

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

BC Jacintho, BMM Fonseca, BW Hounkpe, APRD Santos, CO Vaz, GLTV Mesquita, JD Oliveira, E Paula, FLA Orsi

Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil

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

SC Huber^a, SAL Montalvão^a, SS Martins^a, LQ Silva^a, C Bacchin^a, T Diaz^b, C Wroclawski^c, CC Filho^c, EV Paula^a, JM Annichino-Bizzacchi^a

^a Hemostasis and Thrombosis Laboratory, Centro de Hematologia e Hemoterapia (Hemocentro), Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil

^b Hospital Municipal de Campanha do Anhembi, São Paulo, SP, Brazil

^c Thrombosis and Hemostasis Center, Hospital Sírio Libanês, São Paulo, SP, Brazil

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.



Methods: Data and samples were obtained from June to September 2020. Laboratory evaluation included complete blood counts, PT, aPTT, fibrinogen, D-dimer, factor VIII activity, Von Willebrand Factor (VWF) (activity and antigen), C reactive protein (CRP) and P-selectin (ELISA). Patients were segregated by outcome, with clinical worsening defined as need for ICU, mechanical ventilation, pulmonary embolism, deep vein thrombosis or death. **Results and discussion:** In total 209 were enrolled in the study, of which 24 presented clinical deterioration (11.5%). In both groups there was more male patients. In the group of clinical worsening the mean age was 58.1 and improvement was 53.6 years old. Concerning smoking, 3.2% of patients that improved smoke. Regarding pulmonary infiltrate, it was verified in 50% in the group that worsening versus 41% in clinical improvement. No differences could be observed between patient subgroups regarding the presence of fever (63.2% vs. 62.5%), dry cough (75.1% vs. 87.5%) and dyspnea (65.9% vs. 54.2%) at admission. As main comorbidities, the groups presented chronic obstructive pulmonary disease (2.2% vs 8.3%), asthma (3.2% vs 4.2%), chronic heart failure (1.1% vs 8.3%), arterial hypertension (46% vs 41.7%) and diabetes (28.1% vs 33.3%) in comparing improved with clinical deterioration patients. In general, it was verified a significant decrease in platelet number ($p = 0.0426$), and an increase in the parameters of aPTT ($p = 0.0084$), CRP ($p = 0.0450$), vWF antigen ($p = 0.0022$) and ristocetin cofactor ($p = 0.0032$). **Conclusion:** Our results demonstrate that hemostasis activation is associated with clinical deterioration even at the early phases of Covid-19. The Ethics Research Committee of the University of Campinas approved all of the experimental procedures, and all individuals signed the informed consent form.

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PÚPURA TROMBOCITOPÊNICA TROMBÓTICA (PTT) RECIDIVADA/REFRATÁRIA: EXPERIÊNCIA DO CENTRO UNIVERSITÁRIO EM VITÓRIA – ES

VHR Carvalho, GS Sonsim, SS Marcondes, PADSBA Matos, MP Araujo, MDD Santos, VB Filho, JPA Frechiani, ALRAC Sipolatti

Universidade Federal do Espírito Santo (UFES), Vitória, ES, Brasil

Introdução: A PTT, doença rara que atinge 3/milhão/ano em adultos, é considerada emergência médica com mortalidade de 95% se não tratada. Trata-se de microangiopatia trombótica, causada por deficiência da enzima ADAMTS 13 e caracterizada por oclusão microvascular generalizada por trombos de plaquetas, levando à plaquetopenia. Os critérios para diagnóstico incluem: Anemia hemolítica microangiopática (esquízócitos em sangue periférico), plaquetopenia (< 100 mil), sinais de isquemia em órgãos alvo (alterações neurológicas e renais) e dosagem de ADAMTS 13 $< 10\%$. Seu tratamento de escolha é a plasmáfereze e deve ser instituído precocemente. Caso não haja disponibilidade, o plasma fresco congelado (PFC) deve ser iniciado como opção, até se obter início da

plasmáfereze, além disso, o uso de corticoide é necessário devido predomínio do caráter autoimune da doença. **Objetivo:** Relatar dois casos clínicos de PTT refratária enfatizando aspectos clínicos e tratamento. **Caso 1:** 40 anos, masculino, hipertenso, apresentando quadro de cefaleia, vertigem e plaquetopenia. Suspeitado de PTT no serviço de origem sendo tratado com metiprednisolona e PFC com melhora (plaquetas: 150.000). Dosagem de ADAMTS 13: 5% e Anticorpo anti ADAMTS 13 negativo. Na transferência para este serviço apresentou convulsão, pneumonia broncoaspirativa e lesão renal aguda. PLASMIC score 5 (prejudicado devido uso de PFC). Apresentou novamente piora de provas de hemólise e plaquetopenia (7 mil), sendo iniciado plasmáfereze (6 sessões) com resposta completa e alta médica. Após 90 dias, paciente percebeu icterícia e realizou hemograma por conta própria, sendo readmitido com 19.000 plaquetas, Hb:11 e DHL 462. Reiniciada, então, plasmáfereze (5 sessões) associada ao rituximabe 100 mg/semanal, atingindo remissão e alta com 164.000 plaquetas. **Caso 2:** 49 anos, feminino, DM tipo 2, apresentou inicialmente sangramento muco-cutâneo (tronco e membros) e recebeu diagnóstico inicial de PTI em serviço ambulatorial, com realização de corticóide por 6 meses, sem melhora. À admissão estava assintomática com Hb 9,0 g/dL, plaquetas 9 mil, leucócitos normais, 3 esquízócitos/campo em sangue periférico, DHL:1850, sorologias, função tireoidiana e triagem reumatológica negativas e PLASMIC score: 6. Diante disso, solicitado ADAMTS 13 e iniciado imunoglobulina 0,4 mg/kg/4 dias, associada PFC por 19 dias sem resposta. Após resultado de ADAMTS 13: 0% iniciado plasmáfereze (10 sessões), sem resposta. Associado, então, Rituximabe 375 mg/m²/semanal, no total de 4 infusões, recebendo alta com 177 mil plaquetas. Uma semana após, apresentou plaquetometria de 66 mil com reinício de plasmáfereze (7 sessões) associada à ciclofosfamida 750 mg/m²/mês. Diante dessas medidas, evoluiu com reposta satisfatória (191 mil plaquetas) e alta hospitalar. **Considerações finais:** Sabe-se que 10 % dos casos são refratários e cerca de 34% apresentam recidiva (era pré rituximabe). Nos pacientes refratários as opções de tratamento são: Rituximabe e outros imunossuppressores, como por exemplo: ciclofosfamida, vincristina e ciclosporina. Recentemente, a aprovação do caplacizumabe, também se constitui como opção terapêutica. Apresentamos 2 casos ilustrando estas complicações cujo manejo terapêutico é desafiador considerando as dificuldades de dosagens de ADAMTS 13 e disponibilidades terapêuticas pelo SUS.

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SAFETY AND EFFECTIVENESS OF ANTICOAGULATION BASED ON AN INSTITUTIONAL RECOMMENDATION ON THE MANAGEMENT OF CANCER ASSOCIATED VENOUS THROMBOSIS

C Rothschild, AAGS Brandão, A Duran, AE Zerati, LA Hajjar, GF Saes, CS Bittar, IBSS Costa, SMR Fonseca, MHHDS Rehder, LBO Alves, MDPE Diz, J Pereira, V Rocha

