ORIGINAL: How to Improve the Clinical Suspicion of Pulmonary Embolism in Hospitalized Patients

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Abstract: *Background*: The high number of missed diagnosis of pulmonary embolism antemortem still has not improved.

Objective: To define the causes of misdiagnosis and suggest another way in order to increase the rate of clinical suspicion.

Material and Methods: The cases with autopsy-confirmed of PE from 32986 autopsies were studied retrospectively. The data was classified according to the useful points to investigate the causes of undiagnosed antemorten.

Results: The number of patients that had the diagnosis suspected of PE antemorten was 692 (24.2 %). The dominant cause of misdiagnosis was deficient clinical suspicion (26.4 %). The underlying conditions that most frequently cause unsuspected PE were heart disease 24.6 % (mainly myocardial infarction), pneumonia (23 %) and cancer (15.1 %). Altogether, the percentage of correct clinical diagnosis of PE was 26.9 % (95 % CI).

Conclusions To increase the rate of correct diagnosis of PE, it is necessary to perform the clinical suspicion in the atypical forms that are common, besides the classical markes used.

Keywords: Pulmonary embolism, clinical suspicion, anxiety, sudden dyspnea.

INTRODUCTION

For several decades pulmonary embolism (PE) has remained one of the leading causes of death in hospitalized patients. That is because PE often is not clinically suspected antemortem. It has been shown in autopsy studies with clinico-pathological correlation [1,2]. Indeed, the index of correct diagnosis is still quite low, although some studies have reported modest improvement, but always more than half of the cases that occur are not clinically diagnosed before death. Some studies reveal a correct clinical diagnosis within 25% to 35 % [3]. More recently, over the last ten years ending in 2012 a study with clinico-pathological correlation revealed 31 % of correct diagnosis antemorten [4].

Our purpose is to suggest a new and possible diagnostic strategy to increase the percentage of the accuracy of the clinical antemorten diagnosis of PE.

MATERIAL AND METHODS

The data was obtained from 17 reports of acute PE at autopsy with clinicopathologic correlation, in hospitalized patients from prestigious institutions across the world. The data was adequate for a retrospective study and for the development of the argument of our topic. This vast material of our study includes five groups of periods (10, 5. 4, 2, 1 year). The data was organized as follows: number of autopsies performed; number of PE necropsy-proven, correct diagnosis suspected; lack of clinical diagnosis of PE, as well as the causes of misdiagnosis of PE. Also, the clinical diagnosis before death was compared with postmortem diagnosis.

RESULTS

Of 32986 autopsies performed during the groups of periods studied, 2,631 (7.9 %) cases of PE were found and 692 patients had correct clinical suspicion and diagnosis (Table **1**). During the ten year period, the number of patients that had a correct clinical suspicion was 164 (25.3 %) from 647 PE autopsy-proven. During the five year period PE was suspected 101(22.9%) from 441 cases diagnosed post-mortem. During a four year period, 251 (22.9 %) had clinical suspicion from 1,141 cases of PE diagnosed post-mortem. For a period of 2 years, 5 (23.3%) were suspected from 17 cases of PE diagnosed post-mortem, and for a period of 1 year, 183 (24.4 %) had correct suspicion from 742 PE autopsyproven (Table **1**). The predominant cause of misdiagnosis for PE was failure to suspect in the reports, but it was evident in all of them (Table **2**). Altogether, there was a marked lower rate of clinical suspicion of PE in comparison with PE autopsy-proven. The underlying condition played significant roles in the

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Table 1: Comparison Clinical Suspicion and Post-Morten Diagnosis of PE in Different Countries (Period of10, 5 & 23 Years)

