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Case Report

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Persistent hemothoraxafter video-assisted thoracoscopic surgery secondary to factor V deficiency

Abstract

Coagulation disorders should be considered in unusual post-surgical bleeding, especial in low-complicated procedures even the platelet count and coagulation tests are within normal ranges.

Case presentation: Male patient receive video-assisted thoracoscopic surgery (VATS) due to pleural effusion. In his clinical course, unusual bleeding and persistent and recurrent hemothorax was occurred. Coagulation Factor V disorder and resistance of the activated protein C is diagnosed. Further surgeries and blood product transfusions, tranexamic acid to control the bleeding were required. The final clinical outcome was satisfactory.

Conclusion: Coagulation Factor V deficiency is an uncommon cause of post-operative bleeding and should be considered for in all patients with abnormal bleeding.

Keywords: hemothorax, video-assisted thoracoscopic surgery, abnormal bleeding, factor V

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Introduction

Video-assisted thoracoscopic surgery (VATS) is a surgical procedure with low morbidity or mortality rate in thoracic surgery; even in more complicated lung resection is required. Consequently, in simple procedures, such as pleural biopsies or diagnostic pleuroscopy, the complication rate is very low. Evidence based studies have conclude that patients with limited pulmonary function have better outcome under VATS compared with traditional exploratory thoracotomy.[1]

The incidence of severe intraoperative complications is similar between VATS group and thoracotomy control (1.57% vs. 1.44%). Severe complications are related to major iatrogenic pulmonary vessel injury and most of these complications occurred during upper lobectomy.[2] Hematologic studies reported Factor V deficiency, resistance to activated Protein C, which is associated with moderate to severe hemorrhages in a prevalence of 1 in 1,000,000 of the population.[3] The presence of post-operative bleeding should be alerted by physicians that a coagulation disorder may persist despite normal pre-operative coagulation profile, especially if during surgery no vascular lesion was documented.

Case presentation

A 51-year-old Hispanic male with past medical history of Diabetes and Hypertension, who was admitted in October 2016. He had 1 month history of generalized malaise, fever and a 1 week history of productive cough of white sputum. He is referred to our center with right pleural effusion diagnosed by chest x-ray. His vital signs revealed a temperature of 37°C, pulse 88/min, respiratory rate 24/min, blood pressure of 120/70 mm Hg. His weight is 122.7kg, and height is 1.70m. (BMI of 42.46). On physical examinations, this patient was morbid obesity. Decreasing breath sounds and fremitus with dullness in percussion in one-third of the right lower chest. Mild rales and no wheezing were also noted. The other examinations were within normal ranges.

Laboratory results were Hemoglobin 15.3 g/ml, Hematocrit 44.5%, White cell count 11.08 mil/ul, Platelets 322 mil/ul, Prothrombin time (PT) 12.9 sec., Thromboplastin partial time (PTT) 28.2 sec. INR 1.26, Glucose 333 mgs/ml.CR 0.7 mgs/dl and BUN 11 mgs/dl. His blood type is A Rh (+). The initial chest X-ray revealed loss of lung volume with a right moderate pleural effusion and pneumo-atelectatic infiltration at right lung. A contrasted chest CT confirmed the right side moderate lobulated effusion with a peripheral pseudo-cavitation of the right lower lobe without enhancement of the pleura. No pulmonary masses, cardiomegaly, or mediastinal adenopathy were noted (Figure 1).

The patient is admitted with a diagnosis of:

a) Complicated right pleural effusion, suspected with pulmonary tuberculosis

b) Diabetes Mellitus,

c) Hypertension and

d) Morbid obesity.

Due to the lobulated effusion observed in the computed tomography. The VATS was applied for the diagnosis and the release of adhesions. The patient is taken to the operating room where the procedure is done, revealing a mildly thickened, hyperemic parietal pleura, with multiple pleuro-pulmonary adhesions easy to liberate1200 cc of citrine pleural fluid was drained and sent to pathology and microbiologic studies. Pathology of the pleural biopsy revealed a non-specific chronic inflammatory process and smears and cultures were all negative. On post-operative day #1, the chest tube drained 800cc of bloody secretions and his chest X Ray (CXR) revealed total pulmonary re-expansion with air-fluid levels. At 72 hours post-op, the CXR showed a right apical and lateral density measuring 12 cm in diameter with partial lung collapse. On day #5, he is taken to the operating room again and a limited right thoracotomy is done. Abundant clots at the right base and a retained apico-lateral right hemothorax at the site

were found .The biopsy was performed. Parietal pleural decortication with pleural cavity washings were done, and 2 units of pack red blood cell were transfused and one more unit during post-operative stage because his hemoglobin was fell to 8mgs/dl. He was presented with wound infection and radiologic worsening with persistent opacities that continuous chest tube hemorrhagic drainage was required. His coagulation profile and platelet counts remained within normal ranges. (Table 1). Hematology consultation is requested and the coagulation disorder secondary to Factor V Leiden deficiency and resistance to activated protein C were diagnosed. (Table 2) Starting Tranexamic acid administration are recommended. 2 vials (100 mg/ml) in 250cc of normal saline solution were administered in 30 minutes STAT and repeated every 6 hours. The bleeding was controlled after the third dose and a third surgical revision was performed. A new chest tube was placed. His post-operative course is satisfactory without further bleeding. Complete re-expansion of the right lung was noted (Figure 2) and good control of his diabetes was also obtained. Pathology of the pleural material reported chronic paquipleuritis and subpleural fibrosis.

