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A rare case of fatal pulmonary embolism immediately after scoliosis surgical correction

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Abstract: The incidence of pulmonary embolism in spinal surgery is very rare, especially when a posterior approach is adopted and the mechanisms of this complication in this type of surgery is not completely clear. In this population of patients, in light of the known risk of serious hemorrhagic complications (above all, subdural hematoma), there are no universally accepted guidelines on timing and methods of thrombo-prophylaxis; nowadays the prophylaxis, when considered, is mostly performed only in the post-operative phase. We describe a fatal case of a 59 years old man with no apparent previous risk factors in which the diagnosis of massive pulmonary embolism was made through autopsy and histopathological findings. The event arose immediately after spinal surgery carried out through the posterior approach. We believe that, although the high risk of bleeding in this type of surgery, some strategies of thrombo-prophylaxis should also be considered in the preoperative phase, since, as is illustrated by the case presented here, the embolism may arise suddenly and rapidly become fatal even in this low risk type of surgery.
Key Words: pulmonary embolism, vertebral arthrodesis, spine surgery, scoliosis.

INTRODUCTION

Deep venous thrombosis (DVT) and pulmonary embolism (PE) are very dangerous complications in surgical patients, especially those who undergo major orthopedic surgery, and particularly in hip and knee arthroplasty procedures. In this kind of operation, in the absence of prophylaxis, the incidence of DVT is about 84%, while that of PE ranges from 9% to 30% [1]. In addition to blood stasis and the general state of hypercoagulability encountered during surgical operations, there are many known risk factors for thrombosis, including prolonged immobilization, hormone replacement therapy, previous thromboembolic events, neoplasia, diabetes and hereditary coagulation disorders [2, 3].

Those who undergo spinal surgery are also at risk of developing potentially fatal thromboembolic complications, although the incidence has been shown to be markedly lower in such patients. In this population of surgical patients, however, in light of the relative rarity of such complications and the known risk of serious hemorrhagic complications, there are no universally accepted guidelines on thrombo-prophylaxis [4], and the mechanisms leading to the onset of DVT and PE after this type of surgery are unclear. Moreover, while the incidence of post-operative DVT in the setting of spinal surgery has been more frequently studied, less attention has been devoted to cases of symptomatic PE [5-7].

Mortality due to PE depends on the patient's clinical condition at the time of onset; however, it is estimated to be about 52% in patients with an initial systolic pressure below 90 mmHg, and up to 65% in patients requiring cardiopulmonary resuscitation [8].

Here, we report a rare case of fatal massive pulmonary embolism which arose after a procedure of posterior surgical correction performed on the thoracolumbar spine in a 59-year-old man affected by progressive idiopathic scoliosis. The PE was manifested

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immediately after the operation, when the patient was roused from anesthesia, and proved fatal within about 15 minutes.

CASE REPORT

A 59-year-old man affected by a progressive double scoliosis underwent surgical arthrodesis and thoracolumbar fixation. The man's severe form of scoliosis had led to the onset of paraparesis of the lower limbs about a month earlier and urinary blockage about a week earlier.

Preoperative radiography revealed severe dorsolumbar kypho-scoliosis with deformity of the vertebral bodies at the upper end of the pathological curvature, diffuse spondylotic phenomena and multiple discopathy, without notable findings in the cervical region. Routine preoperative examinations (laboratory analyses, electrocardiogram and chest x-ray) revealed no alterations.

