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RESEARCH ARTICLE

FUNGAL ORIGIN OF IN SITU PULMONARY ARTERY THROMBOSIS: A CASE REPORT

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Abstract

When filling defects are found on CTA, they are almost universally assumed to be emboli from a peripheral deep vein thrombosis. However, new studies have led to the theory that localized inflammation, endothelial cell damage, and disruption of blood flow cause de novo formation of clots within the pulmonary artery or in situ thrombosis. Fungal origin of pulmonary embolism is rare. We report the case of a 31-year-old man previously treated for tuberculosis. He was admitted with haemoptysis and a chest CT scan revealed an obstruction of the right upper pulmonary artery. He was initially diagnosed as a pulmonary embolism of cruoric origin and anticoagulant treatment was given. But the patient had massive hemoptysis a few days later. Aspergillosis serology was positive and the diagnosis of pulmonary aspergillosis complicated by pulmonary embolism in situ was retained. Antifungal treatment was started with good improvement and cessation of the haemoptysis.

Introduction:-

Pulmonary embolism (PE) is defined as anything that obstructs the pulmonary arteries (clot, tumor, fat, or air). Most commonly in clinical practice, PE refers to a blood clot that lodges into pulmonary circulation from peripheral deep vein thrombosis (DVT) [1]. However, new studies have led to the theory that localized inflammation, endothelial cell damage, and disruption of blood flow cause de novo formation of clots within the pulmonary artery or in situ thrombosis [2].Fungal origin is a rare condition. There were only some sporadic cases of pulmonary aspergillosis (PA) with in situ pulmonary artery thrombosis (PAT) reported [3-4]. Here we present a case of PA complicated by in situ PAT in a young man.

Case report:

A 31-year-old male, who got lung tuberculosis 4 years ago. He was admitted to our hospital with moderate haemoptysis for a week. On admission, her blood pressure was 100/50 mmHg, her pulse rate was 91 beats/min and oxygen saturation 94% on room air and the pleuropulmonary examination was unremarkable. Laboratory tests revealed a haemoglobin count of 8,6 g/dl, white blood cell count of 11530 and a CRP of 98 mg/l. Contrast enhanced CT-chest showed nodules and micronodulars with bronchial disposition, excavated lesion of the right fowler and bronchiectasis. CT scan detected a mosaic image in the left basal lung, as well as a thrombus in the right upper lobar pulmonary artery (figure 1). Peripheral DVT is not detected on ultrasound of the extremities. Sputum smear for mycobacterial PCR (XpertMTb/RIF) was negative. For a history of tuberculosis, we completed with aspergillus serology which was positif.

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He was diagnosed as pulmonary embolism and treated with acenocoumarol. Five days later, the patient still had hemoptysis. In addition to anticoagulants, an antifungal treatment with voriconazole was added.Therefore, he was diagnosed as in-situ pulmonary artery thrombosis (PAT) instead of pulmonary thromboembolism (PTE) because of the close relationship of artery and lung parenchyma lesions. Lung scintigraphy showed in the right lung a hypoperfusion of almost the lung parenchyma, more marked in the upper and middle lobe. In addition, a systematized perfusion defect in front of the anterior and upper lingual segments of the left upper lobe had been detected (figure 2).

Coming days, the patient had an episode of heavy hemoptysis. Laboratory tests revealed a haemoglobin count of 5.3 g/dl and INR = 7.13. He was transfused with 2 red blood cells with control haemoglobin at 10.5 g/dl. Anti-coagulation was stopped for persistent hemoptysis and anti-fungal therapy was continued. The patient improved after several weeks and continued oral itraconzole after discharging.

Six months later, the patient had no more haemoptysis. A control angioscan showed that the thrombus was still present in the right upper pulmonary artery with regression of the excavated lesion and nodular images (figure 3). The aspergillus serology was still positive, which confirms more a fungal origin of the thrombus.

Our patient was referred to thoracic surgery for a right upper lobectomy. A thoracic angioscan was redone showing still the persistence of the endoluminal material on the right without its demonstration on the left. However, a Lung scintigraphy still showed defects on the right but also on the left (same results as the first scintigraphy). A cruoricorigin was unlikely given the good improvement of the patient under antifungal treatment. Therefore the surgical indication was not retained; either because of the risk of bleeding or because of the risk of functional aggravation given that the contralateral side is not well perfused.

