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Pulmonary Medicine

UNPROVOKED PULMONARY THROMBOEMBOLISM – CASE SERIES

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ABSTRACT Unprovoked pulmonary thromboembolism is a very difficult diagnosis owing to the fact that PTE should be suspected based on clinical presentation and confirmed with CT-pulmonary angiogram, but since unprovoked requires no identifiable causes are the required criteria makes it even more difficult to start the treatment on early basis. Here is a case series of unprovoked PTE to make aware the prevalence of the same in the ER and to prompt necessary investigations and signs to diagnosis the condition.

KEYWORDS : Unprovoked pulmonary thromboembolism, dyspnoea, chest pain, hemoptysis

INTRODUCTION:

Pulmonary Thromboembolism (PTE) has always been a diagnosis of difficulty at the time of presentation despite the presence of highly specific tests and sensitive imaging methods. Around 60% of the patients who succumbed to PTE were diagnosed during their course of stay at the hospital (1). At the same time <20% to even 9.8% of the selected suspected patients (as per diagnostic criteria) would have PTE (2). This is because most of the times patients would have had a subclinical course of PTE and also the main symptoms such as dyspnoea, cough, chest pain, haemoptysis and syncope, used to diagnose the disease were nonspecific seen in both patients with and without PTE. Provoked PTE are those caused by underlying conditions and having an active cause of embolism such as COPD, inflammation, immobilisation(for at least 4 days in previous month), surgery (within 1 month), cardiac failure, trauma, obesity (with BMI >40), intake of hormonal replacement therapy, stroke, AF and paresis. The pure form of PTE termed as Idiopathic/Unprovoked PTE comprises of the patients having none of the above-mentioned causes. The frequency of unprovoked PTE varies between 16.5% to 51% and can go up to 69-76% as mentioned in some literatures (3,4,5). This case series is done to emphasize on the prevalence of Unprovoked PTE in our institution and to an extent describe the factors to help in favour of diagnosing the condition without any other comorbidities and to start treatment early and adequately as it requires to get an inherited thrombophilia work up done and has a longer duration of treatment.

Case Presentation

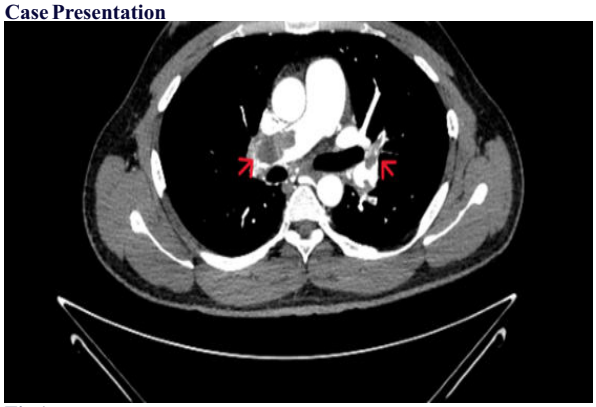

Fig 1

Case 1:

30-year-old male came with complaints of breathlessness and productive cough for 4 days. He was apparently asymptomatic 4 days back after which he developed breathlessness of mMRC Grade III and productive cough with mucoid expectoration and no diurnal variation, He also complaints of fever 4 days back which subsided on medications. He had a past h/o Left lower limb pain 3 months back and was managed symptomatically. He never smoked in his lifetime but consumes alcohol, last intake being 4 days back. He maintained 94% in room air and other vitals were stable. Blood investigations showed polycythaemia and leucocytosis along with hypoxia on ABG. D-dimer was high and 2D ECHO showed mild RA/RV dilatation with mild TR and PASP of 45 mmHg. CTPA confirmed pulmonary thrombus in bilateral pulmonary arteries (fig. 1) and was thrombolysed with alteplase followed by maintenance of dabigatran on discharge. Other culture reports showed no growth and ANA was negative.

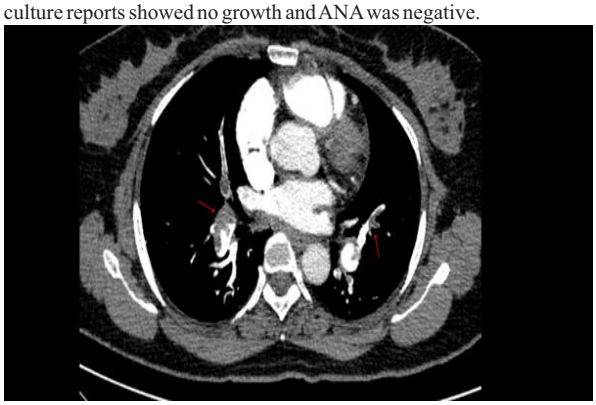

Fig. 2

Case 2:

