachycardia

Case 2

A 62-year-old female who presented with complaints of lethargy, poor appetite, abdominal bloating, and unilateral left leg swelling. She was 11 years post-menopausal and had a laparoscopic total hysterectomy with bilateral salpingo-oophorectomy 2 weeks prior to presentation on account of post-menopausal bleeding and histological findings of mild cellular atypia of the endometrial cells. After her surgery she was less active, missed her thrice-a-week 45-minute walks, and had not commenced ambulation fully. She has background essential hypertension and type 2 diabetes mellitus and was still on her medications, in addition to her post-op antibiotics and analgesics.

At presentation, her vitals were stable, with a blood pressure of 93/60 mmHg and an oxygen saturation of 96% in room air. Initial laboratory and imaging workup revealed low sodium and chloride of 128 mmol/L (135-145 mmol/L) and 87 mmol/L (95-105 mmol/L) respectively, 1+ each of ketones, blood and leucocytes in her urine analysis, D-dimer was 3,470 ng/dl (Ref: 0-500 ng/ml) and ESR 37 mm/Hr. Her electrocardiography revealed a regular sinus rhythm with normal electrical axis and widespread inverted T waves mostly in the precordial leads V1-V6, leads I and avL and the inferior leads II and avF (**figure 2**). This was different from her previous ECG done 8 months earlier which showed a regular sinus rhythm with a normal electrical axis and no ST segment or T wave changes. An emergent lower limb doppler ultrasound scan was done which reported an extensive chronic deep vein thrombus extending from the right common femoral to the popliteal vein with no compressibility. Mild compressibility was seen only at the popliteal vein, with no significant flow seen within them. An

abdominopelvic scan was also done which showed a polycystic liver with a left simple renal cortical cyst, as well as confirming a hysterectomy. She commenced on therapeutic dose of enoxaparin, 80 mg twice a day and wore anti-embolic compression stockings. Her routine oral anti-hypertensives were discontinued, and she was then connected to a cardiac monitor for continuous ECG monitoring. In the ensuing 96 hours after admission, her gastrointestinal symptoms worsened, with increasing abdominal distension, constipation, epigastric tenderness, and vomiting (mostly post-prandial). There was increased weakness and occasional restlessness too. A plain abdominal X-ray (supine & erect) and a CT pulmonary angiography were ordered, the former showed distended bowel loops with air-fluid levels on the erect view, while the later reported a large saddle-shaped embolus at the bifurcation of the pulmonary arteries (**figure 3**), with extensions into the left and right pulmonary arteries (**figure 4**).

A nil-per-oral was ordered and a nasogastric tube inserted which drained feculent effluents. A general surgeon consultation was also ordered. From the 6th to the 9th day of her admission she was managed conservatively with intravenous fluids, small quantities of liquid diet, proton-pump inhibitors, and anticoagulation. On the 9th day of admission, a decision was made to refer her back to the center where she did her laparoscopic surgery.

In the referral center conservative management was continued and after 4 days of admission there was significant improvement in her clinical state, and she was eventually discharged home. Her 1st post-discharge visit was unremarkable, and during the 2nd visit her anticoagulants were changed from rivaroxaban 15 mg twice daily to dabigatran 150 mg twice day, because of complaints of persistent abdominal pains and discomfort with rivaroxaban. By the 3rd visit, which was about a month after discharge, a repeat lower limb doppler scan was done which reported a normal study with no evidence of a deep vein thrombus.

She has been constantly followed up and found to have resumed her regular daily activities while continuing with her oral anticoagulants. Based on the circumstances surrounding the occurrence of the extensive deep vein thrombus and pulmonary embolus, no discussions concerning thrombophilia screening has been had yet.

Case 3

A 24-year-old male who was brought in through the emergency unit with complaints of breathlessness at rest, which is worse with recumbency, dizziness, cough and weakness. His referral note stated that he was earlier rushed into their facility through the emergency unit, with a 3-week history of dyspnea on exertion, orthopnea, dry cough, palpitations, and bilateral leg swelling. At presentation oxygen saturation was < 90% and he was commenced on intranasal oxygen at a flow of 3L/min but was eventually referred out due to a lack of bedspace in their facility.

