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The Clinical Presentation of Thrombotic Microangiopathy

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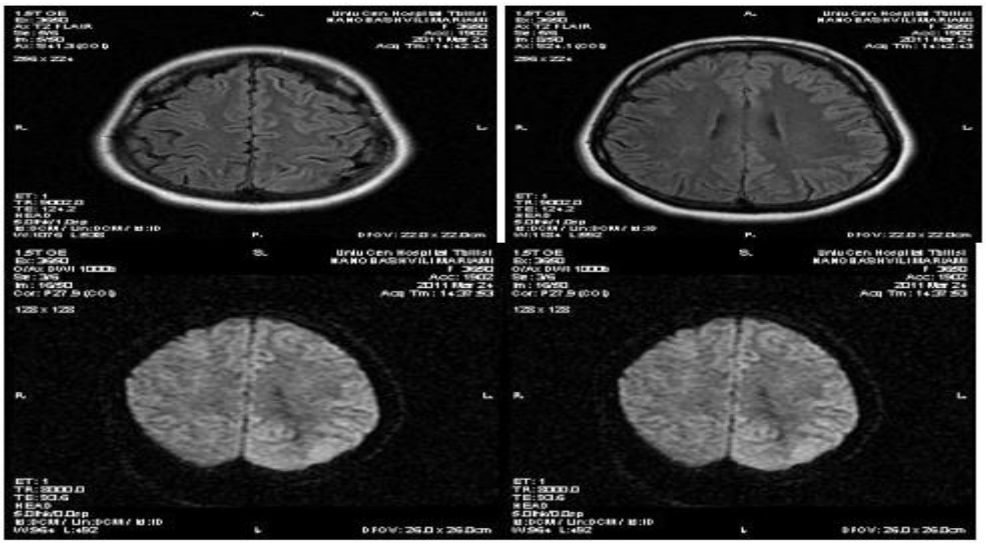
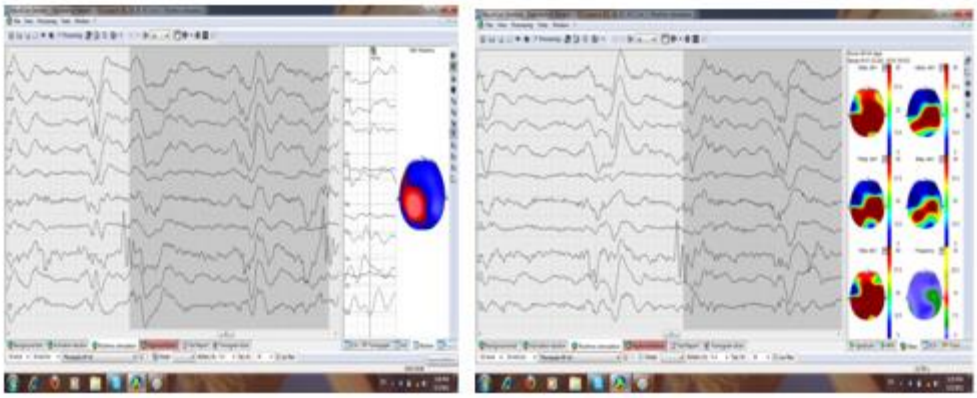
INTRODUCTION

Thrombotic microangiopathy (TMA) is characterized by thrombocytopenia, microangiopathic haemolytic anaemia and end organ damage. Microangiopathic haemolytic anaemia is caused by red blood cell fragmentation in the microvasculature, with schistocytes seen on peripheral blood film. Lactate dehydrogenase (LDH) is raised due to tissue ischemia and cell lysis. Low plasma haptoglobin is a marker of haemolysis as it binds to free haemoglobin and the complex is cleared by macrophages. Coombs test is gener negative. Renal involvement is common to most TMAs due to its vulnerability to occlusion and endothelial damage. ADAMTS13 is an enzyme, which cleaves von Willebrand factor (VWF).[2] Deficiency of ADAMTS13 in TTP results in the formation of ultra large VWF multimers on the endothelium. Platelet attachment to these ultra large multimers occurs in high shear conditions, hemolysis is typically not immune mediated, the direct antiglobulin (Coombs) test is negative. Notably, the clinical findings of MAHA and thrombocytopenia are not universal. Individual features vary,[3, 4] and TMA can be identified on tissue biopsy even in the absence of hematologic abnormalities. This is especially true in subacute or chronic TMA, which may represent a smoldering or previously active process.[6]HUS and TTP is syndroms ,charactarized with microangiopathic hemolityc anemia , trombocytopenia , acute renal falure ,severe neurological violations. In patients with TTP, severely deficient ADAMTS13 activity has been seen in 25–79% of cases at presentation, whereas HUS is not associated with any reduction in activity or absence of ADAMTS13. The combination of clinical and laboratory data, activity of ADAMTS13, and response to plasma exchange allows for better differentiation between these thrombotic microangiopathies,

