‘The silent killer’: A case series on pulmonary embolisms

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'The silent killer': A case series on pulmonary embolisms

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ABSTRACT

Background and Objectives. Pulmonary embolism (PE) is the third most common cause of death among hospitalized patients. The clinical presentation of a PE is highly variable and requires a high degree of suspicion to diagnose especially in a timely manner. A good grasp of various risk factors that may predispose a patient to a venous thromboembolism (VTE) and knowledge of the various presentations possible is required in order to diagnose and initiate potentially life-saving treatment in these patients. Here, we will look at five unique clinical presentations of a PE that highlight the variability of presentation in these cases.

Materials and Methods. 5 unique clinical presentations of pulmonary embolism were chosen and clinical data discussed.

Conclusions. The spectrum of clinical presentation in a case of pulmonary embolism is very wide. A high degree of clinical suspicion is necessary to make a timely diagnosis of a PE, especially in the ER. This is especially pertinent given the fact that mortality in untreated cases is a whopping 30% compared to 8% with timely therapy. Thus it is imperative for clinicians to have a comprehensive understanding of the various presentations possible, to allow timely detection and prevent delays in the potentially lifesaving therapy that must be initiated.

Keywords: pulmonary embolism, thromboembolism, anticoagulation, deep vein thrombosis, hypercoagulable states

Abbreviations:

1. PE: Pulmonary Embolism
2. VTE: Venous Thrombo Embolism
3. NYHA: New York Heart Association
4. JVP: Jugular Venous Pressure
5. CTPA: Computerized Tomography: Pulmonary Angiogram
6. MRI: Magnetic Resonance Imaging
7. USG: Ultrasonogram
8. CXR: Chest Xray
9. BP: Blood Pressure
10. RR: Respiratory Rate
11. ECG: Electrocardiogram
12. TAPSE: Tricuspid Annular Peak Systolic Excursion
13. NOAC: Newer Oral Anticoagulant
14. APLA: Antiphospholipid Antibodies
15. ANA: Anti-Nuclear Antibodies

INTRODUCTION

A pulmonary embolus (PE) refers to an obstruction of either the pulmonary artery or one of its branches usually by a thrombus originating from elsewhere in the body. The diagnosis of a pulmonary embolism is often an extremely challenging task owing to its varied and non-specific presentation. If left untreated, it is often devastating, with an overall mortality rate of up to 30% [1] which drops to around 8% with timely therapy [2]. It is crucial to identify patients early especially those with hemodynamic instability, and initiate appropriate treatment as soon as possible. It is important to have a high index of suspicion for a PE, especially in cases with associated risk factors, so that such cases may be picked up at an early stage, facilitating more

prompt treatment. Here, we will be looking at a series of cases, all with pulmonary embolisms in drastically different clinical settings.

MATERIALS AND METHODS

5 unique clinical presentations of pulmonary embolism were chosen and clinical data discussed.

CASES:

Case 1:

The patient was a 37 year old male, with no known comorbidities. He was a driver by occupation. He presented with breathlessness for 1 week, sudden in onset, Grade II to III NYHA(New York Heart Association), aggravated on exertion. He also had complaints of right lower limb pain, extending from the thigh to the calf x 4 days duration, which was insidious in onset and progressive. He was a smoker (smoked cigarettes 1 pack/day for 8 years, and had stopped 6 years prior), and occasionally consumed alcohol.

On arrival, he was restless and tachypneic, his Blood pressure was 90/60 mmHg, pulse rate was 120/min, and SpO2 94% in room air. Systemic examination revealed no significant abnormalities. His ECG showed a sinus tachycardia (Figure 1), right axis deviation and an RV strain pattern. A CT-PA (Figure 2) was done which revealed filling defects in bilateral pulmonary artery branches. An echocardiogram revealed hypokinesia of the RV free wall with a normal apex- the 'McConell's sign', with a TAPSE of 12mm.

Figure1: His ECG showed a sinus tachycardia, right axis deviation and an RV strain pattern:

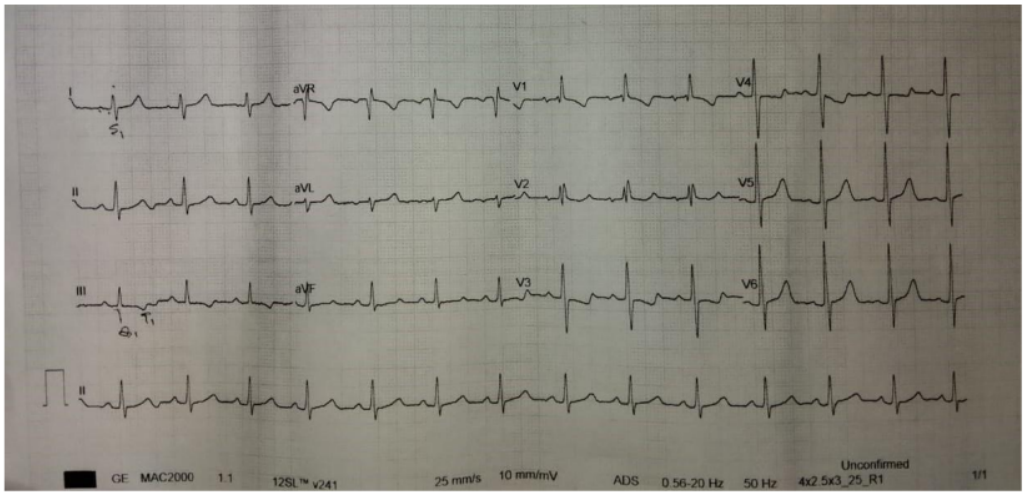
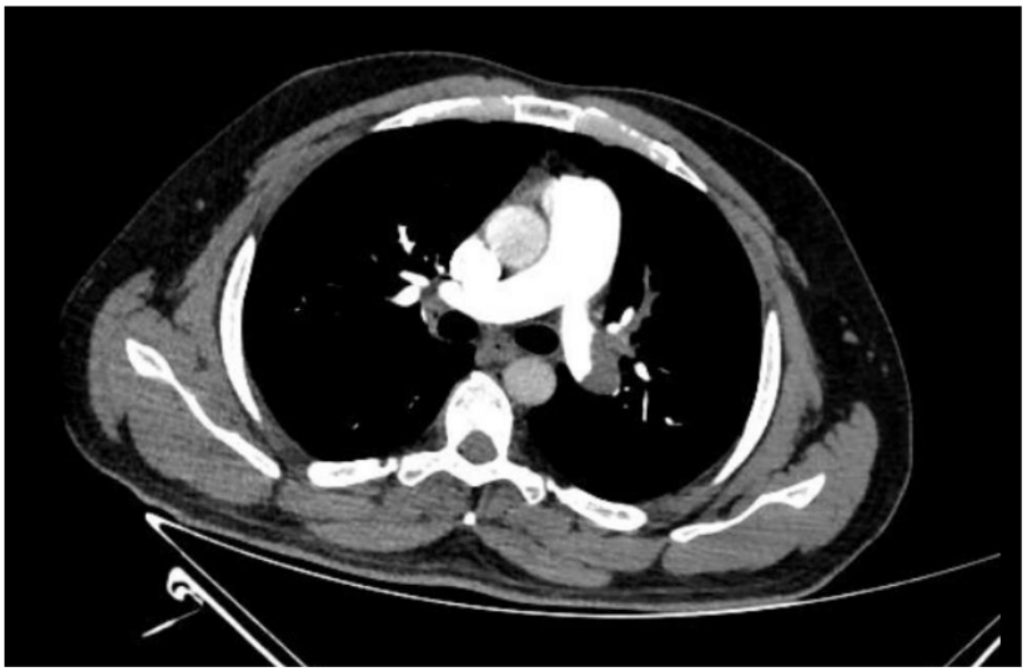


Figure 2: His CT-PA revealed filling defects in bilateral main pulmonary artery branches:



Owing to hemodynamic instability and RV dysfunction, he was thrombolysed with Tenecteplase and later anticoagulated with heparin. USG doppler of the right lower limb showed an Ileofemoral thrombus. He was started on oral acenocoumarol after a period of 'bridging'. Pro thrombotic work up (consisting of Serum homocysteine, Protein C and S levels, Anti Thrombin III levels, APLA antibodies and an ANA-IF) came out negative.

Case 2:

A 62 year old female, known diabetic, came with history of sudden onset weakness of left upper and lower limb and slurring of speech for 3 hours. The weakness was improving and was ⅘ (MRC grading) in both limbs on arrival. An MRI- brain showed an infarct in the right gangliocapsular region. On probing her history further, she revealed that she had had pain in her left calf for 1 day prior to onset of her symptoms. Owing to the improving nature of her neurological deficit and history of left calf pain, a D-dimer (2822 ng/ml) and a USG doppler (Figure 3) was done, which revealed a thrombus in the left popliteal vein. She was started on anticoagulation.

Figure 3: USG doppler of the left lower limb revealed a thrombus in the left popliteal vein.

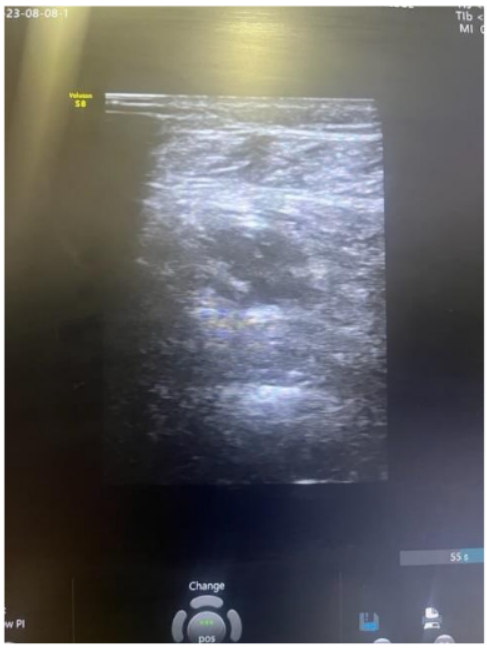
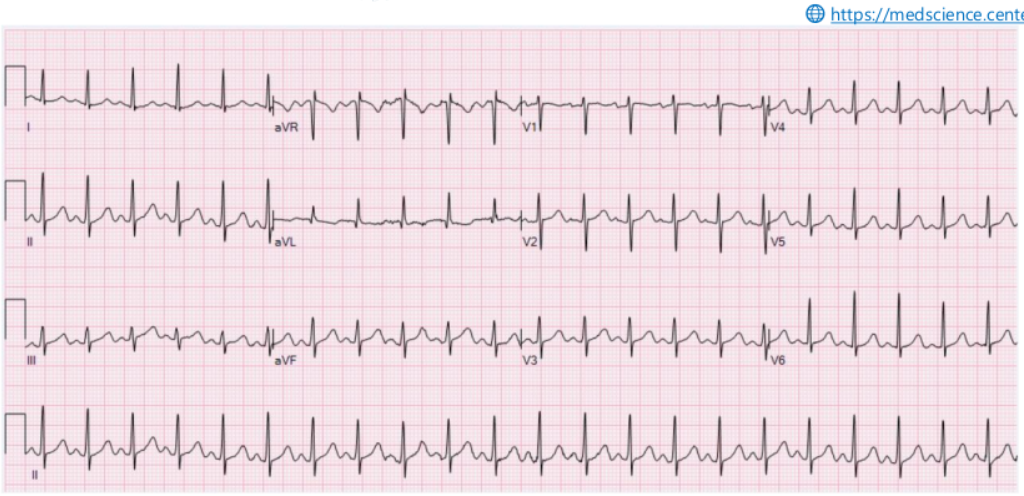