Further questioning of accompanying relatives, especially his younger brother revealed that the patient had been having recurrent episodes of sudden-onset shortness of breath, bouts of cough, palpitations, and dizziness. He was visiting a nearby medical facility where he was managed as a case of heart failure. He received 2 units of blood during the 3-week period and several shots of IV frusemide and antibiotics. On the day he presented to the referral center, he was said to have collapsed while coughing before he was rushed to the emergency room. There was no history of any underlying medical condition, and he used alcohol and marijuana socially.

On presentation, he was acutely ill-looking, pale, icteric and in mild respiratory distress with a respiratory rate of 28 cycles per minute on 100% oxygen supplementation at a flow rate of 3L/min via nasal prongs. There was bilateral leg swelling up to the mid-shin, mild tachycardia, 102/min, a jugular venous pressure of 5 cm and hepatomegaly. The edge of the liver was felt about 8 cm below the right costal margin and was tender.

Initial laboratory workup revealed, PCV of 28%, MCV 72.2 fl (Ref: 83-101), Total WBC 9.98 x 10^9 (Ref: 3.9-10.8) Urea 62 mg/dl (Ref: 15-50), Total bilirubin 11.8 mg/dl (Ref: 0.0-1.2), Direct bilirubin 5.7 mg/dl (Ref: 0.0-0.2), AST 194 IU/L (Ref: 0-37), ALT 146 IU/L (Ref: 0-50) and ALP 268 IU/L (Ref: 78-258). Troponin I was within normal range, D-dimer >10,000 ng/ml (Ref: 0-500), Urinalysis 1+ each of blood and urobilinogen, calcium 2.0 mmol/L (Ref: 2.2-2.7), phosphate 4.8 mmol/L (Ref: 2.5-4.5), uric acid 13.6 mg/dl (Ref: 3.4-7.0).

Rest electrocardiography showed sinus tachycardia with right axis deviation, inverted T waves in the precordial leads V3-V5 and an incomplete right bundle branch block (RBBB) (**figure 5**).

He was commenced on IV frusemide 20 mg 8 hourly, Spironolactone 25 mg daily, Losartan 12.5 mg daily, IV Ceftriaxone 1g 12 hourly and subcutaneous enoxaparin 40 mg daily. Oxygen supplementation was continued at a flow rate of 3L/minute, and he was counselled for ICU care but declined on account of financial constraints.

By day 2 on admission, his clinical condition worsened, and further history had to be taken from his relatives. His brother stated that prior to onset of his symptoms about 3 weeks earlier, the patient did a 20-hour road trip from Lagos state to Abuja, where he departed Lagos by 2 pm and arrived Abuja by 10 am the following day. There were minimal stops over the night, and his seating position was very uncomfortable due to the improper positioning of his legs during the journey. The patient

also complained of chest pain which was aggravated by lying flat and relieved by sitting up, and bilateral pain.

A lower limb doppler and 2D transthoracic echocardiography were ordered and a couple of extra laboratory investigations requested. His viral serology, that is, HbsAg, HCV and HIV all came out negative. PT was 15 secs (Ref: 8-12), aPTT 49 secs (Ref: 27-43) and INR 1.50 (Ref: 1.00-1.25). Doppler ultrasound scan found dilatation of the posterior tibial veins bilaterally with some echogenic intraluminal structures and partial compressibility seen, worse on the right and seen extending to the mid-calf.

Later that day his blood pressure began to drop with his systolic blood pressure falling below 90 mmHg. An acute massive pulmonary embolism was suspected, and thrombolysis considered, an emergency 2D echocardiography was ordered and revealed, left ventricular ejection fraction of 57%, left ventricular internal diameter in diastole of 4.5 cm, left ventricular mass 196 g, E/A ratio of 1.04 and E/E' ratio of 8.6. The right atrial pressure was 10 mmHg (2-6 mmHg), right ventricular systolic pressure 87 mmHg (12-57 mmHg) and tricuspid annular plane systolic excursion was 1.8 cm (>1.6 cm). The right ventricle was severely enlarged, and right atrium moderately enlarged and crushing on the left atrium (**figure 6**). There was moderate-to-severe tricuspid regurgitation, moderate generalized pericardial effusion and septal flattening in diastole and systole consistent with right ventricular pressure and volume overload. He was informed of the need for fibrinolytic therapy, but due financial constraints streptokinase could not be given. Eventually, his enoxaparin was increased to twice daily, 80 mg (am) and 40 mg (pm) and sildenafil 12.5 mg twice daily was also added because of suspected pulmonary hypertension.