In the preoperative period, the patient received no form of anti-thrombotic prophylaxis, which, according to the patient's clinical records, was to have been initiated in the post-operative period: low molecular-weight heparin (LMWH) 2 hours after surgery. The operation was carried out through a posterior approach with the patient in the prone position. Anesthesia was induced by means of sevoflurane; owing to anesthesiological requirements, the patient was curarized for most of the procedure. Sevoflurane was suspended and propofol was started in order to try to record patient's vital signs. The patient was then curarized again and sedation was maintained with sevoflurane. The operation, which lasted a total of 11 hours, involved T3-L5 epispinous incision and skeletonization of the bony plane with destruction of the articulations from T4 to L4. Titanium plates (Depuy) were applied in the sagittal direction and fixed with peduncular screws and clamps. Cruentation of the bony plane was then carried out and bone bracts taken from the operating field were applied. During the operation, which was performed with the aid of evoked potentials and intraoperative blood recovery (about 900 ml), no complications were recorded. At the end of the procedure, however, when the patient was being roused from anesthesia, severe bradycardia (37 bpm) occurred, followed by asystole; the patient died about 15 minutes after the administration of inotropic drugs and a failed attempt at resuscitation.

Two days after the patient's death, a judicial autopsy was ordered in order to ascertain the cause of death and any professional responsibility that the operators might have had in the death. On external inspection of the corpse, the dorsal region was covered by a large gauze, from which two drainage tubes emerged: one in the superior dorsal region and one in the inferior dorsal region. After removal of the gauze, a sutured vertical surgical incision about 40 cm in length was visible along the vertebral column from T3 to L4. Incision of this surgical wound in the dorsal and lumbar regions revealed the presence of metallic bars fixed in place, with plates and screws, and drainage tubes correctly positioned at the site of the surgical operation. In addition, copious hemorrhagic infiltration of the paravertebral muscles was observed (Fig. 1a).

On sectioning the heart (500 g), the right chambers were seen to be dilated and a massive reddish-gray clot was found in the right ventricle; the clot was adherent to the wall of the ventricle (Fig. 1b) and extended into the trunk of the pulmonary artery. This thrombotic formation was made up of a greyish-red coagulation, which adhered to the vessel walls in a mould-like manner and occluded the vessel lumen, straddling the main branches of the pulmonary arteries and extending bilaterally to the medium and small branches of the pulmonary arteries (Fig.1c-d). The venous system was also sectioned distally as far as the popliteal veins bilaterally; this investigation did not reveal macroscopic evidence of venous thrombosis.

Histological examination of the samples confirmed the presence of a pulmonary thromboembolism; on "Histological Age Determination", microscopic features were consistent with phase 1 (1-7 days) according to Fineschi *et al.* [9] (Fig. 2a-b). Involvement of the trunk of the pulmonary artery and the bilateral pulmonary arteries was observed. The lungs presented parenchymal areas characterized by features of vascular congestion with passive hyperemia due to acute pulmonary stasis and by the focal presence of amorphous endoalveolar material (acute pulmonary edema), associated to initial

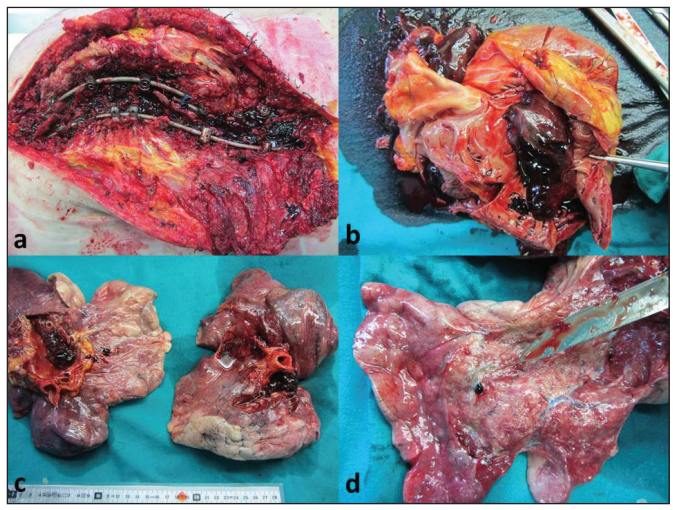

Figure 1. a) Surgical incision about 40 cm in length along the vertebral column from T3 to L4. Metallic bars fixed in place, with plates and screws. Copious hemorrhagic infiltration of the paravertebral muscles. b) Dilated right chambers with a massive reddish-gray thrombus; the thrombus was adherent to the wall of the ventricle. c-d) Thrombotic formation occluding the vessel lumen, straddling the main branches of the pulmonary arteries and extending bilaterally to the medium and small branches of the pulmonary arteries.

