Journal of
Pulmonary & Respiratory Medicine

Giraldo et al., J Pulm Respir Med 2015, 5:6
DOI: 10.4172/2161-105X.1000300

Case Report Open Access

Protective Mechanical Ventilation and Tracheal Gas Insufflation in a Patient with Massive Pulmonary Embolism Caused by the Combined Deficiency of Proteins C and S and Antithrombin III

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Abstract

During pulmonary embolism, the physiology of the ventilation and the perfusion is damaged. A sudden massive increase of the intrapulmonary shunt might result if the clinical setting is not adequately implemented to regulate the inflammatory process. For this reason, the protection of the ventilation and the tracheal gas insufflation are useful tools in modulating the injury, and the hypercoagulability caused by protein C and S and the deficiency of antithrombin III. All caused by the damage of the endothelial barrier, therefore gives origin to interstitial leakage, tissue damage, inflammation, and apoptosis.

Keywords: Condensation; Swirl; Tracheal gas insufflation; Serine proteases; Glycoprotein; Protease activated receptor 1; Protein C; Protein S; Antithrombin III; Thrombin/thrombomodulin complex

Case Report

We present the case of a 17-year-old female patient who is submitted to ICU by the present clinical setting of 24 hours of evolution, consisting of dyspnea, pleuritic pain and oxygenation alteration, not history of importance. Incoming blood pressure 140/100, pulse 145 per minute, breath frequencie 36 per minute, saturation 76% FlO2 (fraction inspiration 02) 50% normal temperature, Glasgow 15/15. As important to the review physical Gallop S3 at the expense of right cavities with reinforcement of S2 pulmonary focus, impulse sternal left side and blow diastolic tricuspid. Rx thorax evidence opacity 2/3 low of the right lung, pulmonary precapillary hypertension, arterial blood gas PaFl02 income of 88 with arterial oxygen pressure of 44 mm Hg, metabolic acidosis with mild consumption base excess and blood pressure of Co_2 33 mm Hg. Alveolar-arterial gradient of oxygen in 179, lactate at 2.9. The EKG documented sinus tachycardia 150 per minute, complex of Mc Ginn White; S v5 and v6 (Figure 1), count of income without Leukocytosis or neutrophils high, Hemoglobin 10 gr/dl and 180,000 platelets, time prothrombin in 15 sec. and thromboplastin time in 33 sec. Orotracheal intubation was performed by acute respiratory failure secondary to possible pulmonary embolism thrombus low clinical pretest. Started protective mechanical ventilation on assisted controlled tidal volume of 6 ml/Kg, Fl0, 1, PEEP (positive end expiration pressure) 8 cm H20, flow rate 70 lt/min, IMV (intermittent mandatory ventilation) of 15, inspiratory pause of 0.1 sec, curve slowed. Thorax CT (Figure 2) reported density of soft tissue in left pulmonary arterial compatible with thrombus, consolidation in the right lower lobe area, associated with important right pleural effusion and left basal atelectasis with air bronchogram, performance thorax ultrasound which dismiss pleural effusion. Documented right pulmonary condensation, broncho alveolar lavage was negative report of Dimer D 7.833 ng/ml. It evolves worsening with deterioration of ventilatory distensibility 33 static and

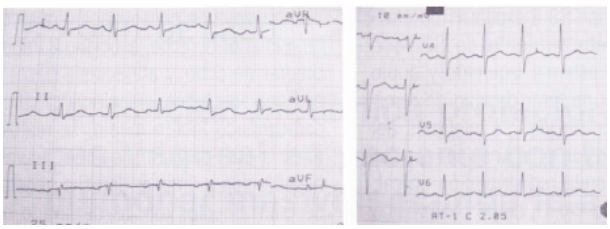

Figure 1: e.k.g. Mc ginn white complex and sinus tachycardia.