Discussion:-

PTE is caused by thrombi detached from deep veins of lower extremities. However, following chest trauma, pulmonary diseases and systemic inflammatory and immunological disorders, pulmonary thrombi may be generated in situ. The currently known mechanism underlying in-situ pulmonary artery thrombosis (PAT) originates from the local hypoxic and inflammatory milieu, which then induces pulmonary vascular endothelial cell dysfunctions [5].

In up to 57% of people diagnosed with PE, DVT may be absent. A high prevalence of isolated PE may suggest localized thrombus formation in the pulmonary arteries instead of embolization from peripheral clots [2]. Tuberculosis-destroyed lung was the most common underlying condition in Korean PAT patients, followed by pulmonary artery stump after lung resection [6].

Septic embolism can develop when fragments of thrombus include micro-organisms. These organisms are typically bacteria or, less commonly, fungi or parasites [7]. Septic pulmonary embolisation (SPE) is a rare but wellrecognised problem in the setting of right-sided endocarditis and septic thrombophlebitis from the jugular, dental or pelvic region and infected central venous catheters [8]. Fungal septic pulmonary embolism is rare. In a huge series of post-mortem examinations in Japan, SPE was found in 2.2% of 11,367 cases of ‘‘critical’’ pulmonary embolism. Infectious endocarditis was responsible for 11% of these cases of SPE. Surprisingly, fungal emboli (from Aspergillus 14.6%, Mucor 12.6% or Candida 7.3%) were found more frequently than bacterial [9].

In our case, the main questions were: Is it a PTE or in-situ PAT? Was the nature of the thrombus cruoric or fungal? Should we treat with anticoagulant, anti-fungal or both?

PTE is distinguished from in-situ PAT by computed tomography pulmonary angiography (CTPA) features. In PTE, filling defects usually can be observed in bilateral pulmonary artery, whereas in-situ thrombus formation happens single often. In patients with PAT, it displays mural thrombus with obtuse angles with vessel wall, but not common in patients with acute PTE [10]. Zhi-Bo Liu et al reported three cases of PA with in situ PAT. Radiology showed that the embolism was single and located in main pulmonary artery adjunct to the lung lesions, distal arteries were unobstructed, the lesions of pulmonary parenchyma and artery fit together, consistent with in-situ PAT.

Aspergillus is widespread in the environment and causes a variety of tracheobronchial and pulmonary disorders, depending upon the alterations of immune status of hosts [10]. It may cause a broad spectrum of disease in the human host, ranging from hypersensitivity reactions to direct angioinvasion.

In angioinvasion pulmonary aspergillosis, the characteristic pathological findings are: blood vessel invasion, thrombo-mycotic occlusion and hemorrhagic infarctions. In vivo experiment, Aspergillus hyphae stimulated tissue factor activity in vascular endothelial cell, revealing the potential mechanism of angioinvasion and thrombosis. In addition, in patients with underlying pulmonary diseases, because of the pulmonary vascular remodeling, blood flow vortex is another risk factor of thrombosis [10].

We retained in our patient an in situ PAT for these reasons: Aspergillus has the characteristic of thromo-mycotic occlusion. Aspergilloma and pulmonary artery affected fit together. Peripheral DVT is not detected on ultrasound of the extremities.

There were only some sporadic cases of PA with in situ PAT reported [3-4]. Thrombi in these cases were fungal thrombi proven by autopsy. Antifungal therapy was diverse which includes: triazole, Amphotericin B, and caspofungin. No matter for fungal thrombi or PA, anti-fungal therapy is essential.Zhi-Bo Liu et al reported three cases: two patients received anti-fungal therapy in time and recovered. But, one patient suffered subacute invasive pulmonary aspergillosis for 5 months speculated by previous CTs, without standard anti-fungal therapy, Aspergillus spoiled vascular and fatal hemoptysis as a severe complication resulted in poor prognosis.For patients with angioinvasion, early diagnosis and antifungal treatment are essential. Voriconazole is approved for first-line therapy in invasive aspergillosis according to guidelines; combination of anti-fungal drugs may help in immunocompromised or critical-ill patients [10]. The necessary of anti-coagulation therapy for in situ PAT patients is unclear. Anti-coagulation should be personalized in PA with in situ PAT. According to the recommendations of the American College of Chest Physicians guideline of antithrombotic therapy for venous thromboembolism (VTE) disease, bleeding estimation should be made in different anti-coagulation individuals [11]. InZhi-Bo Liu et al study, one patient was in high risk of bleeding with more than two bleeding risk factors, and they got cessation of anti-coagulation after occurrence of hemoptysis. Anti-coagulation helped the improvement in one case while aggravated hemoptysis in other one.