Figure 4: Her ECG showed a sinus tachycardia:

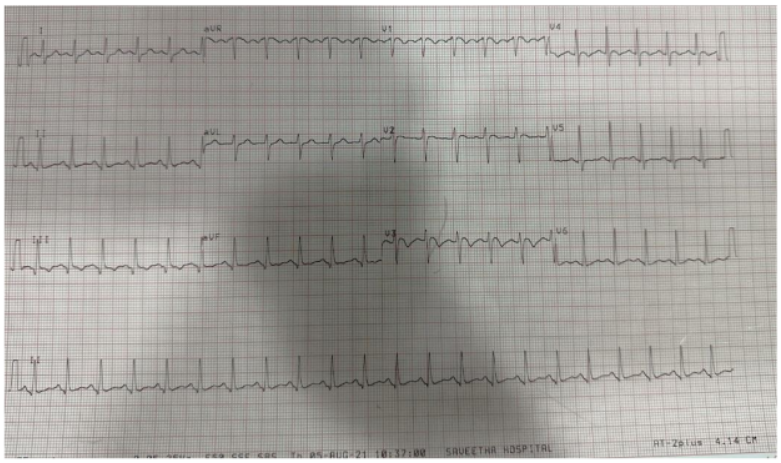


Her Echocardiogram was normal. However, she had a persistent sinus tachycardia (Figure 4) and a low/low normal SpO2 (93-95%). A CTPA was done which revealed a thrombus in the distal left main pulmonary artery. She was continued on anticoagulation and converted to a NOAC (Rivaroxaban) on discharge. A prothrombotic workup is planned.

Case 3:

The patient was a 28 year old male, with no comorbidities. He came with a history of giddiness followed by a fall 1 day prior to presentation. No head injury was sustained. Since then, he complained of breathlessness, Grade 2-3 NYHA, static, aggravated on exertion. He had no history of recent surgeries or immobilization. In fact, he had climbed 100 steps up to a hill side temple 4 days earlier. On arrival to the ER, he was tachypneic. Even though he was lying down, he had his legs folded underneath him and his right calf was mildly tender. His vitals were stable. Systemic examination was normal. ECG showed the 'S1Q3T3' pattern with a sinus tachycardia. (Figure 5) His echocardiogram was normal.

Figure 5: His ECG showed the 'S1Q3T3' pattern with a sinus tachycardia:



In view of the persistent unexplained sinus tachycardia and breathlessness, a CTPA was done which showed a filling defect in a branch of the right pulmonary artery. As there was no hemodynamic instability or RV dysfunction, he was anticoagulated with heparin and primary

reperfusion therapy was not started. On discharge, he was switched to a NOAC(Newer oral anticoagulant). A prothrombotic workup on follow up was significant for a moderately elevated Homocysteine (30 micromol/dl), and normal Folate levels (26 ng/ml).

Case 4:

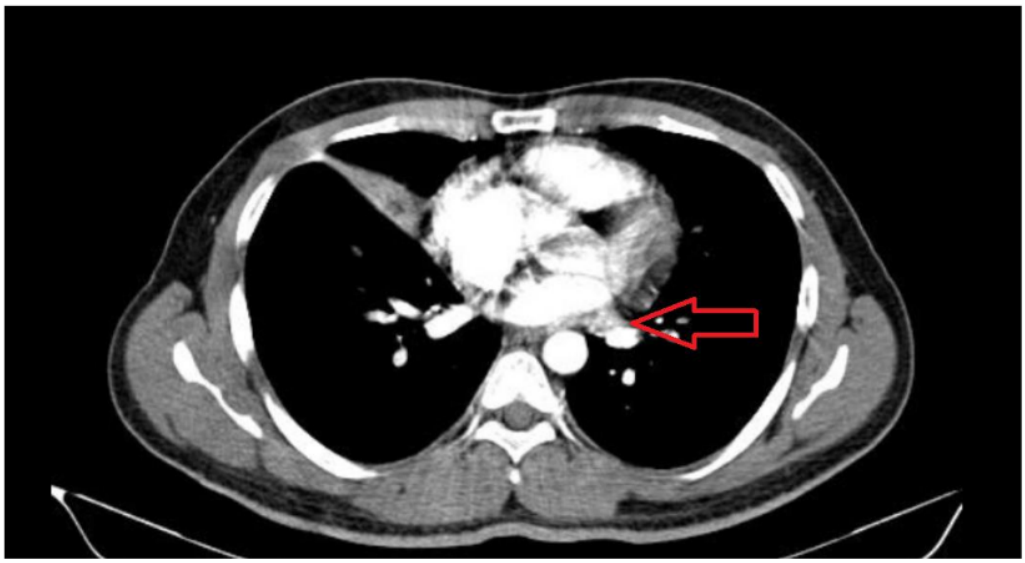
The patient was a 52 year old male, a k/c/o Decompensated Chronic Liver Disease- Ethanol related and Diabetes mellitus, on regular medication. He came with complaints of bilateral leg swelling x 2 weeks and abdominal pain 3 days. On arrival, he had bilateral pitting pedal edema, his blood pressure was 100/70mmHg, pulse rate was 112/min, respiratory rate was 28/min and SpO2: 94% in RA. His JVP(Jugular Venous Pressure) was elevated. Abdominal examination revealed ascites and no tenderness. An RVS3 or 'RV gallop' was heard in the left lower parasternal area. His ECG showed only a sinus tachycardia. An Echocardiogram was done which revealed RA and RV dysfunction (TAPSE: 1.0 cm)**. A D-dimer was sent which was elevated (3809 ng/ml).

