CASE REPORT

Pulmonary embolism presented by syncope in a low-risk patient: a case report [version 1; peer review: 2 approved with reservations]

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Abstract

Introduction: Pulmonary embolism, an emergency that can have fatal consequences, can be presented with a common symptom that can be missed, such as syncope.

Case presentation: We present a case of a young, low-risk male who presented with attacks of syncope and dyspnea followed by massive pulmonary embolism. We also review the pathophysiology of syncope in pulmonary embolism cases and strategy of how to work up with similar cases.

Conclusion: Pulmonary embolism should be considered and excluded in every case of recurrent attacks of syncope.

Keywords
Pulmonary embolism, Syncope, Low risk

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Introduction
Pulmonary embolism (PE) is a medical emergency that can lead to sudden death. This condition is usually associated with factors that may increase the risk of its occurrence, such as age, high tendency for intravascular coagulation and the presence of certain concomitant conditions such as deep venous thrombosis (DVT) and malignancy. In this case, we have a presentation of a young, low-risk patient with only recurrent syncope and dyspnea that was eventually diagnosed as a massive PE. It is an uncommon case of pulmonary embolism of unknown cause that deserves attention. Such a common presentation could have led to misdiagnosis of the condition which could have ended with the sudden death of the patient.

Case presentation
A 30 year old male patient, a farmer from Upper Egypt, attended the cardiology outpatient clinic at Assiut University Hospitals, Egypt, on June 2012 with repeated attacks of syncope. They took place at irregular intervals, about two or three times per month.

The attacks of syncope had started eighteen months earlier, with each one lasting about one minute. There was progressive grade III dyspnea between the initial syncope symptoms and presentation at our clinic, but no evidence of orthopnea, paroxysmal nocturnal dyspnea or lower limb swellings.

General examination found that the patient had a body mass index of 28.4 kg/m². The pulse was 110 beats/min, the respiratory rate was 24 breaths/min and the arterial blood pressure was 110/70 mmHg. There was a raised jugular venous pressure line about 6 centimeters above the level of the sternal angle. There were multiple, soft, painless subcutaneous masses over both thighs and the back of the patient with ill-defined edges. Cardiac examination showed that there was a pansystolic murmur over the tricuspid area which increased with inspiration, ejection systolic murmur over the pulmonary area with accentuated pulmonary component of the second heart sound. Electrocardiography showed sinus tachycardia with inverted T wave in leads II, III, aVF and V₅-V₆. Chest X-Ray revealed cardiomegaly. 2-D transthoracic echocardiography showed a dilated right side of the heart with a 5.7 cm × 1.4 cm mass in the right atrium that protruded through the tricuspid valve towards the right ventricle. Valvular morphology was normal with moderate tricuspid regurgitation and moderate pulmonary hypertension (Figure 1). Liver and kidney function tests were normal. According to this data, the patient was given a Wells score of 1.5, which gave an indication to a low risk of PE.

The patient was diagnosed initially with a cardiac tumor in the right atrium with suspected positional obstruction of right ventricular inflow track causing syncopal attacks, which was managed accordingly with diuretics, aspirin 150 mg/day and bisoprolol 10 mg/day to control heart rate. He underwent a duplex scan of the deep venous system of both lower limbs, which was found to be normal. While the medical team investigated the patient in hospital, a sudden attack of syncope occurred, with a sudden severe hypotension down to 90/60 mmHg. The Wells score of the patient has sharply increased from the initial 1.5 to 8, which indicated a very high risk of the presence of PE. Urgent Multi-slice CT pulmonary angiography found a massive bilateral pulmonary embolism involving the left and the right pulmonary arteries and most of their segmental branches (Figure 2). A diagnosis of high-risk pulmonary embolism was made.

In order to save the patient’s life, we put the patient under thrombolytic therapy. A central venous line was set up, and streptokinase was given initially as a loading dose of 250,000 IU over 30 minutes, followed by a dose of 100,000 IU/hour over 24 hours. After the recovery of the patient from the acute stage, anticoagulant therapy was given, initially in the form of enoxaparin sodium at a dose of 90 mg/kg for seven days. In conjunction, warfarin was given at a daily dose of 5 mg until the international normalized ratio (INR) reached 2.8.