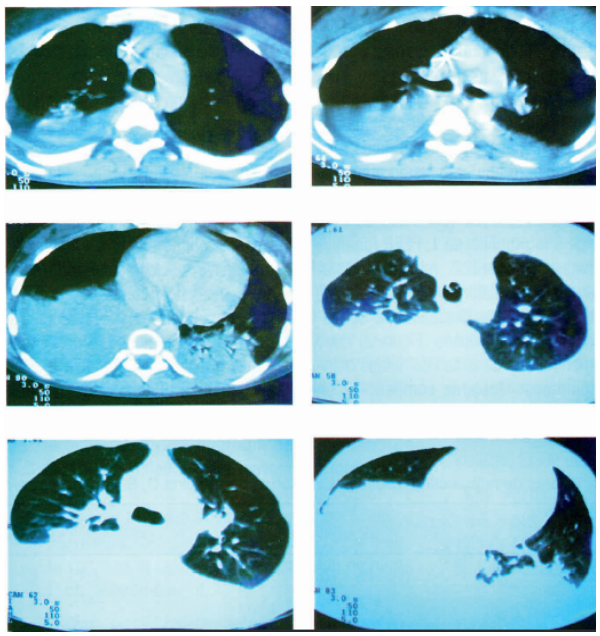

Figure 2: CT. Thorax opacity righ lower lung and air brochogram left lower lung.

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Received September 05, 2015; **Accepted** December 18, 2015; **Published** December 22, 2015

Citation: Giraldo Sanchez JM, Giraldo Arboleda DL, Giraldo Arboleda RA (2015) Patient with Massive Pulmonary Embolism Caused by the Combined Deficiency of Proteins C and S and Antithrombin III. J Pulm Respir Med 5: 300. doi: 10.4172/2161-105X.1000300

dynamic 25 compliance associated with hypoventilation alveolar and oxygenation index increased by 52 therefore starts to 5 liters per minute of tracheal gas Insufflation; with the idea to avoid worsening of the condensation saving positive pressure and tidal volume, autoimmune profile report was negative. Requested functional percentage of protein C and protein S, as well as Antithrombin III plus load antigenic protein C and S, whose results are mentioned in Table 1. Evolving satisfactorily with recovery of oxygenation, ventilation and oxygenation index (Table 2). Scans of the chest control (Figure 3) shows remission absolute of the condensation and the atelectasis, starts process of weaning with adequate tolerance to the SBT (spontaneous breath trial) as well as the T-tube therefore proceed to extubation.

Discussion

Pulmonary thromboembolism, there is a sequence of deleterious effects that eventually damage the gas exchange and lung structure. As a result of the loss generated from Pneumocells type II compromised the production of surfactant with the emergence of atelectasis total or segmental and the lung collapsed according to the severity of the thrombosis and the disbalance between neuro-humoral response mediated by serotonin, endothelin, prostacyclin and nitric oxide modifies regional blood flow pulmonary with increase total lung water

Glycoprotein / Range	Reference range	Result
Functional protein C	71%-176%	6.4%
Antigenic protein C	65%140%	47%
Functional Protein S	76%-178%	45%
Protein S antigen	50%-130%	30%
AT III Functional	84%-123%	65%

Table 1: Reference values and validated results of protein C, S and antithrombin III (ATIII).

Relationship gases/CVM/ TgI	Protect Mechanical Ventilation (P.M.V.)	P.M.V. + TgI	
PaFIO2	88	378	313
Ventilation	33 mmhg	37mmHg	31mmHg
Oxygenation index	52	6	4

Table 2: Relationship of gases in conventional mechanical ventilation and tracheal gas insufflation.

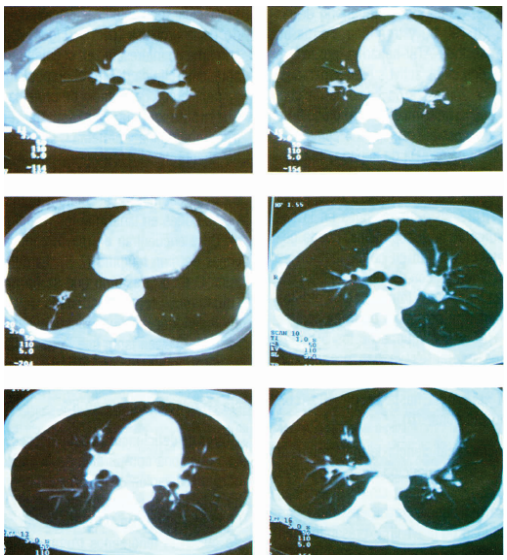

Figure 3: CT Thorax absolute control of condensation and air brochogram.

arise to the appearance of condensation these being the direct cause of the often irreversible lung injury [1-3]. With the administration of PEEP in this kind of patients vascular flow is redistributed to areas with badly perfusion and get against gravity the gas flow therefore can generates atelectasis and collapses in that regions and modifies water lung total distribution worsening condensations [4,5]. With the implementation of tracheal gas insufflation through the mixture of flows arise turbulence in pulmonary compartments of the airway intermediate expiratory brake, non-mechanical PEEP and recruitment without modifying the vascular distribution lung [6].