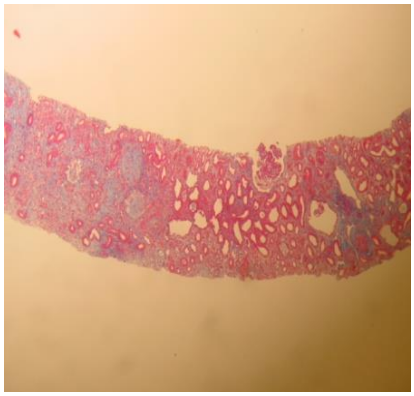
Case-- 32 yars old wumen was admitted in ICU with oligoanuria,chills. Diseases started with diarrhea,vomiting, abdominal pain ,oliguria ,fever .Changes of awareness revealed after generelaized seizuresMRI detected (Flair mode)—cortex damage of left temporal –occipital area(pict2),Lumbar aspirate—protein—0.48g/l,leicocytes—7/mm^3,limph—68%,neutrophils—32%.In lumbar asprate was detected HSV 1 vires. After treatment with aciclovir and repeated investigation of lumbar aspirate , HSV 1 vires was not found .Antibacterial treatment was based on bacteriological investigations and suitable antibacterial therapy.



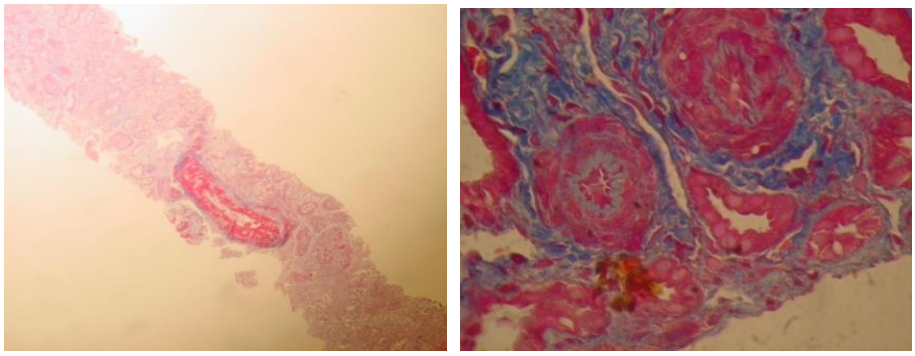
After episodes of focal seizures ,OnEEG revealed generelaized ,spike slow wave activity (pict.1)



Renal biopsy was found 20 glomerulus,in 9 glomerulus was discovered necrotic changing(focal cortical necrosis) ,in 5 glomerulus ---complex replication of basement

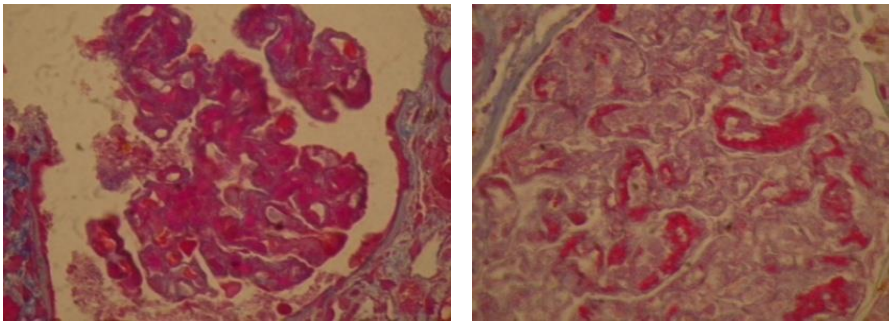


(pict 3,4) membrane and enlargement of mesangial matrix



pict.4 Renal biopsy material

In preglomerular arterioles revealed fibrosis of intima , thrombus into lumen and arterial-arterioles sclerosis . 35% of tubules was necrozed (focaL cortical necrosis) ,remaining part was atrophic with thickening of basament membrane.(pict 5)



In arterial wals and focal glomerulus was found fibrin/ fibrinogen deposits (pict 3,4,5).ADAMTS-13 activity was normal –64.9%(N40-130),ADAMTS -13 antigen was 0.46u/ml,slightly decrased,and antibody was not found

.ADAMTS inhibitor –3.5 u/ml(N<12u/l). At first platelets count was decreased—80000/mm^3,then platelets count returned to normal value. Immunity parameters was normal(schedule1)

Sched.1 Immunological tests

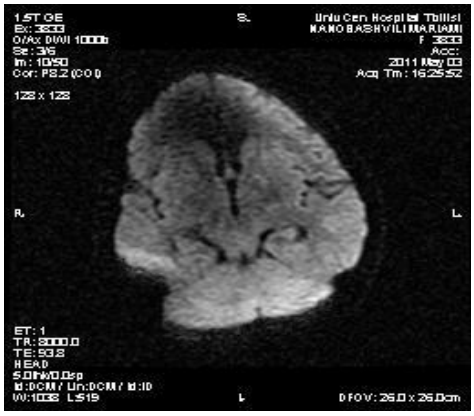
CD3 limphocytes—65%	**IgG 14.3g/l(N8-18)**
CD4 limphocytes –45%(N29-57)	**IgA 3.4g/l(N 0.9-2.5)**
CD4—abs.number—1431(N404—1612)	**IgM—0.2g/l(N0.6—2.8)**
CD8limphocytes—20%(N11-38)	**IgE—9.19 g/l (N<200)**