By the 3rd day on admission tabs bisoprolol 1.25 mg daily was added because of the persistent tachycardia, and during the following 72 hours on admission, his oxygen requirement kept reducing until he was eventually taken off oxygen support. His blood pressure also began to normalize without commencing inotropic support and the major complaint then was bilateral leg pain, for which analgesics (paracetamol/codeine) were added to his treatment regimen. By the 6th day on admission repeat labs showed, PCV of 29%, Sodium 124 mmol/l (135-145), potassium 2.9 mmol/L (3.5-5.0), total bilirubin 4.1 mg/dl (Ref: 0.0-1.2) and direct bilirubin 3.3 mg/dl (Ref: 0.0-0.25), but his liver enzymes had dramatically returned to normal range. He was eventually discharged the next day on request based on financial constraints, enoxaparin was converted to oral rivaroxaban 15 mg twice daily, oral hematinic agents were added, and other prescribed medications continued.

He was seen twice after his discharge, each 1 week apart and was still using his compression stockings and all prescribed medications. He was given a 1-month appointment with a plan to repeat his liver function test, serum electrolytes, urea and creatinine, and a 2D transthoracic echocardiography during his next visit.

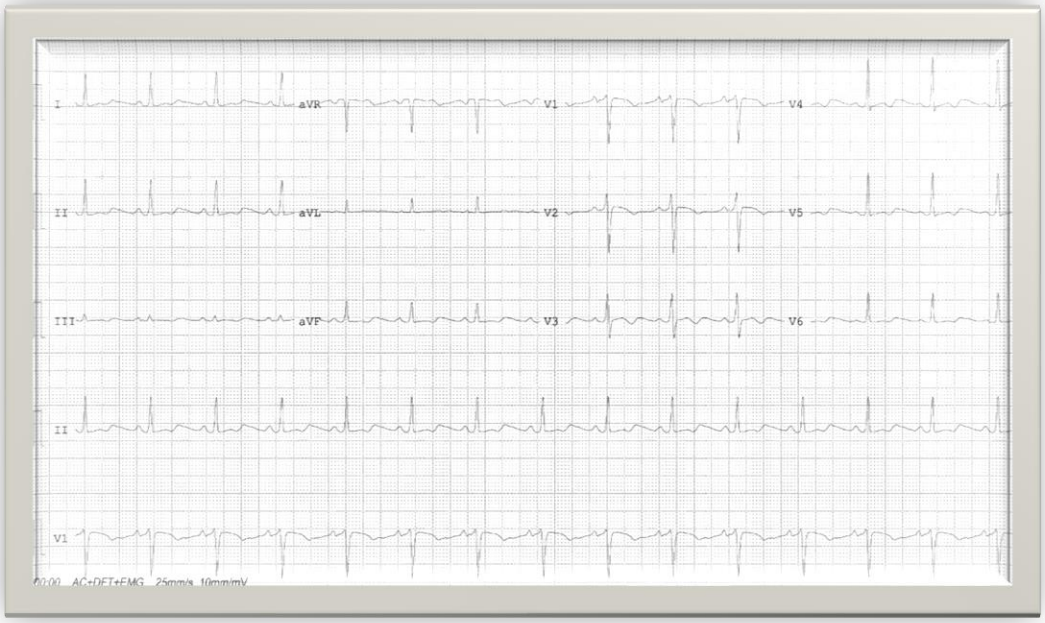

Figure 2 Electrocardiography showing a regular Sinus rhythm with inverted T waves from V1-V6, also seen in leads I, II and avF