Understanding of the clinical presentation of pulmonary thromboembolism by deficiency of protein c S AT III should be considered a series of concepts that reveal a severe inflammatory response with significant Endothelial dysfunction during thrombosis pulmonary. Antithrombin III is a glycoprotein produced in the liver of the Serpin family whose anticoagulant action is derived from the inhibitory effect of the serine protease X, Vll, Xll, lX, and Thrombin. Forms a ternary complex substrate-ATIII-heparin with two surface active sites; one of them for the union with heparin, which induces a conformational change in the molecule AT lll making more accessible the second active Center for the substrate, in the absence of heparin reaction is slower. Its deficiency is an autosomal dominant disorder associated with chromosomal deletions C1q 23-25 or alterations in the sequence amino acid glycoprotein. Can generate severe symptoms when their concentration is lower than 50%, however with reduction of 70% already thrombotic phenomena are experienced, between 10 and 35 years of age the presence of thrombosis is associated in up to 10% and above age 50 up to 85% of patients have already presented hypercoagulability. The presentation of deep venous thrombosis is associated with a 40% of embolism pulmonary.

Types of deficiency: Antithrombin III deficiency type I is associated with decreased ability functional of glicoprotein product of chromosomal deletions, type II deficiency is associated with alteration in the quality of antithrombin lll, expressing itself in conservation or loss of affinity to heparin molecule conservation or loss of the proteolytic activity of the serine protease [7].

Protein C is a glycoprotein produced in the liver causing a carboxylation of residue amino E lysine therefore comes out under the action of vitamin k to circulation in zymogen form where id activated (aPC) slowly by Thrombin (Tm) which through disruption of Arginine, Leucine expressed its active center located in the amino terminal of the heavy chain portion; This reaction it catalyzes by Thrombomodulin (Trd) in the presence of calcium [8,9].

Protein C in addition to intervene inhibiting the FVlll and the FV through marginalization of Endothelial Protein C receptor (EPCR), also acts conditioning platelet adhesiveness in certain flow conditions by of receiver 2 Apo lipoprotein E (apoER2) and glycoprotein 1 beta alpha (GP1ba) [8]. As well as activated protein C (aPC) has anti-inflammatory properties directly relationship with preservation in the integrity of the barrier endothelium by activating (1 par) (Figure 4) protease activated receptor, which is extremely interesting in understanding the presentation clinic of pulmonary thromboembolism in patients with protein C, S deficiency; keep in mind that number of receptors for Thrombomodulin and protein c varies according to the type of glycoprotein. The Thrombomodulin presents many receptors at sites of turbulent flow, capillary valves, pulmonary vasculature and arteries/veins short, and receptors for protein C are found in greater quantity in arteries and veins of great length [8-10]. Protein C deficiency is a disorder that transmitted way autosomic, has been

