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Brief Communication Thombotic Trombocytopenic Purpura: Allergic Reaction to Plasma Proteins During Therapeutic Apheresis

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ABSTRACT: *Thrombotic Thrombocytopenic Purpura (TTP) is a raredisordercharacterized by microangiopathichemolysiswiththrombosis. The golds tandard of treatment is the rapeutic plasma exchangewhichreplenishesthedepleted ADAMTS-13. Herewepresent a rarecomplication: a patient that developed allergy to plasma proteins and remitted afterapheresis with albumin.*

Keywords:*ThromboticThrombocytopenic Purpura, AllergytoPlasma Proteins, Plasma Exchange.*

I. INTRODUCTION

ThromboticMicroangiopathy refers to a group of diseases in whichthehallmarkisthepresence of microvasculopathywithorwithoutthrombosis[1,2].Thrombotic Trombocytopenic Purpura (TTP) isanexample of thesedisorders. Itisdefined by thepentad of microangiopathichaemolyticanaemia, trombocitopenia, neurologicalsymptoms, renal disorders and fever[3]; however,itiswidelyacceptedthatonlythefirsttwocriteriaare neededtofulfilldiagnosis.Neurologicalsymptoms and feverrepresent late events and maydelay interventions[4], therefore, plasma exchangemust be startedimmediately in ordertodecreasemortalityratesfrom 90% to 10% [3-6].Becauseof itsbroadclinicalpresentation, theterm TTP-HaemolyticUremicSyndrome (TTP-HUS) wascreatedtorefertothisgroup of conditions[2,4]. The firstinsightintothepathogenesis of TTP waspublished by Moake in 1982, whofoundthatpatientswithrelapsingcongenital TTP hadunusuallylarge von Willebrand Factor (vWF) multimerswhile in remission[7], a findingthatwasnotpresent in healthypeople. In 1997, Furlan and coworkersdemonstratedthatdeficiency in the activity of the vWF-cleaving protease ADAMTS-13 was the cause of chronic relapsing TTP [8], defining HUS and TTP as different clinical entities, the latter presenting with levels below 5% [9,10].There are fourdifferentpathophysiologicalmechanismsthatexplainfindings in thromboticmicroangiopaties: vWF-plateletaggregates in ADAMTS-13 deficiency, microangiopathy in autoinmune and infectious TTP, tumor cellsthrombosisand fibrin-plateletthrombi in DisseminatedIntravascularCoagulation[10].Despitetheautoimmune[10]or genetic[11]aetiology, thegoldstandard of treatmentistherapeutic plasma exchange (TPE), whichremovestheinhibitors and replenishesthedeficient ADAMTS-13[12,13].Herewedescribe a case ofa patientwithPTT whodevelopedanacuteallergicreactionto plasma proteinsduringTPE**.**

Case Report

A femalepatient of 32 yearsoldwith no important prior medical historyvisitedherprimarycarephysicianforupperlimbshaematomaswithpetechiaealongthethorax and abdomen thatstarteddevelopingin theprevious10 days. Shedeniedheadaches, visual disturbancesoranyneurologicalsymptoms. Shehad no history of recent trauma and wasnottakingmedications. Therewerenosigns of bleeding, no splenomegaly and therest of thephysicalexaminationwas normal. Bloodsamplesshoweda normocytic-normochromicanaemiawith7.5g/dL of haemoglobin, normal leukocytecount, 15.000platelets/mm^3 and normal coagulationtests. Withtheseresultsshewasreferredtothenearesthaematologydepartment,whereperipheralbloodmorpholog yexaminationdemonstratedschizocytes and polychromasia. ThromboticThrombocytopenic Purpura

wasdiagnosed and the patientinforme dabouttherapeuticplasmapheresis, whichstartedimmediately. Lactatedehydrogenase (LDH)levelwas 532U/L,withfibrinogen in 858 mg/dl andnormalrenal functiontests. Thirtyeight minutes afterthefirstsession of plasma exchangeshedevelopedplasma proteinsallergymanifested as generalized cutaneous rashandpruritus. At thatmomentshedidnotpresentbronchospasm, theproceducewas suspended and a fall in plateletsweredocumentedlateronthesameday (Table 1). Because of thisscenariosteroidswereaddedto a dose of 1mg/kg/day and therapeuticapheresiswasrestartedwith5% albuminthenextmorning. No response wasseenwiththefirstsessionas plateletscontinuedtodescendto 8.000/mm^3.ADAMTS-13 activitylevelstakenonadmissionwere0.5%. Five consecutive a pheres is procedures were completed and eventuallyallsigns of TTP disappeared. Beforedischarge, ADAMTS-13 activitylevelreturnedto 90%.Untilnow, 8monthslater, she has notrelapsed.

Discussion

The clinicalpresentation of TTP maydiffer[14]butitremainsunknownwhetherornotthisvariabilityrepresent a prognosticfactor. Plasmapheresisrelated adverse eventshavebeenreportedto be as low as 1.6%[15], however, informationregardingtheincidence of allergicreactionsduring TPEfor TTP islimited[16,17]. Interestingly, ourpatienthada severe ADAMTS-13 deficiency, whichcorrelateswithvWFdependentmicrovascular trombosis [18],and despite no specificreplacementtherapywasgivenforthedeficientprotease, ADAMTS-13 levelsreturnedto normalwithalbumin TPE, suggestingthatanimmunologically-mediatedmechanismwas corrected[13].In this case TTPmay be anearlypresentationof other disease, however,severe ADAMTS-13 deficiencyisextremelyrare in patientswithsecondary TTP[12,18]. Itisalsoquestionablethatsteroidscouldhavehadanyimmediatebeneficial effect in thispatient as ithas notbeenestablishedthattheir useshortentheduration of plasma exchangetherapy[19]. Informationregardingtheoptimaltreatment of plasma-proteinallergicpatientsislimited; someauthorshavedemonstratedthatweeklyinfusions of Rituximab are effective in theacuterefractorypatients[20]butaccesstothisdrugmay be difficult in developingcountries. No data isavailablethatcompares directlyrituximabto TPE in thisscenariobutconsideringthefewavailableinformation,the use of TPE withalbuminmay be a safealternative in patientswithallergicreactions in situationswhereotheralternatives are limited.

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TABLE 1. Laboratory evaluation

	Day Before TPE	Day of TPE	After5 sessions of Albumin TPE
Hemoglobin (g/dL)	7.5	6.8	9.9
Platelets (x mm^3)	15.000	10.000	247.000
LDH (UI/L)	532	760	121
PeripheralBloodSmear	Schizocytes + Polycromasia +	Schizocytes + Polycromasia ++	No Schizocytes

LDH: Lactate Dehydrogenase