Country	Hospital	Autopsy	Period	Years	PE(a-p)	Clin suspicion	Total clin suspicion
BRAZIL	Antonio P	3980	1998-04	10	114	28 (24.6 %)	10 years period
SERBIA	Pathol Inst	3629	1980-90	10	533	136 (21.4 %)	164 (25.3%)
DENMARK	Medical Univ	178	1973-78	5	152	26 (15.0 %)	
USA	Buffalo	733	1991-96	5	67	30 (44.8 %)	5 years period
SPAIN	San Carlos	483	1994-99	5	40	5 (12.5 %)	101 (22.9 %)
ITALY	San Carlo	1545	1989-94	5	182	40 (21.9 %)	
GERMANY	Innere Med	176	1998-02	4	349	91 (26.0 %)	
USA	Mayo Clin	2427	1985-89	4	92	29 (32.0 %)	
USA	Peter Briham	1555	1973-77	4	54	16 (29.6 %)	4 years prriods
NIGERIA	Univ College	1578	1985-89	4	60	9 (15.0 %)	251 (22.8 %)
CANADA	St Vicent	1276	1980-84	4	44	14 (31.8 %)	
SINGAPUR	Forensic Md	10097	1994-98	4	130	43 (33.1 %)	
NORWAY	Gade Inst	4191	1980-84	4	351	37 (10.5 %)	
TRINIDAD	St Agustine	610	4985-89	4	61	12 (19.7 %)	
IRAN	Legal Med	200	2005-06	2	17	5 (29.4 %)	2 years 5 (29.4 %)
AUSTRALIA	St Vicent	232	1992	1	16	2 (12.5 %)	1year 183 (24.6%)
POLISH	Kierownik	13216	--------	1	726	181(25.0%)	
Total	17	32986			2631		692 (26.9%)

PE (a-p) = PE autopsy-proved. *Clin=Clinical.*

Table 2: Underlying Diseases that Caused Incorrect Suspicion of Pulmonary Embolism

Condition	Periods	Percentage	Brief comment in the reports
Heart disease	10 years	24.6 %	Dominated by MI
Pneumonia	10 years	23.7 %	May be ass with elderly
Cancer	10 years	15.1 %	May be ass with elderly too
Stroke	4 years	10.3 %	Difficult suspicion of PE

Other conditions: elderly, surgery, immobilization were found, but without percentage.
MI =myocardial infarction; Ass = associated; PE = pulmonary embolism.

causes of misdiagnosis of PE, dominated by heart disease (24.6 %), mainly myocardial infarction, followed by pneumonia 23.7%, cancer 15.1%, and stroke 10.3 % (Table **2**). Overall, the percentage of correct clinical diagnosis of PE was 26.9 % (95 % confidence interval (CI)).

DISCUSSION

Our study has shown in general that the high rate of PE clinically undiagnosed has not changed as was found in our vast and heterogeneous data. Both the low rate of clinical suspicion, as the cause of misdiagnosis was similar in all the studies reported. It was confirmed that the misdiagnosis of PE is a univerasal problem.

This study has shown that one of the most important cause of misdiagnosis of PE is the failure of its diagnosis antemorten, This causal factor plays also a central role because of the contribution of other secondary factors that hinder an accurate suspicion. The failure of the clinical suspicion and diagnosis is mainly caused by inadequate level of diagnostic ability of the physician on one side, and also the variable and atypical presentations of PE that are frequent as was confirmed in the analysis of our data. That is why the

use of the classical syndrome as a guideline for its clinical suspicion is often not suitable, leading to a wrong diagnosis at the initial assessment. The current clinical syndromes used for suspecting PE are not sufficient [5]. Therefore, we also suggest to pay attention to the atypical presentation of PE that are common and can be the clue for its diagnosis. Obviously, our diagnostic method or strategy does not depend on the markers established. Moreover, it is good to know that the symptoms of presentation of PE may be quite variable. For example, sudden dyspnea is frequent but may be absent [6]. These atypical findings of PE have diagnostic value for PE when physical examination reveals any signs of right ventricular overload, always present in different degrees, and the presence of other risk factors. In our experience, this diagnostic strategy is possible. The clinical presentation may need several days to be completed [7]. These clinical manifestations of PE made us compare it with an “iceberg” which exhibits first the top and then the rest. Supposedly, clinician should suspect PE before other clinical findings appear. Also, some authors found a limited value of ECG as a diagnostic test. In our medical practice, if the result of ECG is not compatible with PE, we obtain it serially, always based on our clinical judgment, The clinical assessment should be made continuously.