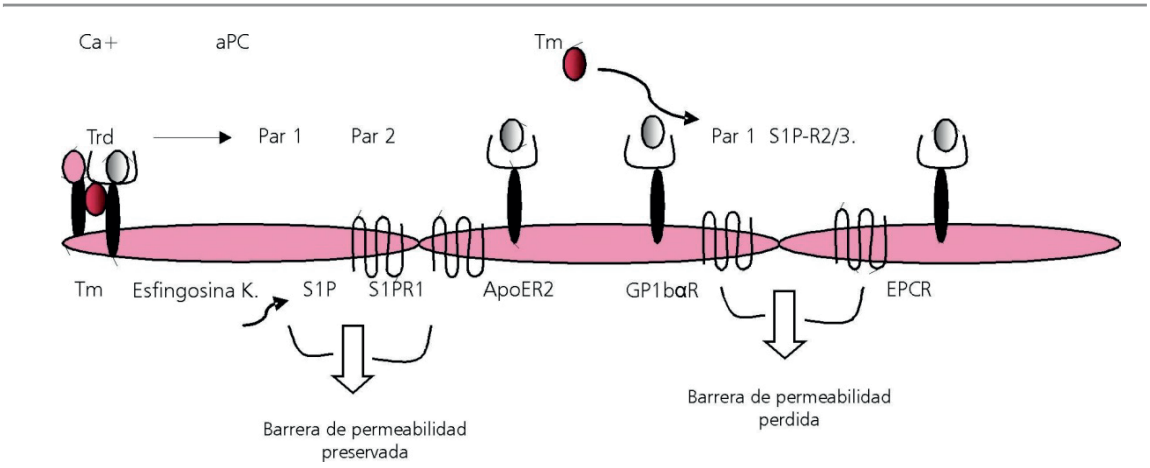

Figure 4: Regulation of vascular permeability by the aPC and Thrombin. Protein C (PC) goes to circulation in the form of zymogen, modified previously by vitamin k; Once in circulation is activated (aPC) slowly by Thrombin (Tm) and in the presence of the Thrombomodulin (Trd) is catalyzes this reaction under the influx of calcium. C-protein binds to its receptor endothelial (EPCR Endothelial PC receiver) protein; small amounts of Thrombin are picked up by the Thrombomodulin to efficiently convert the complex PC-EPCR form aPC-EPCR which starts the activated receptor (par 1 protease activated receptor 1) protease by sphingosine 1 phosphate from the sphingosine kinase; in this way are activated endothelial signals with complex S1PR1 which preserves the barrier of vascular permeability under conditions of inflammation as well in vitro control the action of the lipopolysaccharide and interferon induced by macrophages. The Thrombin molecule interacts with pair 1 and conditions endothelial signals through the S1P-R2/3 complex which causes loss of permeability barrier. Down regulation of the system of c-protein from the complex thrombinase, vitronectins, Activator inhibitor of Tissue plasminogen (PAI1), 4 platelet factor (PAF 4) Act by inhibiting fibrinolysis and the complex aPC, but not its ability to activate Par1. Surface residues of protein c are endothelial ligands known as Receptor 2 (ApoER2 Apolipoprotein E Receptor 2) apolipoprotein and glycoprotein 1ba, from which is inhibited under certain flow conditions platelet adhesiveness. CCM Feb.2010.

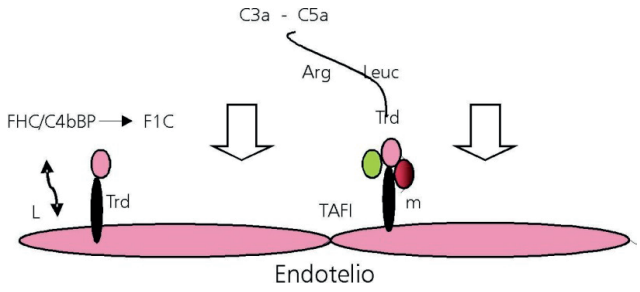

Figure 5: Inflammatory effects of Thrombin/Thrombomodulin complex. The complex Thrombin/Thrombomodulin is a potent inhibitor of fibrinolysis using activation by Thrombin activatable fibrinolysis inhibitor (TAFI thrombin-activatable fibrinolysis inhibitor) which suppresses the production of plasmin by surface cells associated with the fibrin matrix. The complex Thrombin/Thrombomodulin through disruption of Arginine, Leucine inhibits the anaphilotoxins C3a and C5a with reducing the bacterial opsonification, chemotaxis, properdin and platelets sialic acid. Thrombomodulin (Trd) through an extracellular Leucine residue interacts with the complement factor H and 4b of the complement protein portion (C4bBP Complement 4b binding protein) for the production of the 1's complement-mediating factor inactivation of C3b. CCM Feb.2010.

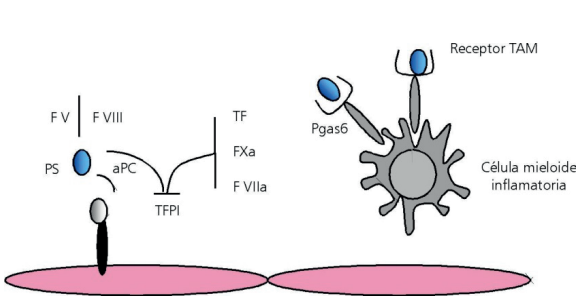

Figure 6: Regulation of inflammation and the anti coagulation by protein S.-dependent pathways By degradation of factor V and factor VIII, protein s activated protein c (aPC) and through the tissue factor inhibitory pathway (TFPI tissue factor pathway inhibitor) suppresses the coagulation ternary complex composed of tissue factor, factor VIIa and factor Xa. The s protein and vitamin k are the only 2 ligands monocytes from a protein Gas6 anti-inflammatory. At the same time protein s through a tyrosin kinase mer stimulates a receptor family tyro/axl/mer in inflammatory myeloid cells giving rise to transgenic and intracellular signals with which promotes phagocytosis in macrophages of the cell apoptoics remains, increases phagocytosis of membrane phospholipids during apoptosis which in turn are inflammatory markers mainly the phosphatidyl serine; and down regulation thanks to such signals routes dependent of nuclear factor kappa beta, System tool like receptor and myD88 molecule. CCM Feb.2010.

identified in individuals randomly with a first event thrombogenic in up to 3%, so that the patients that have been related to severe pulmonary thromboembolism Embolic events his presence relates to 8 %.