rupture of the inter-alveolar septa (initial pulmonary emphysema). Histological examination of the heart revealed mild myocardial sclerosis of the left ventricle, with the concomitant presence of mild "disarray" of the muscle cells associated to inter-myofibrillar edema and minimal focal endovascular granulocyte penetration, signs consistent with very acute EP-related terminal cardiac hypoxia (Fig. 2c-d).

On the basis of the findings of the autopsy and the subsequent histological examinations, the cause of death was attributed to acute cardio-respiratory insufficiency secondary to a massive pulmonary thromboembolism in a subject affected by worsening scoliosis who had undergone thoracolumbar surgical arthrodesis.

DISCUSSION

Cases of fatal pulmonary embolism during elective spinal surgery are extremely rare, if we exclude subjects with spinal traumas, who have a higher risk [10]. Indeed, a study conducted by Oda *et al.* on 110 patients who had undergone posterior spinal surgery revealed no cases of post-operative DVT or PE [11], while another study, which involved 313 patients with spinal disorders, found only one case of symptomatic post-operative DVT and no cases of PE [12].

In a meta-analysis of 14 studies which analyzed data on 4,383 patients who had undergone spinal surgery, it emerged that PE occurred in only 8 cases, with an estimated prevalence of 0.06%, and that only one patient died [13]. In a study conducted on 1229 patients, 8 (0.65%) showed signs of DVT and only one case of fatal PE occurred [14].

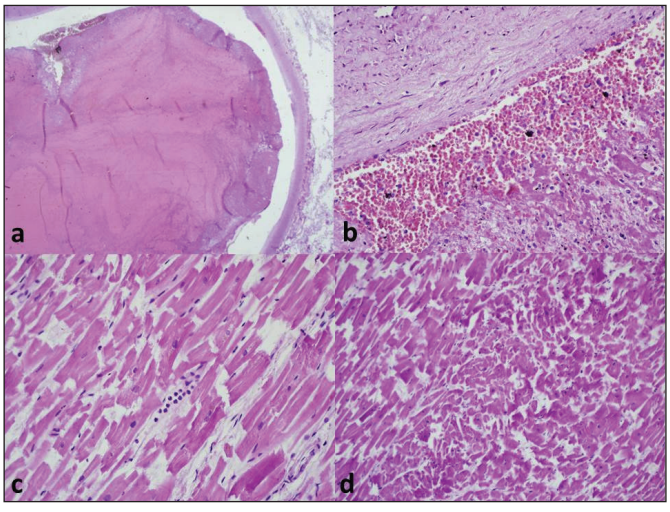

Figure 2. a-b) Phase 1 of the chronological evolution of the process of transformation of thrombo-emboli. No observable reaction between the endothelium of the vessel and the thrombus; erythrocytes conserved and agglomerated; white cells with initial phenomena of pyknosis and monocytes with enlarged nuclei (H&E, 4x, 10x). c-d) "Disarray" of the cardiac muscle cells associated to inter-myofibrillar edema and minimal focal endovascular granulocyte penetration (H&E, 40x, 20x).

Another study, conducted by Smith *et al.* on the records of the Scoliosis Research Society, examined data from 108,419 surgical procedures, including the three most common spinal procedures (Lumbar Discectomy, Anterior Cervical Discectomy and Fusion, Lumbar Stenosis Decompression). The authors reported an overall prevalence of 0.14% of post-operative PE; on excluding patients with traumas or metastatic tumors, the prevalence fell to 0.089% [15].