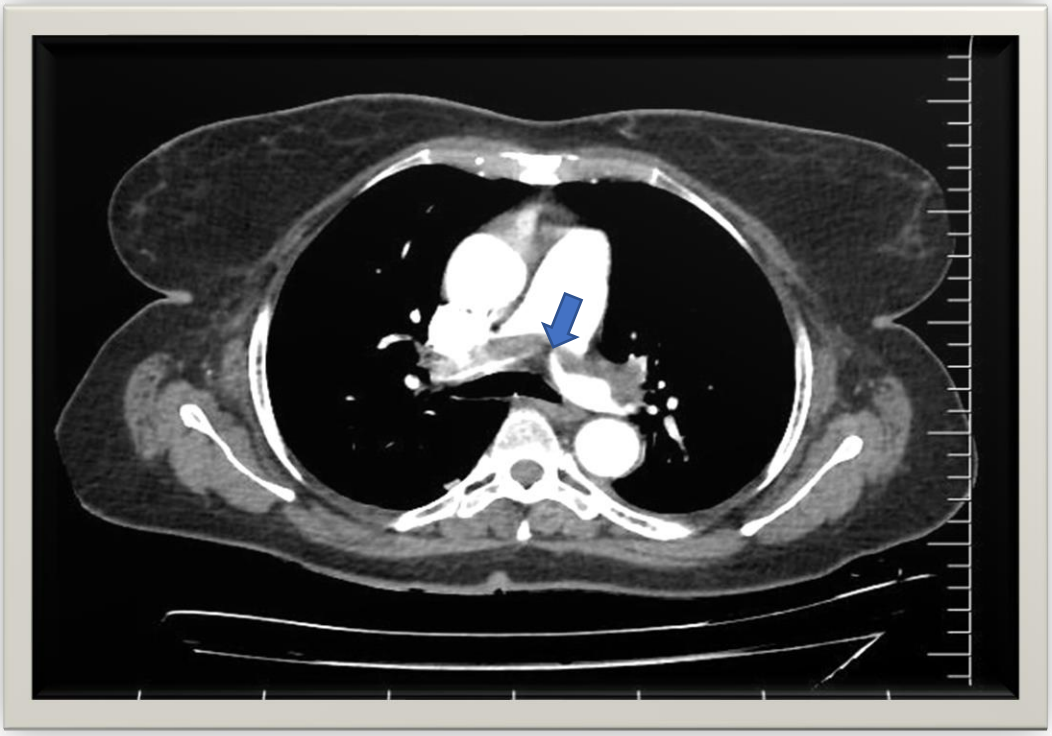

Figure 3: Axial view of CTPA. Blue arrow: Pointing to saddle-shaped embolus lodged at the bifurcation of the pulmonary arteries

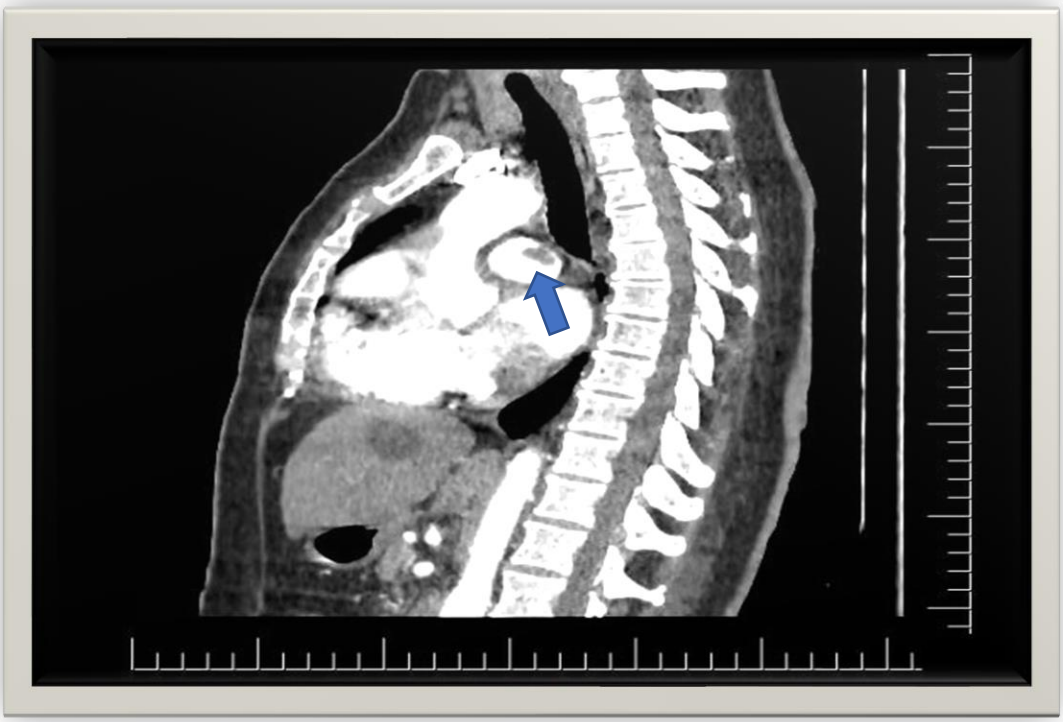

Figure 4. Sagittal view of CTPA. Blue Arrow: Showing a part of the saddle-shaped embolus that extends into the right pulmonary artery