The patient fully recovered from the high-risk pulmonary embolism, and an echocardiogram made 24 hours after recovery showed complete dissolution of the intra-atrial mass with no evidence of any remnants left, suggesting that it was a massive ball thrombus that had a protrusion across the tricuspid valve (thrombus in transit). However, right atrial and ventricular dilation persisted. The patient was discharged after a short period of uneventful monitoring. Right before the discharge of the patient, surgical excisional biopsy of one subcutaneous mass was performed, and pathological assessment revealed superficial subcutaneous lipomas. His brothers also have these lipomas, so we believe that it is of familial origin. Upon taking further history from the patient, it was found that the patient...
and his brothers had a history of familial hyperlipidemia. Tests for
the patient’s hypercoagulable state as assessed by measuring levels
of protein C and S and antithrombin III appeared normal. The
patient was followed up for 6 months and showed no more syncopal
attacks. We do not have details of any further investigations that
may lead to a cause of this condition.

Discussion

PE is a serious medical emergency condition, in which obstruc-
tion of the pulmonary trunk or any of its branches takes place. It
could be partial or complete, which causes sudden obstruction of
the blood flow to the lungs, resulting in dyspnea, hypoxia, chest
pain and insufficient blood flow to the left side of the heart. PE can
be caused by any cause of embolism, including thrombosis, air, fat,
talc or amniotic fluid. About 1–2 people per 1000 may suffer from
pulmonary embolism while 1 in every 100 people over the age of
80 may suffer from this condition.

Signs and symptoms of pulmonary embolism occur suddenly.
Dyspnea, tachypnea, chest pain, cough, and hemoptysis take place.
In more severe cases, cyanosis, syncope and circulatory instability
occur, and sometimes peripheral edema may be present. Sudden
death can occur in the most severe cases. About 25% of PE cases
present as sudden death while 15% of all cases of sudden death are
attributable to PE.

The criteria for diagnosis of PE are put into clinical prediction
systems, such as the Wells score, which was initially proposed by
Wells et al. in 1995 (Table 1). Additional prediction systems to
determine the probability of getting a PE are available, such as the
Geneva rule, which has a similar manner of prediction, but with
some modifications.

Syncope, as a presenting symptom in PE, is not uncommon. While
it can have multiple causes, syncope is still an important sign of PE,
especially if it is accompanied by dyspnea. A study conducted by
Thames et al. in 1977 found that 13% of patients with PE present
initially with syncope. Another study conducted by Calvo-Romero
et al. in 2004, in Spain, showed that 9.1% of patients with PE
presented with syncope. However, the authors concluded that it was
impossible to tell whether syncope could determine the prognosis
in such cases. Apart from these two studies, in 1988, two patients
in Israel were reported to have suddenly died of massive PE af-
after having a hip surgery 3 weeks earlier. Several syncopal episodes
started in the first week after surgery, and they were considered as
a sign of fatal outcome.

The mechanisms that cause syncope in PE are variable. One mecha-
nism is that the presence of PE decreases blood flow to the lungs,
thus leading to hypoxemia and cerebral hypoxia. Another theory
suggests that a vasovagal attack is triggered with the occurrence
of PE. A third mechanism suggests that syncope occurs due to the
arrhythmias that result from overloading of the right ventricle.
A fourth mechanism suggests that PE leads to circulatory obstruct-
ion and decreased left ventricular filling, thus leading to decreased
cardiac output and ultimately diminished cerebral blood flow.

A determinant factor in the diagnosis of the cause of syncope is
the composition of arterial blood gases. Hypoxemia can indicate
the presence of a condition that obstructs normal cardiovascular or
respiratory functions. If there is no airway obstruction, PE is highly
suspected. Advanced imaging techniques, such as multi-slice CT
pulmonary angiography, can give an accurate image of the condi-
tion within the pulmonary vascular tree.