A study conducted by Masuda *et al.* on data from over 47,000 patients (with an estimated prevalence of PE of 0.105%) investigated the factors responsible for the onset of pulmonary embolism after spinal surgery. It emerged that patients at highest risk of thrombotic phenomena in spinal surgery were those of more advanced age (>70 years), those who underwent prolonged anesthesia (>360 minutes) and those who had suffered spinal trauma [16]. To these factors, we may add: greater complexity of the operation performed (correlated with duration), the number of vertebrae involved, and the amount of blood lost.

Moreover, in spinal surgery it has been shown that PE is much more common when procedures are carried out through an anterior, rather than posterior, approach [17-19]. In one group of patients with deformity of the thoracolumbar spine, the overall incidence of PE was 2.2%; however, in those who had undergone surgery through an anterior approach the incidence was higher. In another study, the incidence of PE was 0.65% after posterior surgery, and 2.4% after anterior surgery. This difference may be explained by the fact that the vascular structures are retracted and manipulated during anterior surgery, which might cause endothelial damage and favor the development of thrombotic formations [19].

Regarding the time of onset of thrombotic phenomena following surgical operations, the diagnosis of DVT or PE is generally made weeks after the operation [14]. By contrast, the detection of signs of DVT in the immediate post-operative period or the manifestation of a massive and rapidly fatal PE are rarer phenomena. Indeed, it should be borne in mind that post-surgical immobilization, and therefore venous stasis, can contribute to the pathogenesis of thrombotic phenomena.

For what concerns early PE after spinal surgery, Meng *et al.* reported the case of a suspected pulmonary embolism following a procedure to correct idiopathic scoliosis in an adolescent without evident risk factors; about 2 hours after the procedure, the patient began to suffer from chest pain, dyspnea and reduced blood pressure [20].

A case of fatal PE that occurred early after spinal surgery was reported by Tomar *et al.* in a patient with L4-L5 spondylolisthesis and prolapse of the L5-S1 intervertebral disc who had undergone discectomy and laminectomy through a posterior approach. In this case, the PE appeared about an hour after the patient, who

was conscious and vigilant, had been transferred to the intensive care unit; in about 2 hours, she died, despite thrombolysis and resuscitation maneuvers [21].

In the case that we present here, the patient suffered a fatal pulmonary embolism immediately after thoracolumbar vertebral arthrodesis; progressive bradycardia led to asystole and death within about 15 minutes, which did not allow physicians to entertain the diagnostic suspicion of pulmonary embolism or to implement the investigations required to diagnose or treat the pathology. In the case in point, therefore, the thrombo-embolism was manifested very early and the fatal event played out in such a short time that no adequate diagnostic-therapeutic action could be undertaken. Indeed, it must be borne in mind that the progressive deterioration of the vital parameters was noted when the patient was being roused from anesthesia and had not yet regained consciousness nor achieved clinical stability. It was not therefore possible to detect some of the typical symptoms commonly associated with PE, such as dyspnea or chest pain, but only severe bradycardia, which resulted in cardio-circulatory arrest. The cause of death was therefore not clinically clarified, and anesthesia-related problems were suspected. In this case, the diagnosis of fatal embolism was made on autopsy. Indeed, post-mortem examination revealed the presence of a massive thromboembolism which occluded the pulmonary arteries bilaterally down to the small intra-parenchymal branches. The emboli were compact, opaque, dark grayish-red in color and inelastic. The macroscopic features of the thromboembolic formations observed were compatible with the recent onset of the phenomenon. This hypothesis was subsequently confirmed by histological examination; microscopic analysis through the histological determination of the age of the thromboembolic formations studied established that these formations fell within phase 1 of the chronological evolution of the process of transformation of thrombo-emboli. As thromboembolism constitutes a vital phenomenon, the organism implements a series of reactions to the formation and mobilization of the thrombo-embolus, including the intervention of several types of cells and temporal morphological modifications of the thromboembolic formations themselves. As the formation, organization and decomposition of the thrombus is a process that can be studied from the temporal standpoint, its chronology can be assessed in such a way as to establish the causal relationship between the PE and death. Thromboembolic formations that fall within phase 1 are characterized by the following features: no observable reaction between the endothelium of the vessel and the thrombus; erythrocytes conserved and agglomerated; white cells with initial phenomena of pyknosis, and monocytes with enlarged nuclei [9].