46-year-old female with no known comorbidities, came to casualty with c/o sudden onset of breathlessness for past 3 days, not associated with orthopnoea/PND/diurnal variation. She also c/o productive cough with mucoid expectoration, non-foul smelling and non-blood stained. She also had c/o calf pain followed by right sided chest pain since last night and onset of giddiness since morning of admission. There were no significant past medical or surgical history other than a minor procedure for haemorrhoids 5 years back. On presenting to the ER, she had accelerated hypertension of 180/120mmhg. Other vitals were within normal limits. 2D ECHO done outside showed RA/RV dilated with PASP of 90mmHg. ABG showed respiratory alkalosis with hypoxia and elevated d-dimer levels. I/v/o suspecting PTE, CTPA was proceeded and showed bilateral pulmonary thromboembolism located within the MPA bifurcation, lobar branches and all segmental

branches with dilated pulmonary arteries and mild cardiomegaly (fig. 2). She was categorised as intermediate-low risk PTE and started on treatment dose of low molecular weight heparin and improved. She was discharged with 3 months of Apixaban and PDE5 inhibitors. ANA was negative. On further work up bilateral lower limb venous doppler was negative for DVT.

Case 3:

54-year-old male who is a former smoker of index 200, with no known comorbidities presented to the OPD with c/o haemoptysis of minimal amount for past 4 months, last episode 4 days back. He had c/o exertional dyspnoea for past 1 month due to which he had reduced food intake and associated with weight loss. He had occasional episodes of low-grade fever, on and off during this last 1month. On presentation he had tachypnoea and other vitals were stable and chest Xray had shown right middle zone non homogenous opacities with mild density. In view of elevated D-dimer values and normal levels of infective markers, he was proceeded with CT pulmonary angiogram which showed segmental thrombus in right middle lobe medial segment (fig. 3). Tuberculosis work-up turned out to be negative and sputum culture had grown moderate growth of Pseudomonas aeruginosa sensitive to ciprofloxacin. He has had no other history of provoking factors and was started on T. Rivaroxaban for next 3 months being categorised under low risk for PTE.

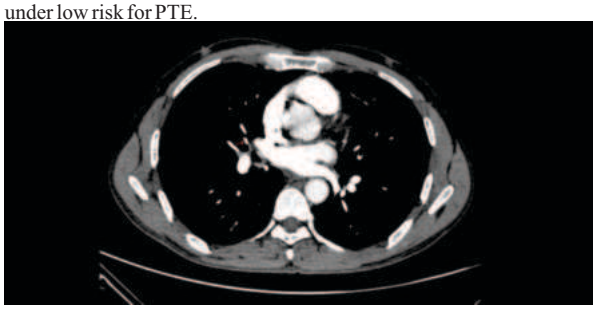

Fig. 3

Parameters	CASE 1	CASE 2	CASE 3
Sex	Male	Female	Male
Age	30	46	54
PR	98	86	88
Blood Pressure	110/90	180/120	120/80
SpO2	94	95	98
ABG (pH/pCO2/pO2)	7.43/24.2/66	7.46/26.5/73	7.48/29/59.8
ECG changes	s1q3t3	q3t3, t inversion in V3	Sinus tachycardia
Hb	17.9	9.2	12
TC	15.6	10.44	7.45
D-dimer	3.16	7.14	9.73
CRP	26	32	9
2D ECHO	RA/RV dilation with PASP 45mmHg	RA/RV dilation with PASP 90mmHg	RA/RV mildly dilated
WELLs Score	6	6	5
PESI Score	81	46	65

DISCUSSION:

Acute pulmonary embolism (PE) is a form of venous thromboembolism (VTE) that is common and sometimes fatal. The clinical presentation of PE is variable and often nonspecific making the diagnosis challenging. The evaluation of patients with suspected PE should be efficient so that patients can be diagnosed, and therapy administered quickly to reduce the associated morbidity and mortality. Death from hemodynamically unstable PE often occurs within the first two hours, and the risk remains elevated for up to 72 hours after presentation (9). In a study done by Natalia Stoeva et. al., it has been found that unprovoked PTE occurs at a younger age, more frequently in males, manifests with a heavier thrombotic burden, higher Well's score and lower one month mortality rate than provoked PTE (6). UPE in older adults is not uncommon (14.5%) but has lower incidence than as that seen in adults (7) and is associated with a better prognosis in terms of a higher cumulative survival within the first year of admission, but cumulative survival of UPE patients decreases and becomes equal to the cumulative survival of PPE patients during the next 2 years (8).

