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CASE REPORT

Acquired factor V deficiency in a patient with pulmonary tuberculosis

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Acquired factor V deficiency in a patient with pulmonary tuberculosis. J.L. Aliaga, J. de Gracia, R. Vidal, M. Pico, P. Flores, G. Sampol.
ABSTRACT: A 29 yr old man with pulmonary tuberculosis and concomitant acquired plasma coagulation factor V deficiency is reported. The case is discussed together with three previously described cases. The bleeding tendency in a patient with pulmonary tuberculosis may be caused by a coagulation factor antibody and may be corrected by chemotherapy, as in the case described. Special therapeutic approaches are required in some cases.
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Tuberculosis may be associated with non-specific haematologic alterations such as normocytic and normochromic and even microcytic and hypochromic anaemias due to chronic infection, or with anomalies of the white cell count. These alterations are usually banal and reversible following effective chemotherapy. However, more severe haematologic alterations such as leukaemoid reactions [1], severe cytopenias and coagulation disorders may also be seen. Of these, the acquired factor V deficiency associated with active pulmonary tuberculosis has been reported in only three cases in the literature to date [2]. We present a case of acquired factor V deficiency associated with active pulmonary tuberculosis.

Case Report

A 29 yr old man was admitted to the hospital following a 3 month history of weight loss, and one month with right pleuritic pain. He had smoked one pack of cigarettes daily for 14 yrs. He denied both drug abuse and excessive alcohol ingestion, and was not on any drug therapy. There was no history of a bleeding disorder either in the patient or his family.

On admission, the axillary temperature was 38°C, and physical examination revealed a pleural effusion on the right side. An X-ray film of the chest showed infiltrates in both lung apexes as well as a right pleural effusion. The erythrocyte sedimentation rate (ESR) was 117 $mm \cdot h^{-1}$, prothrombin time 47 percent, the activated partial thromboplastin time 44 s with a control of 30 s, and index (patient's time in seconds/control's time in seconds) of 1.4 (1–1.2), fibrinogen 5.5 $g \cdot l^{-1}$ (1.5–2.5 $g \cdot l^{-1}$); platelet count, $420 \times 10^9 \cdot l^{-1}$ Other values, hepatic and renal function, and urine analysis were normal. Pleural fluid contained no red cells but white cells with lymphyocytes predominant (79%); glucose was 7.0 $mg \cdot l^{-1}$, protein 56.5 $mg \cdot l^{-1}$, lactic dehydrogenase (LDH), 1.173 $IU \cdot l^{-1}$ and adenosine deaminase (ADA) 85 $IU \cdot l^{-1}$.

No acid-fast bacilli or other micro-organisms were seen, and cytologic examination for tumour cells was negative. Sputum showed acid-fast bacilli in the smear and *Mycobacterium tuberculosis* in culture.

Before chemotherapy the haemostatic study (table 1) showed a decrease in factor V values, an increase in fibroinogen degradation products and a slight decrease in antithrombin III. With the exception of fibrinogen which remained high, all parameters had returned to

Table 1. – Coagulation studies. Results obtained with patient plasma samples

Test	15 days Before Treatment	15 days After Treatment	Reference value Range
Prothrombin time	51%	71%	80–100%
Activated partial thrombloplastin time	1.4	1	Index 1–1.2
Thrombin time s	25	21	18–22
Platelet count x $10^9 \cdot l^{-1}$	442	334	140–400
Factor II	101%	109%	70–100%
Factor V	49%	81%	70–100%
Factor VII y Factor X	75%	99%	70–100%
Factor I $g \cdot l^{-1}$	5.7	5.6	1.5–2.5
AT III	76%	77%	80–100%
FDP $\mu g \cdot ml^{-1}$	16	-	

AT: antithrombin; FDP: fibrinogen degradation products; Index: patient's time in seconds/control's time in seconds.

normal 15 days after initiating chemotherapy with rifampicin 600 mg·day^{-1} and isoniazid 300 mg·day^{-1} both for 9 months and ethambutol 25 mg·kg·$^{-1}$day^{-1} for 2 months. At follow-up one year later the patient was asymptomatic and coagulation studies were normal.