The set of morphological and microscopic features of the thromboembolic formations found during autopsy indicated the recent onset of a massive pulmonary thromboembolism, which was defined as an early complication of the spinal surgery that the patient had undergone. Moreover, histological analysis of the samples taken during autopsy revealed indirect signs of the massive pulmonary embolism that caused the patient's death. These consisted of alterations attributable to acute heart failure with very acute and terminal cardiac hypoxia (acute pulmonary edema with initial pulmonary emphysema and "disarray" of the muscle cells associated to inter-myofibrillar edema and minimal focal endovascular granulocyte penetration).

Subsequent section of the venous system during post-mortem examination did not reveal the presence of residual thrombotic material adherent to the venous walls; it was not therefore possible to identify the site of origin of the pulmonary embolism. Nevertheless, we cannot exclude the possibility that the clot broke away from a thrombotic formation that had developed within the venous system, in that thrombotic material may undergo dislodgement and embolization without leaving macroscopically detectable traces [22].

Analysis of the patient's clinical history revealed that his worsening scoliosis had caused paraparesis, which had prevented him from standing upright for about a month. Immobility is a known risk factor for DVT. Preoperative objective examination did not reveal any clinical signs of thrombosis (thus, the DVT, if already present, was asymptomatic); however, no Doppler ultrasound (DUS) study of the lower limbs was carried out before the surgical procedure. Thus, it cannot be ascertained whether the patient already had some degree of DVT before surgery. If he did, it can be hypothesized that these thrombotic formations were of recent origin, given the fact that no residual thrombotic material was found in the venous system during autopsy, and considering the low degree of adhesion to the vessel wall, which enabled the thrombus to detach completely and to migrate, causing massive occlusion of the pulmonary circulation.

In the case presented, in the pathogenesis of the thrombosis and subsequent massive embolism, we cannot rule out the possibility that the formation of the thrombus (and its subsequent embolization) took place during the surgical operation, given the considerable duration and high complexity of the procedure. Indeed, the patient was anesthetized for about 11 hours. Moreover, there is evidence to suggest that the prone position of the patient during spinal surgery can, by reducing blood flow to the extremities, facilitate the onset of thrombotic phenomena [23]. In addition, it seems that the position of the patient can give rise to continuous pressure in the inguinal region, thereby reducing blood flow and favoring the formation of thrombi; in this regard, the left iliac vein is a vulnerable site owing to its anatomical relationship (iliac compression syndrome) [14].

With regard to the risk factors connected with the thoracolumbar arthrodesis procedure performed, some considerations should be made. Although operations carried out by means of an anterior approach are associated with a higher risk of thromboembolic phenomena, owing to the greater endothelial damage caused by manipulation of the vessels, there is evidence to suggest that the use of spinal implants in degenerative pathologies of the lumbar spine may give rise to micro-emboli of fat and bone marrow; these may, in themselves, cause obstruction or become enlarged through the addition of blood clots. [24] In the case under examination, the surgical operation was particularly complex and lengthy, involving a large number of vertebrae from T4 to L4, with the application of titanium plates fixed in the sagittal directions, peduncular screws and clamps. Cruentation of the bony plane was carried out and bone bracts taken from the operating field were applied; moreover, intraoperative bleeding was profuse (about 900 ml).

Although the pathogenesis of the phenomenon is not completely clear, it may be hypothesized that several factors concurred in the massive and early genesis of the fatal thromboembolism; the paraparesis and consequent venous stasis that had been ongoing for about a month certainly constituted a risk factor for DVT; the same is also true of the prolonged anesthesia time, the complexity of the procedure and the patient's position during the operation, which was maintained for 11 hours.