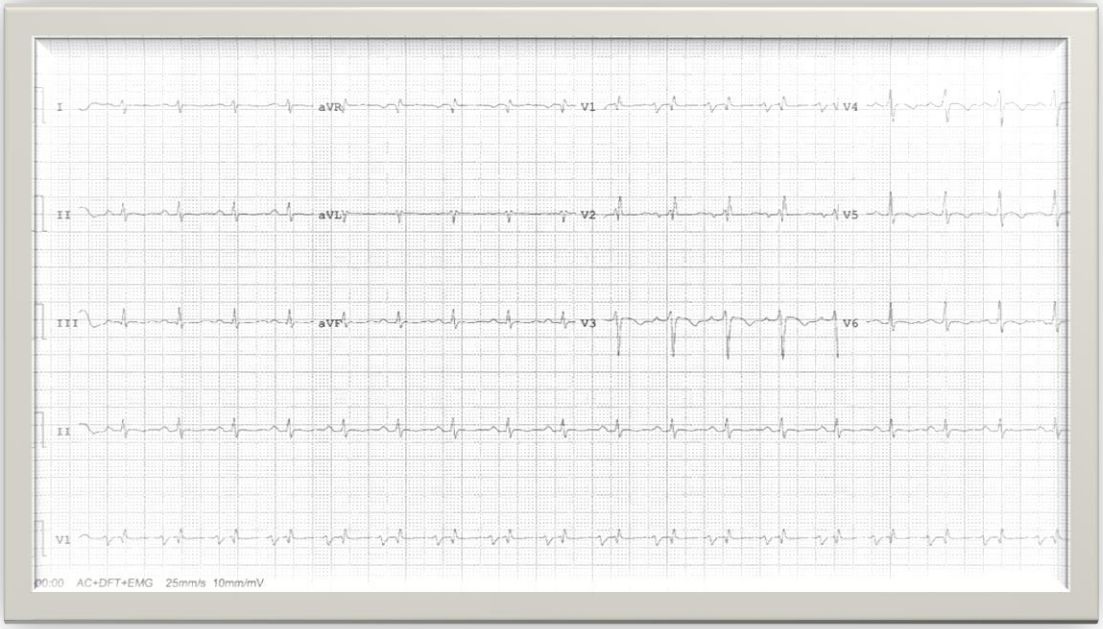

Figure 5. Electrocardiography showing a Sinus rhythm with right axis deviation, inverted T waves in precordial leads V3-V5 and incomplete right bundle branch block.