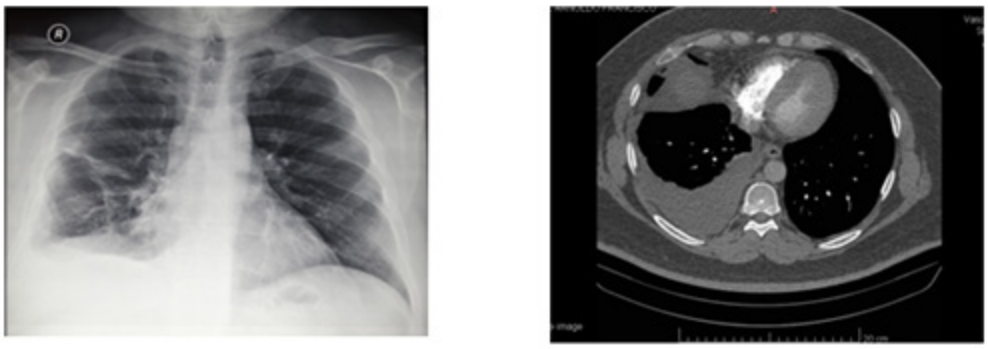

Figure 1 Chest X-ray and Chest CT on admission (10/10/2016).

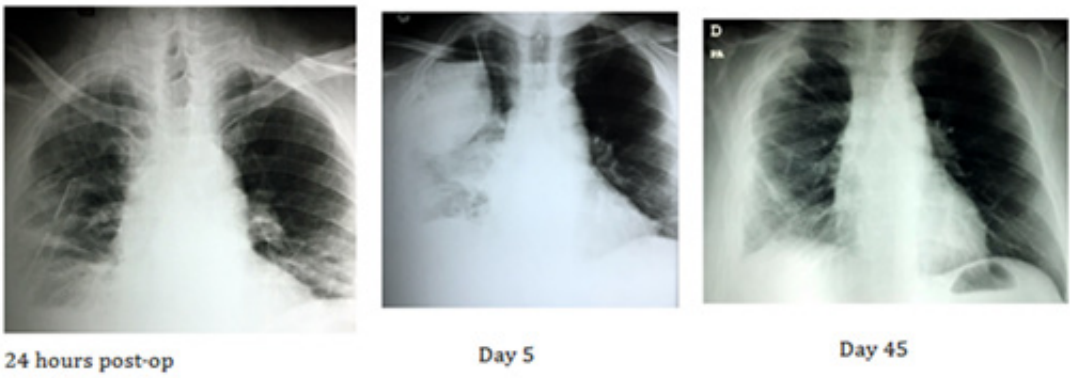

Figure 2 Post-operative radiologic course.

Table 1 Laboratory results

	Hbg/ml	Hct %	Platelets mil/Ul	Transfusions units	PT sec.	aPTT sec.	INR
10.10.16	15.3	44.5	322		12.9	28.2	1.26
15.10.16	12.4	37.6	402		11.1	31.2	0.75
17.10.16	8	24.2	411	2	11.1	30.1	0.75
19.10.16	9.6	29.3	476				
20.10.16	8.9	26.7	517				
22.10.16	9.4	28.6	691	1	12	26.5	0.85
24.10.16	10.4	32.2	709				
26.10.16	12	36.1	540				
10.11.16	12.9	40.4	289		12.3	32.2	0.88

Hb: Hemoglobin; Hct: Hematocrit; PT: Prothrombin Time; aPTT: Activated partial thromboplastin time; INR: International normalized Ratio

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Table 2 Coagulation profile results

Exam		Results	Measure	Normal Value
	TP	12.5	Sec.	10.2
Prothrombin Time (PT)	% Activity	81	%	1
	I.N.R.	1.23		1
Partial Tromboplastina Time (aPTT)		29	Sec.	22 - 34
Fibrinogen		833	mg/ml	308 - 613
Protein "C"		121.9	%	72 - 160
Protein "S"		137.28	%	60 - 150
Antitrombin III		103	%	83 - 128
Factor V of Leiden		1.96		2.61 - 3.32
Factor Von Willebrand		223.5	%	
	Quantification of IgA	6.4	g/L	0.7 - 4.0
Immunoglogulins (G.M.A)	Quantification of IgG	11.5	g/L	16-Jul
	Quantification of IgM	1.2	g/L	0.4 - 2.3
Immunoglobulin IgE		266.9	UI/mL	< 100