Types of deficiency: deficiency of protein C type I is related to loss of functional capacity but preservation of antigenic load protein and the type ll where preserving their functional capacity but antigen load is empty. With less than 50% consumption thrombogenics phenomena are presents and the more severe forms is less than 5% activity are more seriously [7]. It is important known that the protein C deficiency not only generates hypercoagulability, also serious inflammatory disorders mediated by Thrombin/Thrombomodulin complex product from this situation and inhibition of fibrinolysis and alteration in the complement way (Figure 5). Protein S is a glycoprotein produced in the liver that acts as a non-enzymatic protein C cofactor, is produced by degradation of factor VIII and factor V activating protein c (aPC), Additionally generating inactivation of the ternary complex of coagulation of tissue

factor, factor Xa and factor Vlla; through the inhibitory way of the tissue factor [8,9]. Protein S also recognizes properties anti-inflammatory and modulator of intracellular signals (Figure 6). Those properties relate directly to the process of apoptosis and determine in the gene encoding for the response of the host against infection and tissue injury [11-13].

Conclusion

Thanks to recent advances in the understanding of the system of protein C as a regulator of inflammation, it´s allowed the understanding the clinical presentation and image of thromboembolic mainly pulmonary events. Protein C, S deficiency is a fairly uncommon clinical case, however the understanding of each one of the inflammation-related functions has allowed the investigative development of therapeutic interventions for the medical application. Possibly in short time regulation in apoptosis and the response of the host against the injury, also can be controlled all this events with understanding of these systems.

Conflict of Interest

No declared conflicts of interest.

References

1. Goldhaber SZ (2008) Deep venous thrombosis and pulmonary thromboembolism. Harrison s principles of internal medicine: 1651-1658.
2. (2000) Intensive therapie argentina society. (3ªedn): 746-752.
3. Tapson V (2002) The Hearth. Pulmonary embolism. Hurst ll: l679-1692.
4. Dueñas C, Ortíz G, González M (2004) Mechanical Ventilation Applied In Critical lll Patient. Tribune: 67-78.
5. Cressoni M, Caironi P, Polli F, Carlesso E, Chiumello D, et al. (2008) Anatomical and functional intrapulmonary shunt in acute respiratory distress syndrome.Crit Care Med 36: 669-675.
6. Mentzelopoulos SD, Roussos C, Koutsoukou A, Sourlas S, Malachias S, et al. (2007) Acute effects of combined high-frequency oscillation and tracheal gas insufflation in severe acute respiratory distress syndrome.Crit Care Med 35: 1500-1508.
7. Cuker A, Pollak ES (2009) Coagulations Hemostasis and Disorders: Protein C Deficiency. Hospital of the University of Pennsylvania Hematology/Oncology. Coagulation Hemostasis and disorders protein C Deficiency.
8. Weiler H (2010) Regulation of inflammation by the protein C system.Crit Care Med 38: S18-25.
9. Baue AE, Faist E, Fry DE (2000) Multiple organ dysfunction Pathophysiology, prevention and therapy. Springer: 438-446.
10. Ortiz-Ruiz. G. Perafan M. Faist E. Sepsis. 1 -13 Springer 2004.
11. Jia YT, Ma B, Wei W, Xu Y, Wang Y, et al. (2007) Sustained activation of nuclear factor-kappaB by reactive oxygen species is involved in the pathogenesis of stress-induced gastric damage in rats.Crit Care Med 35: 1582-1591.
12. Abraham E, Singer M (2007) Mechanisms of sepsis-induced organ dysfunction. Crit Care Med 35: 2408-2416.
13. Ni Chonghaile M, Higgins BD, Costello JF, Laffey JG (2008) Hypercapnic acidosis attenuates severe acute bacterial pneumonia-induced lung injury by a neutrophil-independent machanisms CCM 36: 3135-3144.