The Nigerian Health Journal, Volume 22, Issue 3

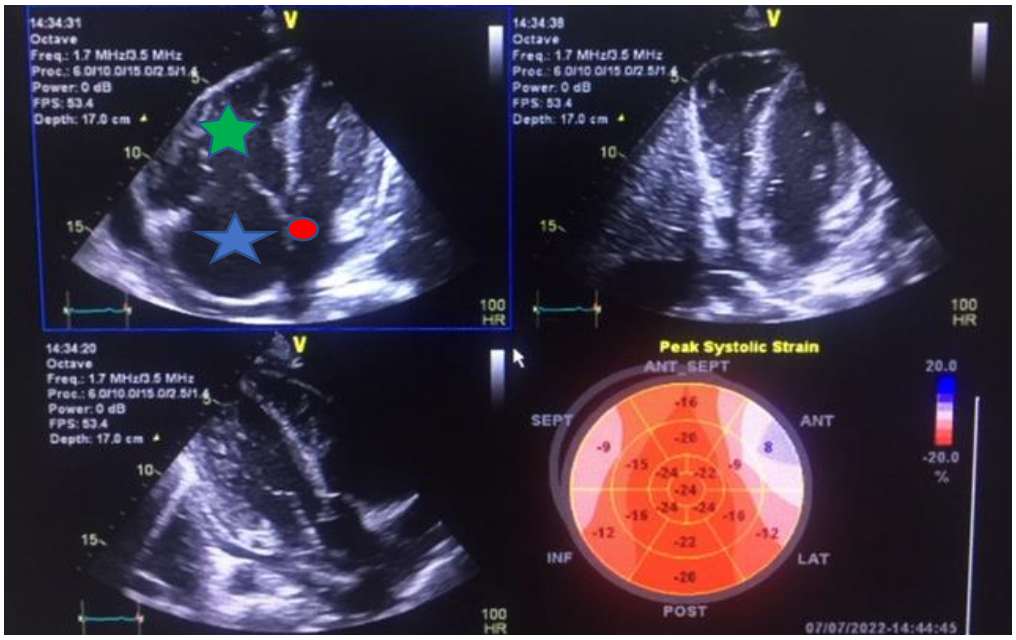

Figure 6. Trans-thoracic Echocardiography image showing severely enlarged right ventricular (green star) and moderately enlarged right atrium (blue star) crushing on the left atrium (red dot).

Discussion

Approximately 80% of all patients that have had a pulmonary embolism have also had at least one episode of in-patient care during the preceding 8 years before index event[4]. The six most common comorbidities were cardiac, vascular, malignancies, gastrointestinal, injuries and infectious, and out of all these, cardiovascular diseases were by far the most common comorbidity registered[4]. Within the vascular group of diseases, venous diseases were the most frequent, with more than 50% of patients with deep venous thrombosis having a simultaneous pulmonary embolism at presentation. The majority of the clinical features of acute pulmonary embolism are non-specific and its presentation can be variable. Often, the classic presentation of sudden onset shortness of breath, cough with pleuritic chest pains and hypoxia are absent, making clinching its diagnosis difficult even for the wary physician. It can also be asymptomatic or present with atypical presentations like fever, epigastric pain, pulmonary oedema, or delirium.

The 3rd case was initially managed as a case of heart failure for about 3 weeks before presentation, and after presenting in respiratory distress, jaundice, distended neck veins and hepatomegaly, acute right heart failure was still considered the most likely diagnosis. His liver enzymes were also initially markedly deranged which was suggestive of significant hepatic congestion, and it was only after his 2D advanced trans-thoracic echocardiography which showed evidence of right ventricular pressure and volume overload that acute pulmonary embolism became top on the list.

In case 1, the clinical picture was more like sepsis, after she presented looking acutely ill with high grade fever, tachypnea, tachycardia, localized abdominal pain and an ultrasound diagnosis of cholelithiasis. Three days into her admission she became hypotensive and delirious and was suspected of being in septic shock. Only after a review of her case notes that suggested a previous history of unilateral leg swelling coupled with an elevated D-dimer level and a lower limb doppler ultrasound which confirmed deep venous thrombosis was acute pulmonary embolism strongly considered.

One of the classifications of pulmonary embolism divides it into two major classes, massive pulmonary embolism, defined as obstruction of the pulmonary arterial tree that exceeds 50% of the cross-sectional area and the other, submassive that causes 25-50% occlusion[10]. The former is usually thought to cause acute and severe cardiopulmonary failure from right ventricular overload[10]. But a recent study replaced this classification with hemodynamically unstable PE (previously called massive or high-risk PE) and hemodynamically stable PE (previously called submassive or intermediate-risk PE)[11]. The former is characterized by a PE that results in a drop in systolic blood pressure below 90 mmHg, a drop in systolic blood pressure of more than 40 mmHg below baseline, or hypotension that requires vasopressors or inotropes. So here, it states that massive does not describe the size of the pulmonary embolus, but rather describes it

The Nigerian Health Journal, Volume 22, Issue 3

hemodynamic effect[11]. This recent study seems to be more accurate than seen in case 2 where the patient was mostly stable. Aside from the earlier complaints of unilateral leg swelling, most of her other complaints were more in keeping with clinical features of a partial intestinal obstruction. A CT pulmonary angiography was done for her, and a picture of an axial view of her scan showed a large saddle-shaped embolus lodged at the bifurcation of her pulmonary arteries, arguably occluding up to 50% of its cross-sectional area. But her vital signs remained relatively stable.