The most common symptoms in patients with PE were identified in the Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED) group. They include the following:

- Dyspnea at rest or with exertion (73 percent)
- Pleuritic pain (66 percent)
- Cough (37 percent)
- Orthopnea (28 percent)
- Calf or thigh pain and/or swelling (44 percent)
- Wheezing (21 percent)
- Hemoptysis (13 percent)

Less common presentations include transient or persistent arrhythmias (eg, atrial fibrillation), presyncope, syncope, and hemodynamic collapse (<10 percent each) (14, 15)

Although the true incidence of asymptomatic PE is unknown, one systematic review of 28 studies found that, among the 5233 patients who had a deep vein thrombosis (DVT), one-third also had asymptomatic PE (16).

Common presenting signs on examination include [17]:

- Tachypnea (54 percent)
- Calf or thigh swelling, erythema, edema, tenderness, palpable cords (47 percent)
- Tachycardia (24 percent)
- Rales (18 percent)
- Decreased breath sounds (17 percent)
- An accentuated pulmonic component of the second heart sound (15 percent)
- Jugular venous distension (14 percent)
- Fever, mimicking pneumonia (3 percent)

The most frequent causes of an inherited (primary) hypercoagulable state are the factor V Leiden mutation and the prothrombin gene mutation, which together account for 50 to 60 percent of cases. Defects in protein S, protein C, and antithrombin (formerly known as antithrombin III) account for most of the remaining cases (10, 11).

The absolute risk of thrombosis among patients with inherited thrombophilia was evaluated in a report of 150 pedigrees, which compared the risk for thrombosis in individuals with inherited thrombophilia due to factor V Leiden or to antithrombin, protein C, or protein S deficiency. The lifetime probability of developing thrombosis compared with those with no defect was 8.5 times higher for carriers of protein S deficiency, 8.1 for antithrombin deficiency, 7.3 for protein C deficiency, and 2.2 for factor V Leiden (12).

Obesity also appears to be a contributing factor for further increasing the risk of VTE in a number of high-risk settings (13).

Common abnormalities seen on ABGs include one or more of the following (18)

Hypoxemia (74 percent)

Widened alveolar-arterial gradient for oxygen (62 to 86 percent)

Respiratory alkalosis and hypocapnia (41 percent)

However they can be normal too in upto 18% of the patients

ECG abnormalities that are associated with a poor prognosis in patients diagnosed with PE include (19):

- Atrial arrhythmias (eg, atrial fibrillation)
- Bradycardia (<50 beats per minute) or tachycardia (>100 beats per minute)
- New right bundle branch block
- Inferior Q-waves (leads II, III, and aVF)
- Anterior ST-segment changes and T-wave inversion
- S1Q3T3 pattern

Thrombolytic therapy can be considered after risk stratifying all patients with PE as per PESI scoring system as follows. For low risk to intermediately low risk patients, mere oral anticoagulants or NOACs would suffice. For intermediately high risk patients, thrombolysis can be done based on clinical judgement. For high risk patients immediate thrombolytic therapy administration is required provided there are no contra indication for major risks of bleeding manifestations. Initial support of supplemental oxygen, NIV, IV fluids and vasopressors are given as per patient presentation.

In the above-mentioned case reports, all patients were planned for inherited thrombophilia work up post 6 months of treatment with Newer oral anticoagulants and have been regularly following up with our OPD. Even though systemic infection causes provoked pulmonary embolism, the fact that the patient in case report 3 has had symptoms for 4 months, there were no elevated infective markers, and that likely infection must have been colonised in the later stages cannot categorise the patient under provoked causes and needs to be evaluated for inherited factors.

CONCLUSION:

Pulmonary embolism is a challenging diagnosis at the ER having a wide range of clinical presentation, ranging form being asymptomatic to hemodynamical instability. Most of the time lack of a provoking factor may sometimes mislead the clinicians to overlook the diagnosis of pulmonary thromboembolism. It is of extreme importance to consider the possibility of unprovoked PTE and thereby o start on thrombolysis treatment as early as possible to avoid further patient mortalities and morbidities. As pulmonary embolism is a diagnosis of clinical presentation, it is imperative to have a high level of suspicion so that potential curable patients are not missed.

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There are no Conflicts of Interest for this series.