With regard to strategies of prevention, in the case described no form of chemical or mechanical prophylaxis was undertaken prior to surgery; LMWH was to have been administered two hours after the procedure, i.e. in the perioperative phase. In general, in spinal surgery there are no peremptory guidelines that lay down the timing or modalities of strategies to prevent the onset of thromboembolic phenomena. Indeed, in this type of surgery, heavy bleeding may occur, which may have devastating neurological consequences (above all, subdural hematoma). The literature does not report sufficient evidence concerning the risk-benefit ratio of pharmacological anti-thromboembolic prophylaxis, the ideal strategy (whether chemical or physical) and the optimal timing of treatment initiation. Many authors do not recommend anticoagulant prophylaxis in spinal surgery, in that the neurological damage caused by possible hemorrhage at these surgical sites may outweigh the benefit yielded by the reduction of the risk of DVT [16, 24].

Moreover, most evidence suggests that prophylaxis, when necessary, should be implemented after, rather than before, the surgical operation. The guidelines of the American College of Chest Physicians suggest that, in patients undergoing spinal surgery who have additional risk factors, such as advanced age, tumors, neurological impairment, or previous episodes of venous thromboembolism (VTE), or those undergoing surgery by means of an anterior approach, one of the following prophylactic strategies should be adopted: post-operative low-dose unfractionated heparin (LDUH) (Grade 1B), post-operative low-molecular-weight heparin (LMWH) (Grade 1B) or an optimal use of peri-operative intermittent pneumatic compression (IPC) [25].

For what concerns methods of post-surgical screening in order to identify patients with DVT, and therefore at risk of PE, a study conducted by Ikeda *et al.* suggested that perioperative DUS to detect DVT following spinal surgery might usefully be undertaken in female patients, non-ambulatory, and those with more elevated preoperative serum D-dimer levels [26]. Some authors suggest that pharmacological prophylaxis is probably not indicated if surgical procedures are performed through a posterior approach, given the rarity of thromboembolic complications, while it may have a role to play if an anterior approach is adopted [18].

The case reported here shows that PE may occur very early and be rapidly fatal even in spinal operations performed through the posterior approach; it is therefore important to draw up efficacious and timely strategies of prevention. Indeed, it must be borne in mind that most patients with post-operative PE die within an hour of the onset of symptoms [27]. Moreover, even if the diagnosis of PE were reached rapidly, any treatment would be complicated by the fact that thrombolytic therapy is not indicated in the first 14 days after a surgical operation, in that it may lead to major bleeding and death [20].

In the case presented here, only by means of thorough post-mortem examination and subsequent histological analyses was it possible to identify the cause of death. Indeed, the rapidity with which the patient went into fatal cardiac arrest prevented any post-operative diagnostic examinations from being carried out. From the medico-legal standpoint, analysis of the clinical events and scrutiny of the guidelines on thromboembolic prophylaxis in spinal surgery enable us to exonerate the operators who performed the surgical operation from any professional responsibility. Specifically, the current lack of precise scientific indications concerning strategies for the prevention of thromboembolic phenomena in vertebral surgery did not enable the operators to determine whether prophylaxis should be undertaken earlier. Thus, the decision to initiate prophylaxis in the perioperative phase (2 hours after the operation) could be considered appropriate and in line with current recommendations.

The present report describes a rare case of fatal massive pulmonary embolism which arose acutely in the immediate post-operative phase following spinal surgery carried out through the posterior approach. Although the incidence of PE is low in spinal surgery, especially when a posterior approach is adopted, the management of antithrombotic prophylaxis should include careful assessment of the relative thrombotic and hemorrhagic risks, in addition to the thorough study of individual

risk factors. Moreover, the timing and the strategies of prophylaxis (to date chiefly oriented to the post-operative phase) should also be considered in the preoperative phase, since, as is illustrated by the case presented here, the embolism may arise suddenly and rapidly become fatal even before it can be diagnosed and treated.

Conflict of interest. The authors declare that there is no conflict of interest.

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