The underlying condition was an important cause of unsuspected PE with pre-dominance of heart disease (mainly MI), followed by pneumonia and cancer. By the way, one of the authors in the data, considered that the diagnosis of PE was more obvious in patients with heart disease and cancer [8]. Other diseases may masquerade PE, but PE may masquerades other diseases too In our medical practice, it was detected masquerade by a clinical picture of an asthmatic attack complicated with atelectasis. In this data the diagnosis of suspected PE increased when deep venous thrombosis was detected. This finding agrees with the results of other studies [5].

Massive pulmonary embolism (MPE) was found as an important cause of misdiagnosis, but there was controversy in the results of the reports of our data, because, while some author improved the clinical suspicion, other had a significant drop in the index of diagnosis [9,10]. These controvetial results were found within the same study in two similar groups [11]. These contradictory results suggest the importance of the personal factor in the clinical suspicion and diagnosis of PE. We believe that the clinical suspicion of PE should be made as a presuntive and premonitory diagnosis based on the wide constellation at the onset, mainly the risk factors. Recently, a suspicion was confirmed immediately by transesophageal echocardiography which was followed by successful embolectomy, using clinical diagnosis alone [12]. In this data some studies found significant delay in the diagnosis of PE [13,14]. This can be due to error in the initial assessment and/or delay of the confirmative diagnosis. Thus, this deficiency may lead to an unfavourable outcome of the disease.

After having analyzed the factors that interfere for the correct clinical diagnosis before death, and suggested how to overcome them, it is essential that the physician have a adequate skill level for suspicion in order to makes an accuraty diagnosis of PE. The diagnostic capacity of the physicians may be increased by several ways. It has been shown that the diagnostic ability increases with physician’s level of training beside senior physicians [15]. It should include the learning of the autopsy evaluation. However, we believe that the most important point in the diagnostic process of PE is to have an accurate medical record, with a detailed medical history and a confident physical examination. This is the cornerstone for a successful diagnosis, although usually is not mentioned. When these steps are not correctly performed leads then they lead inevitably to a diagnostic error. While the physicians take the medical history, they may observe the condition, attitude or anxiety in the patient. Anxiety has been a valuable symptom for us to recognize PE. It has presented as a single finding and may be of severe intensity, followed immediately by circulatory collapse and death. It has also presented with mild intensity, sometimes perceived only in the facial expression of the patient. In this clinical event as was mentioned above, the diagnosis of PE is reinforced when the physical examination reveals any of the signs of right ventricular dysfunction (RVD). confirmed by echocardiography (ECHO). RVD has a great value for the early diagnosis of PE [16], even in absence of overt hemodynamic instability [17] and an increased risk of mortality in patients hemodynamically stable [18].

The differential diagnosis for PE is an important step of the clinical assessment that should be exhausted, and may be the only diagnostic tool for successful clinical suspicion.

Once the clinical suspicion is made several diagnostic tests are necessary in order to confirm the diagnosis. CT pulmonaty angiography and CT venography are the most often used imaging diagnostic tests. These methods are recommend by the PIOPED investigators, who state that any discordance with the clinical assessment demands further evaluation, depending on clinical judgment [19]. In contrast with V/Q scans, they allow direct visualization of the pulmonary arterial circulation but require the injection of a contrast agent. V/Q scans have a high proportion of inconclusive test results. On the other hand, there are no contraindications, nor risks as occur when contrast material is injected. Suspected deep vein thrombosis is best assessed by means of compression duplex ultrasound examination. Chest radiography is negative in the majority of cases of PE. However, it is recommended to rule in or out other abnormalities and before ordering a V/Q scan procedure. D-dimer blood test is used to rule out the presence of a thrombus.

This study has shown that the clinical diagnosis of pulmonary embolism confirms the axiomatic and eternal phrase pronounced by Claude Bernard: “there is no disease, but sick patients".

CONCLUSIONS

The diagnosis of suspected PE using only the markers established are not sufficient. It is necessary to detect this process by considering the atypical presentations that are common. This is a challenge for the physicians but the only way to rise the index of correct diagnosis. For this purpose we have defined the causalfactors of misdiagnosis and, suggest how to overcome them. At the same time we have provided our observations and experience for the clinical diagnosis of this elusive and deadly disease.

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