In view of persistent sinus tachycardia and the above findings a CT-PA was done, which revealed a filling defect in a branch of the left main pulmonary artery. He was anticoagulated and later started on oral NOACs. He was unfortunately not willing for further prothrombotic workup.

Case 5:

A 25 year old male, with no known comorbidities, came with complaints of fever x 2 days, with chills and rigor, cough with scanty expectoration and breathlessness x 1 day. On arrival, his blood pressure was 100/60mmHg, pulse rate was 118/min, SpO2: 94% in RA, and Temp: 99.8F. Systemic examination revealed no significant abnormalities. His CXR was normal. His ECG showed sinus tachycardia with the 'S1Q3T3' pattern. The echocardiogram revealed dilated right ventricle with a basal RV/LV ratio of 1.2. A CTPA (Figure 6) was done and it showed a thrombus in the left lower lobar artery.

Figure 6: A CT-PA showed a thrombus in the left lower lobar artery:



As he was hemodynamically stable, he was anticoagulated with heparin and later switched to oral acenocoumarol. His PT/INR is monitored regularly. On follow up, a prothrombotic workup was

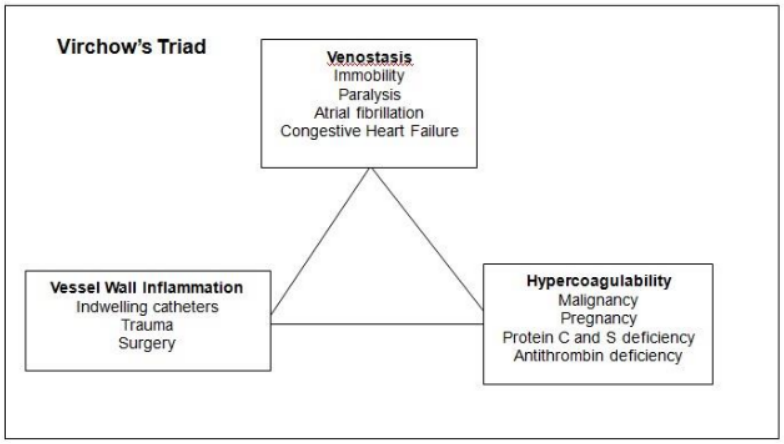
done consisting of Serum homocysteine, Protein C and S levels, Anti Thrombin III levels, APLA antibodies and an ANA-IF was done, which were all negative.

DISCUSSION

A pulmonary embolism (PE) is a serious and potentially fatal complication occurring due to thrombus formation in the deep venous circulation of the pulmonary vasculature. It is the third most common cause of death among hospitalized patients [3]. It's management requires early diagnosis through a systematic diagnostic approach with an understanding of common risk factors involved.

A deep venous thrombosis (DVT) and a PE are two manifestations of the same disease. Their risk factors are similar and include the conditions that favor formation of a thrombus within the vessel i.e, the Virchow's triad (venous stasis, a hypercoagulable state and endothelial injury) [4]. (Figure 7) Venous stasis is seen with immobility, in postoperative patients, polycythemia, pregnancy, etc. Hypercoagulable states include patients on oral contraceptive pills (OCPs), protein C and S deficiencies, antithrombin III deficiency, hyperhomocysteinemia, the APLA syndrome, malignancies, surgeries etc. Endothelial injury may occur with trauma, surgeries, indwelling catheters etc.

Figure 7: Virchow's triad of venostasis, hypercoagulability and vessel wall inflammation:



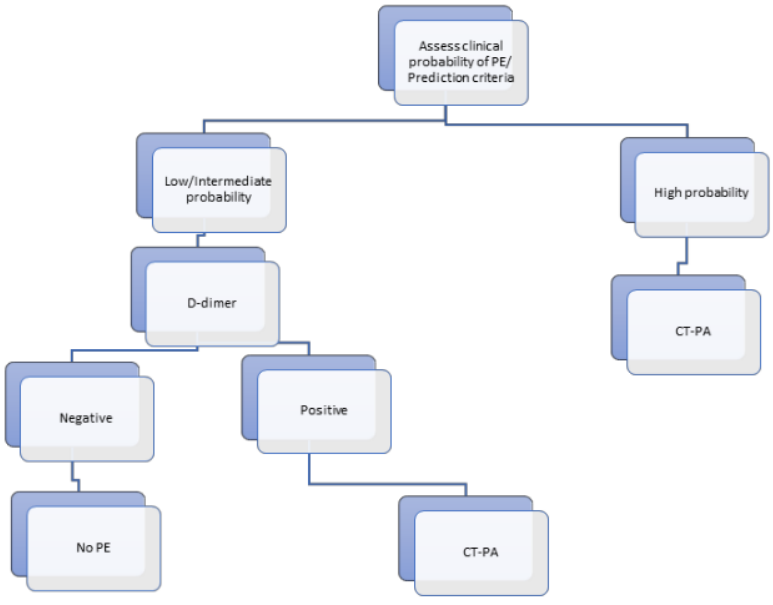
Case 1 was a chronic smoker, Cases 2 and 4 were chronic diabetics, contributing to the procoagulable state, while Cases 3 and 5 had no identifiable risk factors.

The clinical diagnosis of a PE is challenging for a couple of reasons: Firstly, the signs and symptoms commonly associated are not specific for this disorder. Common signs and symptoms include dyspnea, tachypnea, chest pain on deep inspiration, cough, hemoptysis and rarely syncope. Secondly, the clinical findings vary widely depending on the patient's preexisting cardiac and pulmonary status and the size of the embolus.

Among our patients, three of them presented with complaints of breathlessness. Four of the five were tachypneic on presentation.

Once a PE is suspected, an integrated approach is advised. (Figure 8) Various predictive scores such as the Well's score, the pulmonary embolism rule-out criteria (PERC), the Geneva score etc can be utilized.

Figure 8: An algorithm to assess the clinical probability of PE:



The D-dimer is a degradation product of cross linked fibrin[5]. It reflects an ongoing activation of the hemostatic system. The significance of the D-dimer test in PE lies in its high negative predictive value[6]. Thus it's value lies in ruling out the diagnosis of a PE, rather than as a

confirmatory test, as it's positive predictive value is low. It is quite nonspecific and is also elevated after trauma, a myocardial infarction, sepsis, surgery, burns, arrhythmias, disseminated intravascular coagulation, etc.

The CTPA (Computerized tomographic pulmonary angiography) has emerged as the method of choice [7] for imaging in the evaluation of a patient with PE. It provides adequate visualization up to the subsegmental level of pulmonary architecture. However cost and availability in many centers, exposure to iodine contrast, and the attendant radiation exposure are limitations.

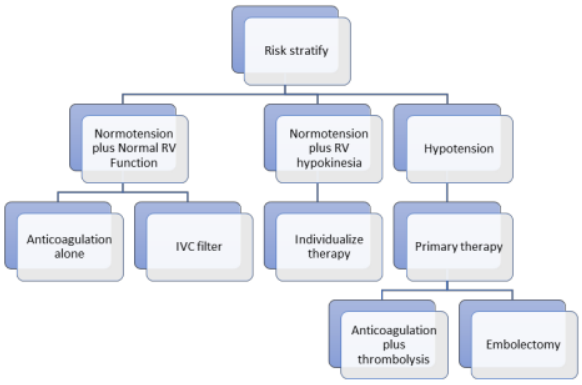
The echocardiogram is a valuable tool in the diagnosis of a PE. Various findings [8] in acute PE include the McConnell's sign(Case 1), RV dilatation with basal RV/LV ratio > 0.1(Case 5), a flattened interventricular septum, decreased TAPSE (tricuspid annular peak systolic excursion) <16 mm, and the 60/60 sign (coexistence of acceleration time of pulmonary ejection <60 msec, and mid systolic 'notch' with a mildly elevated peak systolic gradient i.e, <60 mmHg at the tricuspid valve.)

The classical 'S1Q3T3' or McGinn White sign, denoting RV strain is seen in 15-25% [9] of patients with PE. However the most common abnormalities are sinus tachycardia and nonspecific ST-T changes, seen in around 40% of cases Other findings include a new right bundle branch block (complete or incomplete), rightward shift of the QRS axis, T wave inversions in V1-V4 etc.

All five of our cases had a sinus tachycardia, and two of them (Cases 3 and 5) had the 'S1Q3T3' sign.

Once the diagnosis of an acute PE is made, management (Figure 9) is based on whether there is attendant hemodynamic instability, or RV hypokinesia.

Figure 9: An algorithm on the approach to risk stratification in PE:



If there is hemodynamic instability or hypotension [10], primary therapy with either thrombolysis plus anticoagulation or embolectomy (surgical or catheter-directed) is advised. Commonly used regimens are 100 mg of alteplase, a recombinant tissue plasminogen activator (tPA) as an infusion over 2 hours or streptokinase 250,000 IU loading dose followed by an infusion of 100,000 IU/hr over 12-24 hrs. Even though the sooner thrombolysis is administered, the more effective it is, it may be administered up to 14 days after the onset of PE. Following hemodynamic stabilization, these patients can be switched over to oral anticoagulation.

Anticoagulation alone is sufficient in most cases without hypotension. Three major strategies for anticoagulation in PE exist:

1. Parenteral therapy with unfractionated heparin(UFH), low molecular weight heparin (LMWH), or fondaparinux 'bridged' to warfarin
2. Parenteral therapy switched after 5 days to a novel anticoagulant (NOAC) such as dabigatran or edoxaban.
3. Oral anticoagulation monotherapy with rivaroxaban or apixaban with a 3 week or 1 week loading dose respectively, followed by a maintenance dose.