In our case, though there was no histopathology evidence, we supposed these thrombotic events were attributed to PAT according to clinical and radiological features. We started anticoagulation with antifungal treatment. Few days later, anticoagulation was stopped after a massive haemoptysis. Only the antifungal treatment helped improvement. So, fungal origin of the thrombus is retained.

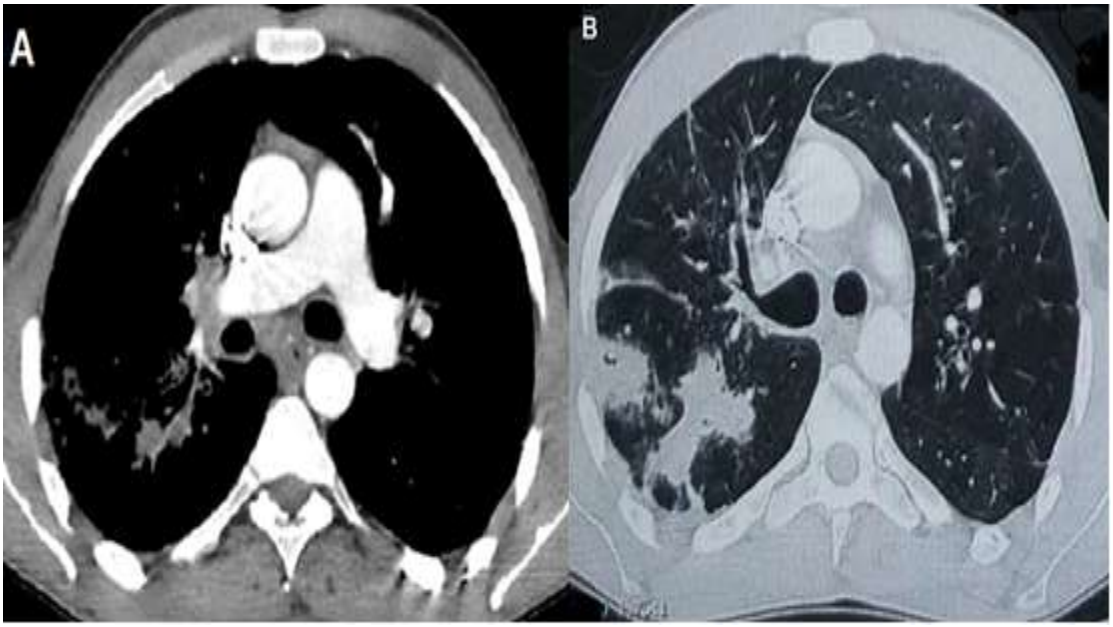

Figure 1:- (A) Mediastinal window and (B) parenchymal window images of CT scan schowinga thrombus in the right upper lobar pulmonary artery and excavated lesion of the right fowler.

