

questionado. Para diminuir as possíveis interações com os resultados laboratoriais, a HBPM foi suspensa durante 24 horas e procedeu-se à quantificação dos níveis de atividade de PC e PS livre, que demonstraram níveis normais de PC e PS (127% e 59%, respectivamente), concluindo-se que a doente afinal não tinha uma trombofilia. Ao fim de 15 anos de hipocoagulação com varfarina – um fármaco com múltiplas interações alimentares e medicamentosas conhecidas e que, neste caso, levou a múltiplas intoxicações dicumarínicas – foi possível suspender a terapêutica. **Conclusão:** Os AVK são uma das principais causas de deficiências adquiridas de PC e/ou PS. Apesar disso, e de outras desvantagens associadas aos AVK, ainda são amplamente utilizados como tratamento anticoagulante. Portanto, devemos ter em consideração a interferência dos hipocoagulantes e do estado inflamatório agudo nos controlos analíticos realizados e a necessidade de repetir resultados de testes anormais para confirmação de diagnósticos, especialmente na ausência de história familiar.

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EVALUATION OF A GENE SIGNATURE RELATED TO THROMBOTIC MANIFESTATIONS IN ANTIPHOSPHOLIPID SYNDROME

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Introduction: Whether different manifestations of thrombotic antiphospholipid syndrome (APS) share pathological mechanisms has not been established. Transcriptome analysis may constitute a new approach to evaluate the mechanisms behind thrombotic manifestations in APS. **Aim:** To determine in patients with primary thrombotic APS (t-PAPS) the expression of genes already related to venous and arterial thrombosis in the general population. **Method:** mRNA was obtained from total leucocyte; gene expression was measured by qPCR and the results were analyzed by QuantStudio™ Software. **Results:** 83 t-PAPS and 85 controls were included. The median age on the enrollment day was 40 years old (IQR 31 - 51) in patients and 38 (IQR 29 - 53) in controls, 66% of patients and controls were women and cardiovascular risk factors were more prevalent among t-PAPS than in controls (37% vs 11%). TXK ($p < 0.001$), BACH2 ($p = 0.005$), and SERPINB2 ($p = 0.003$) mRNA expressions were down-regulated while TNFAIP6 mRNA expression was up-regulated ($p = 0.003$) in t-PAPS compared to controls. A slightly increased gene expression of ANXA3 was observed in t-PAPS patients compared to controls, but it was not statistically significant. In subgroups analysis, patients were divided according to different manifestations of t-PAPS. TXK, BACH2, SERPINB2 and TNFAIP6 mRNA expressions were more pronounced in some subgroups. TXK mRNA expression was decreased mainly among patients with triple aPL positivity ($p < 0.0001$); BACH2 and SERPINB2 mRNA expressions were decreased in patients with a single thrombotic event ($p = 0.002$ and $p = 0.003$, respectively); and TNFAIP6 mRNA

expression was particularly elevated in patients who had multiple thrombosis ($p = 0.01$). **Discussion:** The results showed a distinct pattern of gene expression between APS patients and controls. TXK regulates the development, function, and differentiation of T-cells and NKT-cells of the adaptive immune response. BACH2 is crucial for the maintenance of regulatory T-cell function and B-cell maturation. Both genes were down-regulated in t-PAPS, suggesting that the regulation of adaptive immune response is impaired in the disease. TNFAIP6, which is involved in cell-cell and cell-matrix interactions during inflammation, was up-regulated in t-PAPS, suggesting an increased pro-inflammatory response. Finally, SERPINB2, which inhibits the monocyte-derived urokinase-type plasminogen activator and is responsible for platelet and coagulation cascades activation, was down-regulated in t-PAPS patients. Although down-regulation of SERPINB2 appears to be a contradictory result, it may be evidence of an imbalance in the coagulation process, such as hypocoagulability. Therefore, we observed that innate immunity and hemostasis pathways are involved in the pathogenesis of thrombotic manifestations in t-PAPS at a transcriptome level. However, more study is needed to evaluate the pathways related to these genes, especially at cellular and biochemical levels. **Conclusion:** In this study, the expression of genes previously associated with thrombosis in the general population was validated in patients with t-PAPS. The main difference in gene expression was related to the regulation of cellular and humoral immunity. These genes were also associated with t-PAPS severity such as multiple thrombosis and triple antibody positivity. Our findings suggest that the deregulation of innate immunity and hemostasis is associated with the pathogenesis of t-PAPS at a molecular level.

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HEMOSTATIC ALTERATIONS WITH DISEASE SEVERITY IN THE EARLY SYMPTOMATIC PHASE OF COVID-19

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Introduction: The main factors associated with disease severity in Covid-19 are age, sex, body weight, hypertension, and diabetes. Biomarkers of hemostatic activation have been shown to be independent predictors of disease severity in different populations. **Aim:** To evaluate whether biomarkers of hemostatic activation were associated with clinical outcomes in patients admitted to a field hospital set up to provide initial care to patients in the early symptomatic phase of Covid-19.