Three NOACs have been approved for use in VTE: the oral Xa inhibitors rivaroxaban and edoxaban and the oral thrombin inhibitor, dabigatran [11].

Among our cases, only Case 1 presented with hemodynamic instability, and was thrombolysed with a tPA. The others were hemodynamically stable on presentation and were given anticoagulation alone. Two of our patients were started on oral acenocoumarol and three were given NOACs for long term anticoagulation. All five have not had any further thrombotic episodes.

Duration of anticoagulation after an episode of PE is still controversial. The terms 'provoked' and 'unprovoked' are no longer used due to a similar risk of recurrence of VTE in patients with 'provoked' as 'unprovoked' VTE after discontinuation. In general all patients with PE must be anticoagulated for a period of at least 3 months [9]. Discontinuation after this period is only recommended when the index VTE event was due to a major identifiable risk factor like surgery, or major trauma. In all other patient groups, indefinite anticoagulation is recommended.

Conclusion:

As shown above, the spectrum of clinical presentation in a case of pulmonary embolism is very wide. A high degree of clinical suspicion is necessary to make a timely diagnosis of a PE, especially in the ER. This is especially pertinent given the fact that mortality in untreated cases is a whopping 30% compared to 8% with timely therapy [2]. Thus it is imperative for clinicians to have a comprehensive understanding of the various presentations possible, to allow timely detection and prevent delays in the potentially lifesaving therapy that must be initiated.

CONCLUSION

As shown above, the spectrum of clinical presentation in a case of pulmonary embolism is very wide. A high degree of clinical suspicion is necessary to make a timely diagnosis of a PE, especially in the ER. This is especially pertinent given the fact that mortality in untreated cases is a whopping 30% compared to 8% with timely therapy [2]. Thus it is imperative for clinicians to have a comprehensive understanding of the various presentations possible, to allow timely detection and prevent delays in the potentially lifesaving therapy that must be initiated.

CONFLICT OF INTEREST

None to declare.

AUTHOR'S CONTRIBUTIONS

Conceptualization, Dr. Sharan bose and Dr. Ananthakumar P.K; methodology, Dr. Sharan Bose; validation: Dr. Ananathakumar P.K, Dr. Rajalakshmi K.V; formal analysis: Dr. Sharan Bose and Dr. Jibin Simon; investigation: Dr. Sharan Bose and Dr. Jibin Simon; resources, data curation: Dr. Sharan Bose and Dr. Jibin Simon; writing—original draft preparation: Dr. Sharan Bose; writing—review and editing: Dr. Sharan Bose, and Dr. Ananthakumar P.K; supervision: Dr. Rajalakshmi K.V; project administration: Dr. Sharan Bose. All authors have read and agreed to the published version of the manuscript.

ACKNOWLEDGEMENTS

None

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FIGURES:

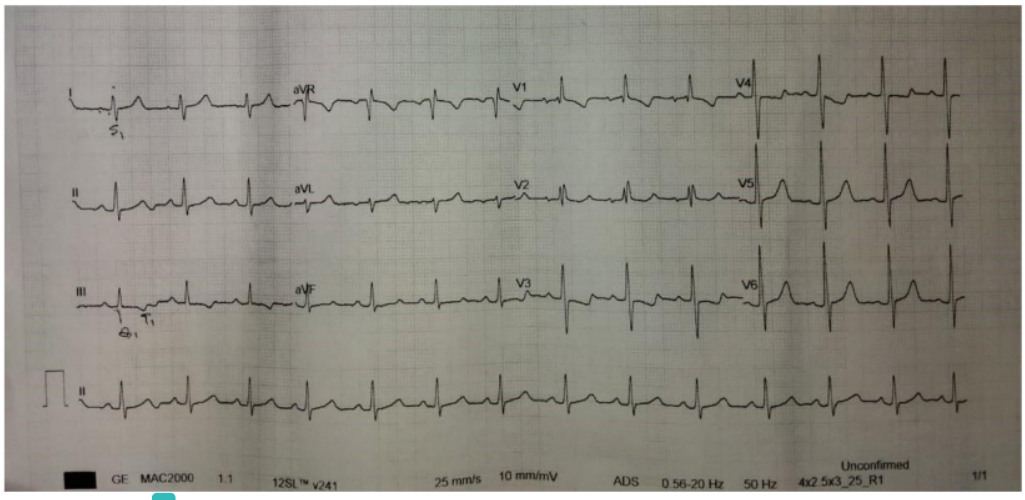
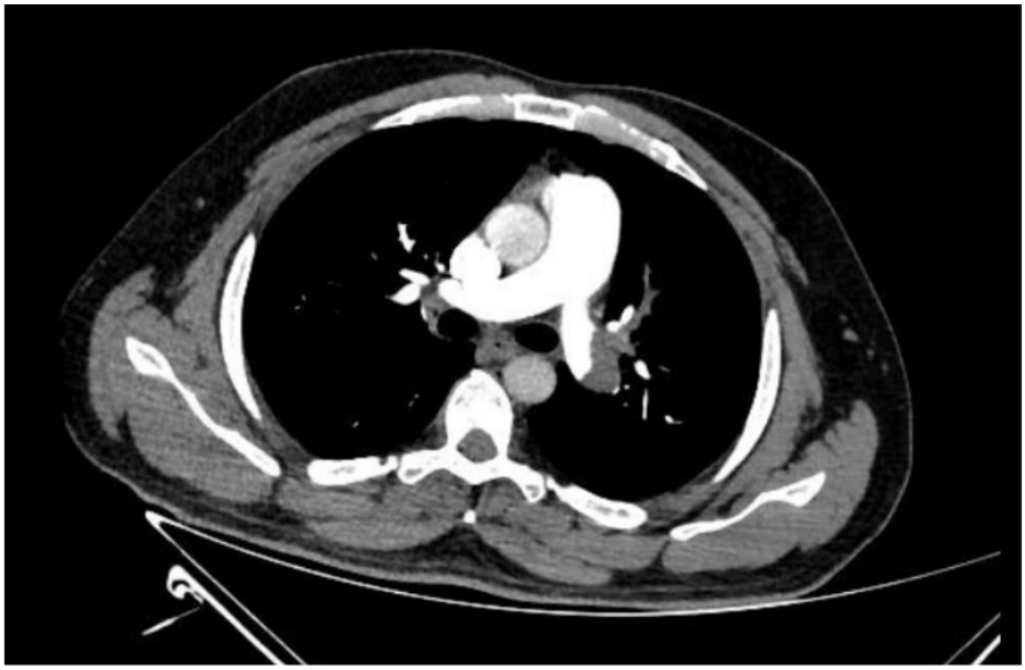