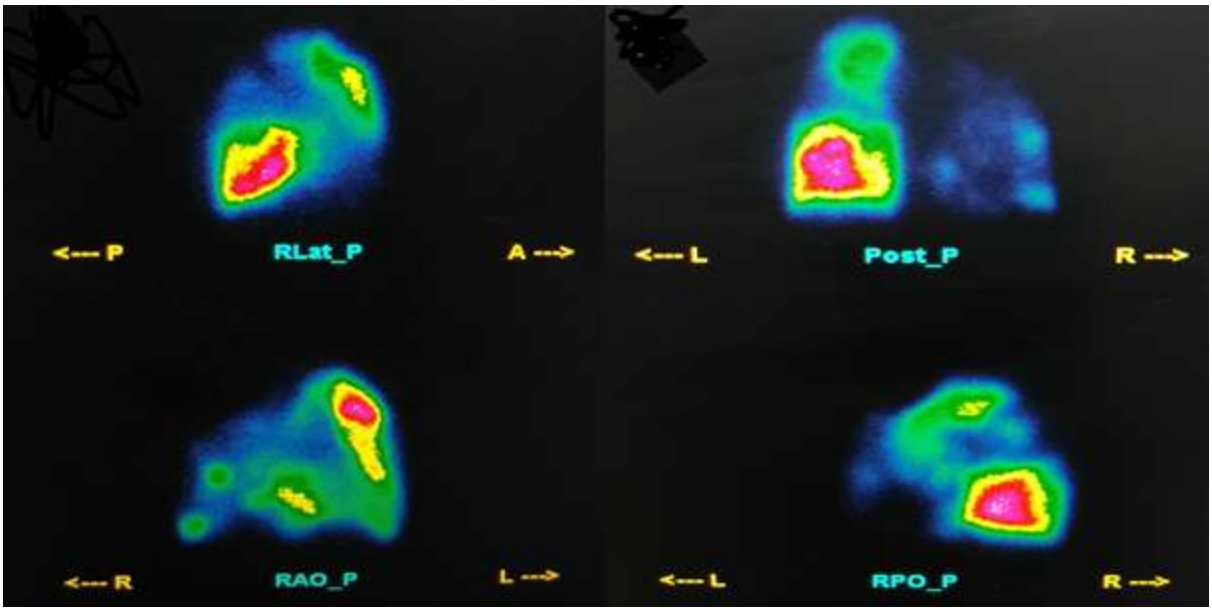

Figure 2:- Images of lung scintigraphy showing in the right lung a hypoperfusion of almost the lung parenchyma, more marked in the upper and middle lobe with a systematized perfusion defect in front of the anterior and upper lingual segments of the left upper lobe.

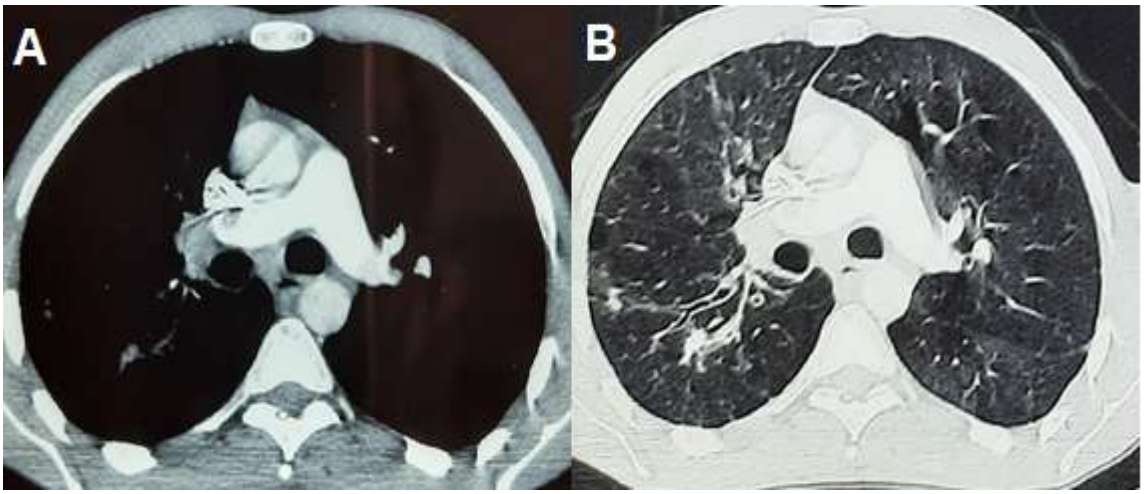

Figure 3:- (A) Mediastinal window and (B) parenchymal window images of CT scan after six schowing that the thrombus was still present in the right upper pulmonary artery with regression of the excavated lesion and nodular images.

Conclusion:-

In summary, when the lesions of pulmonary parenchymal and artery fit together, differential diagnosis of PTE and PAT should be conducted. It is important to notice the correlation between PA and in situ PAT rather than simply PTE due to the therapy is more than anti-thromboembolism. To avoid fatal hemoptysis and slow down vascular invasion, an antifungaltreatment is essential. Anti-coagulation depends on the riskbenefit ratio.

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