While the diagnosis of acute pulmonary embolism should be fast and accurate, bearing in mind that is a potentially life-threatening condition, it is worthy of note that anticoagulation is associated with the risk of major bleeding. The diagnosis of acute pulmonary embolism relies majorly on the assessment of the clinical pretest probability, which can be obtained from the history of risk factors and a physical examination; D-dimer measurements and imaging studies, mainly a multi-detector computed tomography pulmonary angiography (MD-CTPA)[11]. MD-CTPA recently replaced pulmonary angiography as a first-line imaging test for acute pulmonary embolism[12]. D-dimer has a high sensitivity of 97% but a specificity of 47%, hence its value in screening for or ruling out PE, while MD-CTPA has a sensitivity of 94% and a specificity of 98%, hence its value in diagnosing or ruling in PE[13]. The majority of other laboratory investigations and imaging studies have value in pointing to alternative diagnoses.

Evidence based literature supports the practice of determining the pretest probability of pulmonary embolism before proceeding with diagnostic testing[14]. There are 3 major scoring systems which have been validated for assessing pretest probability and they include the Modified Wells Scoring System, the Revised Geneva Scoring System and the Pulmonary Embolism Rule Out Criteria (PERC)[15]. Simplified versions of the Wells score and Geneva score have been developed, and amongst the four scoring systems (the modified and simplified scoring systems together), none has been proven to be superior to the other and the choice for a specific scoring system is dependent on local preferences[12]. The following diagnostic algorithm is followed for clinically suspected PE. After the clinical scoring system patients are classified as either 'PE likely' or 'PE unlikely', depending on their score. If PE is unlikely, then a D-dimer is done. D-dimer has a high sensitivity so a negative D-dimer in the 'PE unlikely' group rules out PE. But if D-dimer is elevated, then a MD-CTPA is ordered to confirm the diagnosis of PE. In the 'PE likely' group, a MD-CTPA is done to confirm or exclude the diagnosis[12]. Once a diagnosis is confirmed treatment can commence immediately. Lower leg compression ultrasonography (CUS), that shows a proximal deep vein thrombus in a patient suspected of PE, has an important positive predictive value, sufficient to confirm PE without further testing[16]. But as a standalone it cannot rule out PE even in patients with low clinical pretest probability[17].

In Cardiocare Multispecialty hospital, the preferred scoring system is the modified Wells Scoring system which has a total score of 12.5 points. It scores 3 points each for the 'presence of clinical signs of deep venous thrombosis', and for 'a differential diagnosis that is less likely than PE'. It scores 1.5 points each for 'a previous deep venous thrombosis or PE', 'heart rate > 100 beats/min' and 'a history of recent surgery or immobilization (within the last 30 days). And finally, it scores 1 point each for a 'history of hemoptysis' and the 'presence of a malignancy within the past 6 months'[12]. Scores equal to or less than 4, are considered 'PE unlikely, while scores greater than 4 are considered 'PE likely'[12].

The first case had a modified Wells score between 1 to 2.5 (PE unlikely) as there was tachycardia and a past history of left leg swelling, but it was not documented if a deep venous thrombus was confirmed. But after a D-dimer that was four times the upper limit, 2,410 ng/ml (reference range: 0-500 ng/ml), and a positive lower leg compression ultrasound scan, PE became the first diagnosis while she was in the ICU. The second case was considered 'PE likely' with a modified Wells score of 4.5, as she had unilateral leg swelling on presentation and a history of laparoscopic total hysterectomy with bilateral salpingo-oophorectomy about 3 weeks prior to presentation. And because she was hemodynamically stable, she was able to do lower leg compression ultrasound scan and a MD-CTPA which revealed a saddle-embolus in the bifurcation of the pulmonary arteries, confirming a pulmonary embolism. The last case, presented as a case of acute right ventricular failure, and just like the first case was categorized in the 'PE unlikely' group with a modified Wells score of 1. But after a D-dimer of 10,000 ng/dl (reference range: 0-500 ng/ml) and a positive lower leg compression ultrasound scan, a PE became top on the differential list.