Figure 1: His ECG showed a sinus tachycardia, right axis deviation and an RV strain pattern:



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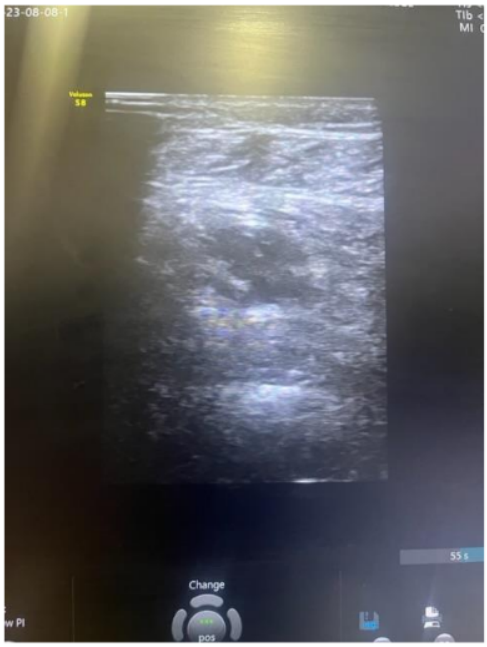
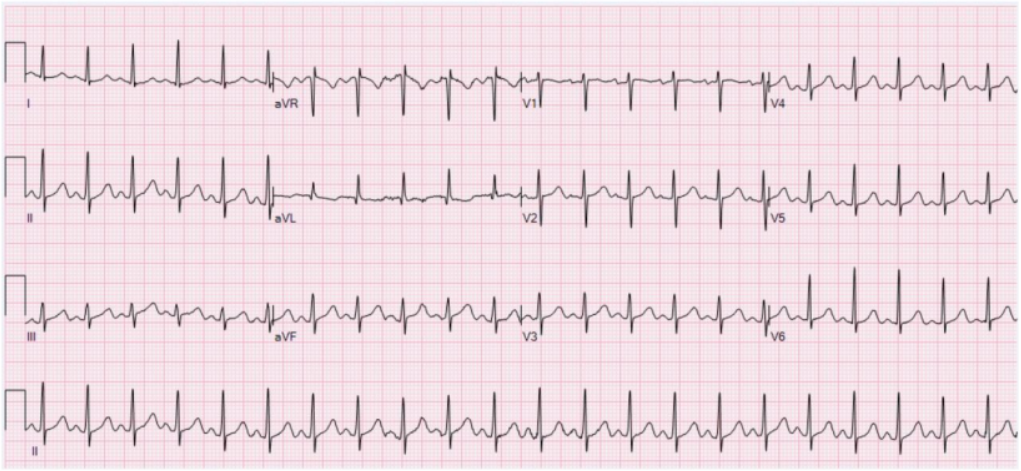


Figure 3: USG doppler of the left lower limb revealed a thrombus in the left popliteal vein.



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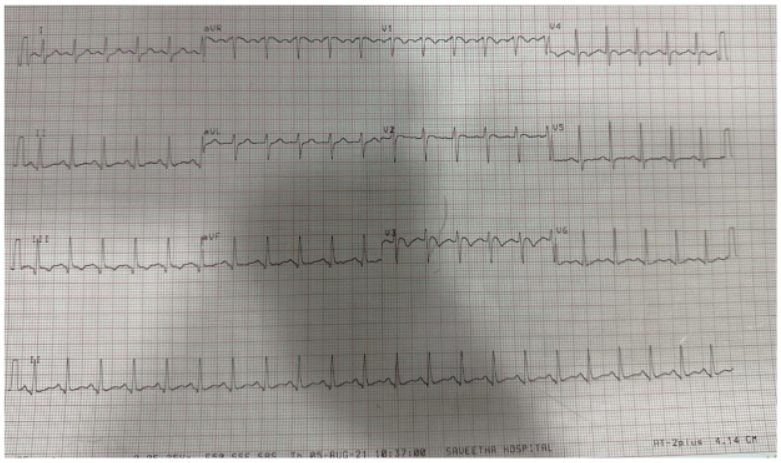