REFERENCES:

1. A.T. Cohen, G. Agnelli, F.A. Anderson, J.I. Arcelus, D. Bergqvist, J.G. Brecht, I.A. Greer, J.A. Heit, J.L. Hutchinson, A.K. Kakkar, D. Mottier, E. Oger, M.M. Samama, M. Spannagl, VTE Impact Assessment Group in Europe (VITAE). Venous thromboembolism (VTE) in Europe. The number of VTE events and associated morbidity and mortality, Thromb Haemost 98 (2007) 756–764.
2. M.D. Mamlouk, E. van Sonnenberg, R. Gosalia, D. Drachman, D. Gridley, J.G. Zamora, G. Casola, S. Ornstein, Pulmonary embolism at CT angiography: implications for appropriateness, cost, and radiation exposure in 2003 patients, Radiology 256 (2010) 625–632.
3. M. Miniati, C. Cenci, S. Monti, D. Poli, Clinical presentation of acute pulmonary embolism: survey of 800 cases, PLoS One 7 (2012) e30891.
4. R.H. White, H. Zhou, P.S. Romano, Incidence of idiopathic deep venous thrombosis and secondary thromboembolism among Ethnic Groups in California, Ann. Intern. Med. 128 (1998) 737–740.
5. E. Gjonbrataj, J.N. Kim, J. Gjonbrataj, H.I. Jung, H.J. Kim, W.-I. Choi, Risk factors associated with provoked pulmonary embolism, Korean J Intern Med 32 (2017) 95–101.
6. Natalia Stoeva, Galina Kirova, Milena Staneva, Diana Lekova, Anton Penev, Rumiana Bakalova, Recognition of unprovoked (idiopathic) pulmonary embolism–Prospective observational study, Respiratory Medicine 135 (2018) 57–61.
7. Agnelli G, Becattini C. Acute pulmonary embolism. *N Engl J Med.* 2010;363:266–74.
8. Aharoni, M., Horesh, N., Rogowski, O., Kremer, A., Mayan, H., & Justo, D. (2021). Unprovoked pulmonary embolism in older adults: incidence and prognosis. *Archives of medical science : AMS*, *17*(2), 337–342
9. COON WW, WILLIS PW. Deep venous thrombosis and pulmonary embolism: prediction, prevention and treatment. *Am J Cardiol*. 1959;4:611-621.
10. Crowther MA, Kelton JG. Congenital thrombophilic states associated with venous thrombosis: a qualitative overview and proposed classification system. *Ann Intern Med*. 2003;138(2):128-134.
11. Mateo J, Oliver A, Borrell M, Sala N, Fontcuberta J. Laboratory evaluation and clinical characteristics of 2,132 consecutive unselected patients with venous thromboembolism--results of the Spanish Multicentric Study on Thrombophilia (EMET-Study). *Thromb Haemost*. 1997;77(3):444-451.
12. Martinelli I, Mannucci PM, De Stefano V, et al. Different risks of thrombosis in four coagulation defects associated with inherited thrombophilia: a study of 150 families. *Blood*. 1998;92(7):2353-2358.
13. Wattanakit K, Lutsey PL, Bell EJ, et al. Association between cardiovascular disease risk factors and occurrence of venous thromboembolism. A time-dependent analysis. *Thromb Haemost*. 2012;108(3):508-515.
14. Stein PD, Terrin ML, Hales CA, et al. Clinical, laboratory, roentgenographic, and electrocardiographic findings in patients with acute pulmonary embolism and no pre-existing cardiac or pulmonary disease. *Chest*. 1991;100(3):598-603.
15. Castelli R, Tarsia P, Tantardini C, Pantaleo G, Guariglia A, Porro F. Syncope in patients with pulmonary embolism: comparison between patients with syncope as the presenting symptom of pulmonary embolism and patients with pulmonary embolism without syncope. *Vasc Med*. 2003;8(4):257-261.
16. Stein PD, Matta F, Musani MH, Diaczok B. Silent pulmonary embolism in patients with deep venous thrombosis: a systematic review. *Am J Med*. 2010;123(5):426-431.
17. Stein PD, Beemath A, Matta F, et al. Clinical characteristics of patients with acute pulmonary embolism: data from PIOPED II. *Am J Med*. 2007;120(10):871-879.
18. Stein PD, Goldhaber SZ, Henry JW, Miller AC. Arterial blood gas analysis in the assessment of suspected acute pulmonary embolism. *Chest*. 1996;109(1):78-81.
19. Panos RJ, Barish RA, Whye DW Jr, Groleau G. The electrocardiographic manifestations of pulmonary embolism. *J Emerg Med*. 1988;6(4):301-307.