Lipomas are common benign tumors formed of adipose tissue.
They are the most common soft tissue tumor. The most common
lipoma is the superficial subcutaneous lipoma. They can be found
wherever fat is present under the skin surface. The tendency to
develop them is not exclusively hereditary. Nevertheless, there are
familial conditions that may include the presence of lipomas,
such as familial multiple lipomatosis. In 1989, it was reported in
Israel that there could be an association between familial combined
hyperlipidemia and the presence of nonsymmetric subcutaneous
lipomatosis in a family, which is similar to this case. A growing
body of evidence suggests the presence of a relationship between
hyperlipidemia and the occurrence of DVT. Therefore, we feel
this co-occurrence is worth noting.

In this case, the ball thrombus (thrombus in transit), which was
present in the right atrium, caused transient obstruction to the tri-
cuspid valve, thus causing a transient obstruction to the outflow of
the right atrium. That obstruction caused a transient obstruction
to the left ventricular filling that brought about decreased cerebral
blood flow. The ball thrombus probably got displaced as the
position of the patient changed so that blood flow was restored and
the syncopal episode ended. Eventually, the ball thrombus caused
further thrombosis and released emboli that were large enough to
occlude the pulmonary trunk and its main branches. Fortunately
for the patient, the medical team successfully managed to initiate
thrombolytic therapy in time, and the ball thrombus, along with the
other emboli, were lysed. A similar case in Turkey was reported in
2009, but it was different in that the patient had a high risk due to
long-term occupational immobilization and the presence of DVT.
Also a similar case series was reported in 1998 by Wolfe and Allen.
They reported three cases that initially presented with syncope and
later diagnosed with PE, and one of these cases ended up fatally.
An interesting aspect of the case presented here is that the medi-
cal team initially evaluated the patient as low risk according to the
Wells score. Duplex scans and tests for hypercoagulable state were normal, unlike the results usually found in most patients with PE. That leaves us with a question as to what could have caused that thrombus to occur. Additional investigations are necessary to find a cause of this condition, such as an undiagnosed malignancy or a familial cause.

**Conclusion**
Pulmonary embolism is a medical emergency that can be presented by a common symptom such as syncope. Physicians should pay attention to this presentation and check for pulmonary embolism in cases of syncope with dyspnea. Such cases can be easily missed, which may end up with sudden death if not diagnosed and treated promptly.

**Consent**
Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Author contributions**
AO was a major contributor to the writing of the manuscript. He also gathered and analyzed the patient’s data about syncope and pulmonary embolism. AT performed the acute treatment to the patient and was a major contributor in writing the manuscript. AH performed and supervised the treatment of the patient and the manuscript writing process. All of the three authors have read and approved the final manuscript.

**Competing interests**
No competing interests were disclosed.

**Grant information**
The author(s) declared that no grants were involved in supporting this work.

**Acknowledgements**
We would like to express our sincere and deepest gratitude towards the Medical Sector Reform Group of Egypt for their continuous support throughout the case report preparation process as a part of the Mentor-Student Research Project. Our special thanks go to Dr. Noha A. Moussa and Omnia M. Omar for their tremendous efforts as coordinators of this project. We are also grateful to Dr. Sameh Nashat for performing echocardiography to the patient and providing us with the results.

### Table 1. Criteria for diagnosis of pulmonary embolism, according to Wells Scoring System. Adapted from Neff MJ (2003)¹⁶. DVT: deep vein thrombosis, PE: pulmonary embolism.

<table>
<thead>
<tr>
<th>Clinical characteristic</th>
<th>Points</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of DVT</td>
<td>+3.0</td>
</tr>
<tr>
<td>Alternative diagnosis</td>
<td>+3.0</td>
</tr>
<tr>
<td>Tachycardia</td>
<td>+1.5</td>
</tr>
<tr>
<td>Immobilization over 3 days</td>
<td>+1.5</td>
</tr>
<tr>
<td>Surgery within four weeks</td>
<td>+1.5</td>
</tr>
<tr>
<td>Hemoptyis</td>
<td>+1.0</td>
</tr>
<tr>
<td>Malignancy</td>
<td>+1.0</td>
</tr>
</tbody>
</table>