The rest electrocardiography (ECG) is one of the imaging studies that can be used to support the diagnosis of acute pulmonary embolism. It can lead to a number of ECG abnormalities, but the findings are neither sensitive nor specific for the diagnosis of acute PE. The greatest utility in patients with suspected PE is in ruling out other life-threatening diagnoses like an acute myocardial infarction[18]. In 1935 McGinn and White described an association between acute pulmonary embolism and specific ECG changes when they noted S1Q3T3 (prominent S wave in lead 1, Q wave and inverted T wave in lead III) in 7 patients with acute cor pulmonale[19]. Since then, this pattern has historically

The Nigerian Health Journal, Volume 22, Issue 3

been associated with pulmonary embolism, but actually is a sign of acute pressure and volume overload of the right ventricle because of pulmonary hypertension and denotes right ventricular strain[18]. This ECG pattern has been found to be present in 15% to 25% of patients diagnosed with pulmonary embolism and there is neither sensitive or specific in diagnosing pulmonary embolism[18].

The most frequent ECG sign found in patients with acute PE is sinus tachycardia[20]. Other findings include complete right bundle branch block, inverted T waves in V1-V4, ST segment elevation in avR and atrial fibrillation[20]. Just like the clinical presentation, the ECG findings in acute pulmonary embolism are quite variable and can be easily missed.

The variability in ECG changes seen in acute pulmonary embolism is evident in the presented cases, the first case only had sinus tachycardia, which is the commonest ECG change seen in acute pulmonary embolism but is also not specific for it. The second case had a regular sinus rhythm with normal electrical axis and inverted T waves in leads V1-V4 (as well as in the lateral and inferior leads), while the last case had sinus tachycardia with right axis deviation, inverted T waves in the precordial leads V3-V5 and an incomplete right bundle branch block (RBBB).

Amongst the variable presentations of acute pulmonary embolism, it can also present with hypotension and shock, a type known as 'hemodynamically unstable PE'. According to the Trust guidelines for management of suspected PE associated with shock or hypotension, a management algorithm which was adapted from the European Society of Cardiology 2014 guideline should be followed. It states that if the patient is stable enough to have an urgent CTPA, then it should be done[21]. When CTPA is unavailable or patient is too unstable for transfer, then an echocardiography may help rule out PE as a cause for the hemodynamic instability, provided there is no evidence of right heart dysfunction. But when efforts to confirm a diagnosis are not possible, then thrombolysis should be considered on a case-by-case basis[21].

Based on this guideline the patient in case 1 had to be thrombolized after successfully passing a fibrinolytic checklist, as she was not considered stable enough to be transferred for a CTPA and the 2D echocardiography machine was unavailable at that time. But in the case of the third patient, even though he was considered unstable to be transferred for a CTPA, he was able to do a 2D trans-thoracic echocardiography that showed evidence of right ventricular pressure and volume overload. A case for fibrinolytic therapy was made but treatment was stalled due to financial constraints. Therapeutic doses of low molecular weight heparin were commenced, and his clinical state improved remarkably within the next 48 hours.

It is evident from the cases discussed that the clinical presentation of acute pulmonary embolism is variable and can also be subtle. This means that there is a high chance that the diagnosis can be missed. A high index of suspicion coupled with the use of standard pretest scoring systems and a treatment algorithm has the potential to uncover the diagnosis and also streamlined the management of this medical emergency. However, as observed in these cases, the Well's score did not correlate with the severity or clinical outcome of the pulmonary embolism. In case 2 the score was 4.5 (PE likely), but she seemed to be the most stable clinically, of the 3. The other 2 cases initially fell into the 'PE unlikely' group but exhibited more severe clinical features. It is hoped that soon, a more robust pretest scoring systems will be developed that will not only determine the likelihood of PE but will also predict the severity and possible outcome of this life-threatening medical disorder.

Conclusion

Acute pulmonary embolism is a potentially life-threatening medical emergency that is associated with significant morbidity and mortality. Its clinical presentation is highly variable ranging from being totally asymptomatic to presenting with acute respiratory symptoms, to presenting with shock, hypotension, and even sudden death. This makes it easy for the unsuspecting physician to miss the diagnosis. Regular use of clinical scoring systems is currently being advocated, to enable rapid classification of patients and early identification of patients who have a high probability of having PE. The D-dimer levels and MD-CTPA are indispensable investigations in the diagnosis of PE, while other investigations including the ECG are more useful for confirming or ruling out alternate diagnosis. A high index of suspicion, early diagnosis, and immediate treatment will not only reduce the morbidity and mortality from the acute embolic event but will also lower the rate of early recurrent PE and reduce the sequelae of chronic embolism.

Conflict of Interest: There are no conflicts of interest to declare.

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