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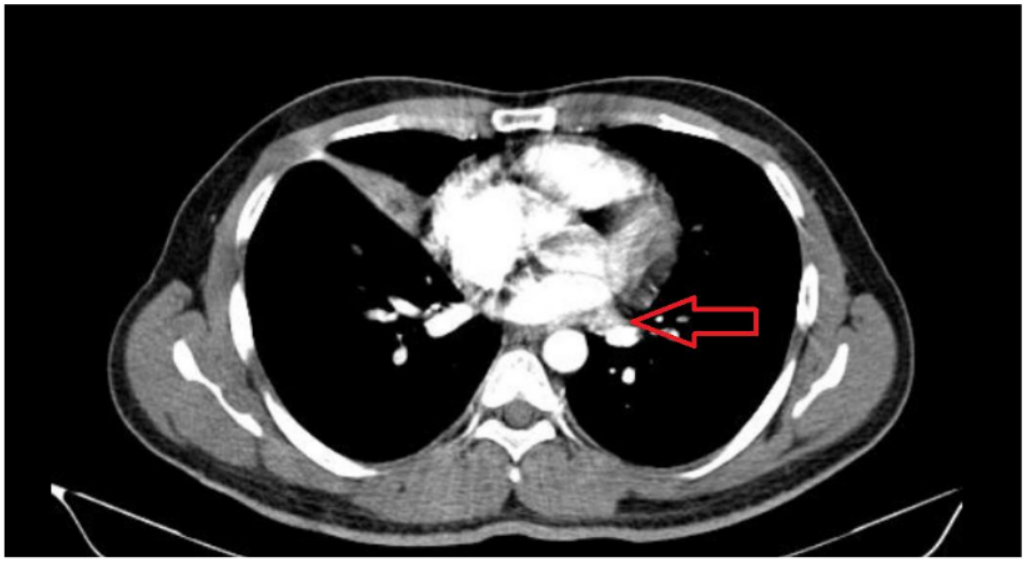
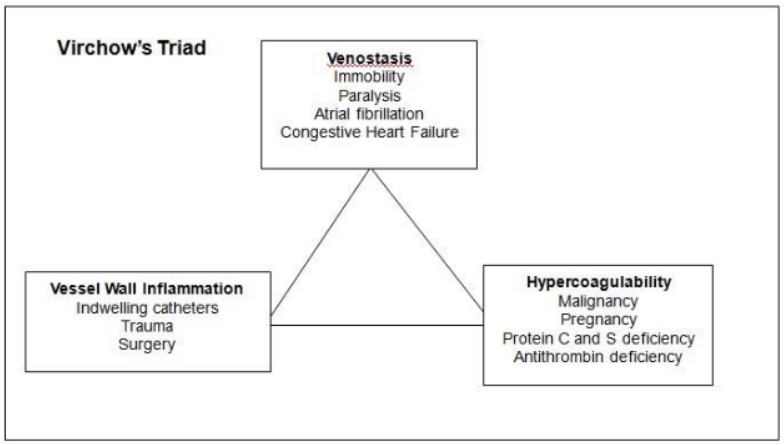


Figure 6: A CT-PA showed a thrombus in the left lower lobar artery:



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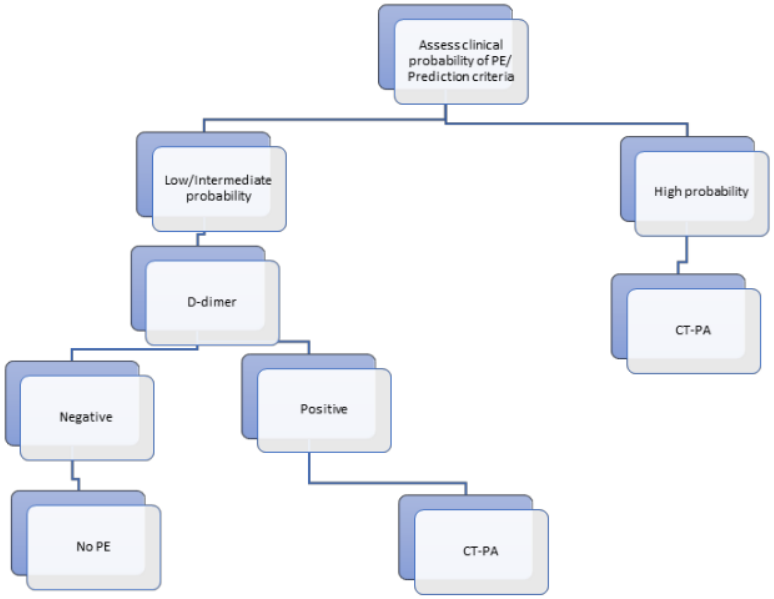

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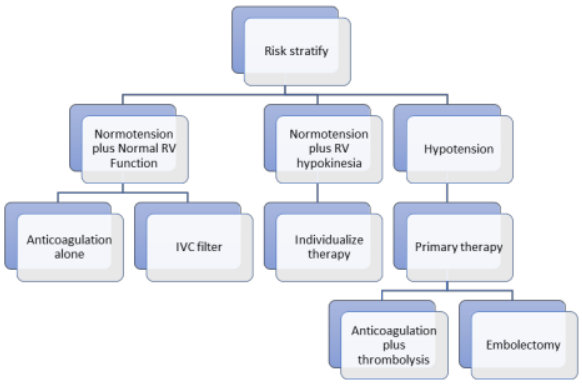

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