**Classic clinical interpretation**

<table>
<thead>
<tr>
<th>Patient’s score</th>
<th>Risk level</th>
<th>Probability of PE</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 2.0</td>
<td>Low-risk</td>
<td>15% (Low)</td>
</tr>
<tr>
<td>2.0 – 6.0</td>
<td>Moderate</td>
<td>29% (Medium)</td>
</tr>
<tr>
<td>More than 6.0</td>
<td>High-risk</td>
<td>59% (High)</td>
</tr>
</tbody>
</table>

**Alternative clinical interpretation**

<table>
<thead>
<tr>
<th>Patient’s score</th>
<th>Likelihood of having PE</th>
<th>Recommended next step</th>
</tr>
</thead>
<tbody>
<tr>
<td>Less than 4</td>
<td>Less likely to have PE</td>
<td>D-dimer test</td>
</tr>
<tr>
<td>4 and above</td>
<td>More likely to have PE</td>
<td>Diagnostic imaging</td>
</tr>
</tbody>
</table>
References

Open Peer Review

Current Peer Review Status: ?

Version 1

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Massimo Miniati
Dipartimento di Area Critica Medico Chirurgica, University of Florence, Florence, Italy

The clinical case is well-described and, as such, it is worthy of indexation. My major concern is the use of the prediction model introduced by Wells. Even though it has been widely used, it has a very limited value in predicting pulmonary embolism (PE).

In the reported case, the Wells score was 1.5 - indicating low clinical probability. In my opinion, instead, the clinical presentation is strongly suggestive of PE.

By applying the prediction model we introduced in 2008 (Miniati et al., 2008) the clinical probability of PE would be 86%. Our model allows the estimation of the probability of PE by adding the regression coefficients that apply to a given patient. The probability can be calculated at once by using dedicated software that can be downloaded at www.ifc.cnr.it/pisamodel.

I am not saying that the authors should make use of our model, but I think that the availability of other models should be acknowledged in the manuscript.
Also, I may say that syncope is a relatively frequent presentation of PE even in young and otherwise healthy subjects. In a survey of 800 patients with an established diagnosis of PE (Miniati et al., 2012) the prevalence of syncope was 24%.

In sum, I believe that the manuscript is of interest but requires revision.

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
Martin Rohacek
Department of Emergency Medicine, University Hospital Bern, Bern, Switzerland

The authors present a case of pulmonary embolism (PE) presenting with syncope and hemodynamic instability.

Comments:
- The Wells score is a validated tool to define the pre-test probability of PE before performing diagnostic tests such as D-dimer tests and CTPA (computed tomography pulmonary angiography), but not to predict outcomes such as mortality. The authors state that the Wells score "sharply increased from 1.5 to 8" after a drop in the blood pressure (BP). BP drop is not a criterion of a Wells score. Thus, the Wells score did not rise to 8, but remained 1.5, and the patient remained low risk for PE. But, the drop in BP speaks for a hemodynamically relevant PE, which can be treated with thrombolytic agents. The drop in BP worsens the outcome of the patient, but is not a reason to describe this case of PE as "high-risk pulmonary embolism".

- "In order to save the patient's life": Hemodynamically relevant PE is not a 100% killer. Please discuss mortality rates of hemodynamically relevant PE.

Competing Interests: No competing interests were disclosed.

I have read this submission. I believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reader Comment 28 Mar 2014

Aly Tohamy, Cardiology Department, Assiut University Hospital, Egypt

Dear Dr Martin,

We confirm that the patient is low risk for pulmonary embolism, So we state and report the case (as you see in case report title).

Although the patient is low risk for pulmonary embolism, he develops hemodynamically relevant pulmonary embolism with huge right atrial mass.

Secondly, the in-hospital all-cause case fatality rate was lower in unstable patients who received thrombolytic therapy than those who did not - 15% vs 47% (Stein PD and Matta F (Am J Med. 2012)).

Competing Interests: No competing interests were disclosed.
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