Discussion

Factor V is a plasma cofactor of coagulation which accelerates the conversion of prothrombin to thrombin. The decrease in its plasma concentration carries an increased risk of bleeding. Two pools of factor V are depicted, one in platelets (20%), the other in plasma (80%). The relative contribution of each pool to coagulation is unknown, although recent studies emphasize the value of platelets [2].

Twenty seven cases of acquired factor V deficit were recently revised [2]. All cases were related to a circulating inhibitor of sudden presentation and short duration, of the IgG or IgM type, capable of neutralizing the coagulation activity. The aetiology and pathophysiologic mechanism of presentation is unknown, but there seems to be a close relationship with major surgery and aminoglycoside treatment. In the majority of cases, the change in coagulation does not produce haemorrhagic diathesis, even in patients with very high titres of circulating inhibitor or factor V activity below 1%, although severe fatal haemorrhages have been described in some cases [3]. This variability in bleeding tendency, especially in those patients with total inhibition of the plasma factor V, appears to be related to the inaccessibility of circulating immunoglobulins to the platelet factor V fraction [2]. Most inhibitors usually disappear spontaneously within four to six weeks without specific therapy. However, in some cases, treatment with steroids or other immunosuppressor agents is necessary when the inhibitor persists [4], or in the case of severe bleeding, platelet transfusion or administration of concentrated activated factor IX may be required [5].

Although very few cases of acquired factor V deficit together with pulmonary tuberculosis have been described in detail to date, the review of clinical data in our patient together with the three cases previously described shows: 1) no sex predominance; 2) ages varying between 23–66 yrs; 3) severe bleeding in only one patient; 4) the mean value of factor V inhibitor titre was lower in patients with pulmonary tuberculosis (1:4) when compared to patients without (1:89); 5) the inhibitor disappeared within 2–6 weeks after beginning tuberculostatic treatment in most patients.

As the association of factor V deficit and pulmonary tuberculosis in the cases described caused haemorrhagic problems in only one case [6], and as the factor V deficit appears to correct itself soon after specific treatment is undertaken, the real incidence of this anomaly may be higher than that described to date.

Coagulation studies should be performed in all cases of haemorrhagic diathesis in pulmonary tuberculosis patients. In such cases, early diagnosis would enable specific treatment with platelets or activated factor IX. However, a greater number of cases is required for a more complete understanding of this entity.

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References

1. Vidal R, Monsó E, Oristrell J *et al.* – Alteraciones hematológicas en la tuberculosis miliar. Estudio de 93 pacientes. *Rev Clin Esp,* 1985, 176, 22–25.
2. Nesheim ME, Nichols WL, Cole TI *et al.* – Isolation and study of an acquired inhibitor of human coagulation factor V. *J Clin Invest,* 1986, 77, 405–415.
3. Coots MC, Muhleman AF, Gluek HI. – Hemorrhagic death associated with a high titer factor V inhibitor. *Am J Hematol,* 1978, 4, 193–206.
4. Chong H, Koneti A, Beckett C, Colmen RW. – Immune complexes containing factor V in a patient with an acquired neutralizing antibody. *Blood,* 1985, 65, 810–818.
5. Vickars LM, Coupland RW, Naiman SC. – The response of an acquired factor V inhibitor to activated factor IX concentrate. *Transfusion,* 1985, 25, 51–53.
6. Onoura CA, Lindenbaum J, Nessel HL. – Massive hemorrhage associated with circulating antibodies to factor V. *Am J Med Sci,* 1973, 265, 407–417.

Déficience acquise en facteur V chez un patient atteint de tuberculose pulmonaire. Observation clinique. J. Aliaga, J. de Gracia, R. Vidal, M. Pico, P. Flores, G. Sampol.
RÉSUMÉ: Le cas d'un homme 29 ans, atteint d'une tuberculose pulmonaire et d'une déficience concomitante acquise en facteur V de coagulation plasmatique, est discuté simultanément avec trois observations décrites antérieurement. Les tendances hémorragiques chez un patient atteint de tuberculose pulmonaire peuvent être provoquées par un anticorps de facteur de coagulation, et peuvent être corrigées par la chimiothérapie, comme dans l'observation décrite. Dans certains cas, des approches thérapeutiques particulières sont indispensables. *Eur Respir J., 1990, 3, 109–110.*