Discussion

The prevention of post-operative complications depends on the duration of the procedure, grade of invasiveness and the precise indication of the procedure. Video-assisted thoracoscopic surgery (VATS) has become a standard therapeutic modality for spontaneous pneumothorax, diagnostic biopsies for multiple pulmonary and pleural diseases,[4,5] management of complicated pleural effusions and, for major resections of pulmonary masses with a much lower rate of complications than open thoracotomy.[6,7] VATS bleeding complications has been reported as low as 0.6%, the majority of which are mild and " in layers" to 4.3% in major resections due to vascular injuries in 50% of the cases.[8] In the actual case, VATS was performed for a pleural effusion drainage and biopsy with a presumptive diagnosis of pleural tuberculosis, having no trans-operative complications. Prolong hospitalization course was characterized by unusual bleeding through the chest tube requiring further surgeries to evaluate and control the cause of the bleeding. A work-up for coagulation disorders was performed and revealed a disorder of Factor V deficiency and resistance to activated Protein C.

Coagulation Factor V which is synthesized by the liver and possibly by megakaryocytes is present in serum as a single-chain polypeptide (80%) and in platelet a-granules (20%). Factor V plays an important role in the anticoagulant pathway because its inactivated form participates in the inactivation of factor VIII via activated protein C (APC). It has a dual action as a pro-coagulant, with mutations, predisposing to thrombosis[3] and as an anticoagulant, with its deficiency being associated to variable severity of bleeding tendencies depending on the Factor V level.[9] Factor V deficiencies are classified as

1) Congenital (Owren parahemophilia),
2) Combined Factor V and Factor VIII deficiency,
3) Acquired due to severe hepatic disease or disseminated intravascular coagulopathy and more commonly, secondary to the development of Factor V inhibitors, i.e. antibodies that bind to Factor V and promote its degradation and/or block its activity, and
4) Platelet Factor V deficiency.[9]

In many countries were consanguineous marriages occur, the congenital form is genetically transmitted as an autonomic recessive pattern, as seen in Iran, where this coagulation disorder occurs 10 times that seen in the western civilization[10] but has also been reported in Italy, USA and Canada.[9] Acquired deficiency associated with Factor V inhibition has been reported in hepatic dysfunction,[11] antibiotics such as cefuroxime or metronidazole,[12] b-lactamase production,[13] and autoimmune diseases are the most common etiologies and, the excessive administration of protamine[14] and tuberculosis[15] being less frequent. The most common symptoms associated with Factor V deficiency are bleeding from mucous membranes (e.g. epistaxis, hematuria, menorrhagia in females)and post-traumatic bleeding following surgery or delivery, which occur in approximately half of all Factor V-deficient individuals.[9,11] Hemarthroses and muscle hematomas are present in only one quarter of Factor V-deficient patients, and severe bleeding manifestations (e.g. pulmonary, intracranial, or gastro-intestinal hemorrhages)are rare and confined to patients with undetectable Factor Vlevels.[9,13,16] Diagnosis requires the measurement of plasma Factor V antigen and/or activity levels.[17] In our case, pleural bleeding post VATS biopsy of a patient with pleural disease with a negative history of previous bleedings, hepatic dysfunction or autoimmune disease.

The therapeutic strategies are focused on

a) Control of the hemorrhage with the administration of fresh frozen plasma, platelet transfusions, prothrombin complex concentrates and recombinant Factor VII and,
b) Eradication of antibodies, which has become the gold standard, with the use of systemic steroids, cyclophosphamide, rituximab, IV immunoglobulin, plasmapheresis and immune-absorption.[11-18] In this actual case, the patient received tranexamic acid, which is an anti-fibrinolysis complex with a potent inhibitory effect on

the activation of fibrinolysis and, with higher concentrations, a non-competitive inhibitor of plasmin. Its use has been studied in a systematic review in the Cochrane library with more than 3000 patients in the prevention of post-partum hemorrhage,[19] intractable hematuria in polycystic renal disease,[20] for the reduction of blood transfusions during By-pass coronary surgery[21] and poly-trauma patients.[22]

Conclusion

The complex pathophysiology of congenital Factor V deficiency is just starting to be unraveled since it is uncommon and the prevalence is likely to be underestimated because mild cases are usually undetected. Given that the Factor V levels required for minimal hemostasis is extremely low, subtle differences in plasma and/or platelet Factor V levels may be crucial to clinical outcome. It should be suspected in patients with un-explained bleeding complications with the usual coagulation profile work-up and a positive family history for bleeding disorders.

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None.

Conflicts of interest

We declare that we have no conflict of interest associated with this publication.

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