Antinuclear antibody was not found . In peripheral blood revealed leicocytosis: white blood cell count--41000/mm^3, anisocytosis, shisocytosis, poikilocytosis, Neutrophils count 31.4mg/d l Secondary coagulation hemostasis was changed :decreased antithrombin III, increased soluble fibrin-monomer complex(sched.2)

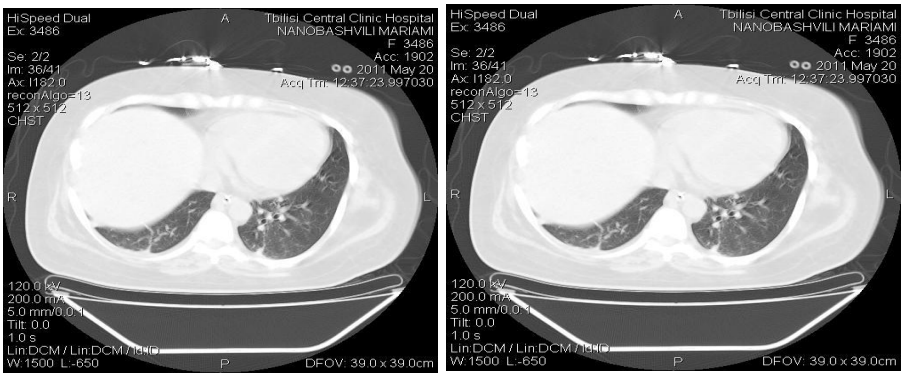
Shed.2 Tests of coagulation hemostasis

FDP --21mg%	**AT-III----70%**
D-dimer 9000 ng/ml(<500ng/ml)	

Chest Ct scan ---detected pneumonia, abdominal CT scan---fluid accumulation .Brain MRI—detected (T2,Flair) ischemic damage in left subcortical nodes(pict6) Brain MRI—detected (T2,Flair) ischemic damage in left subcortical nodes(pict6)

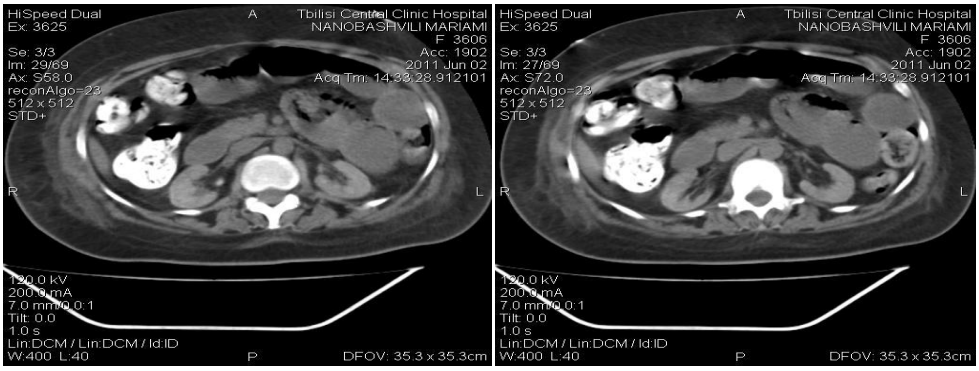


After 25 day from hospitalization neurological state improuved, awareness was adequate, without cognitive violations. lasted renal replacement therapy . Chest Ct scan (pict8) detected improument of lung radiological findings.



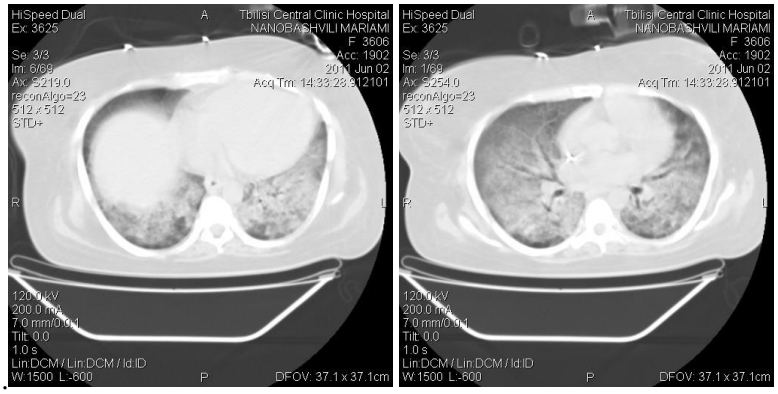
Pict8. Chest CT scan

Patient was extubated, parameters of spontaneous breathing was normal. After one weak revealed abdominal distension,vomiting .Abdomen CT scan and angiography was found bowel distenssion, dynamic obstruction and excluded mezenteric thrombosis. (pict 9)

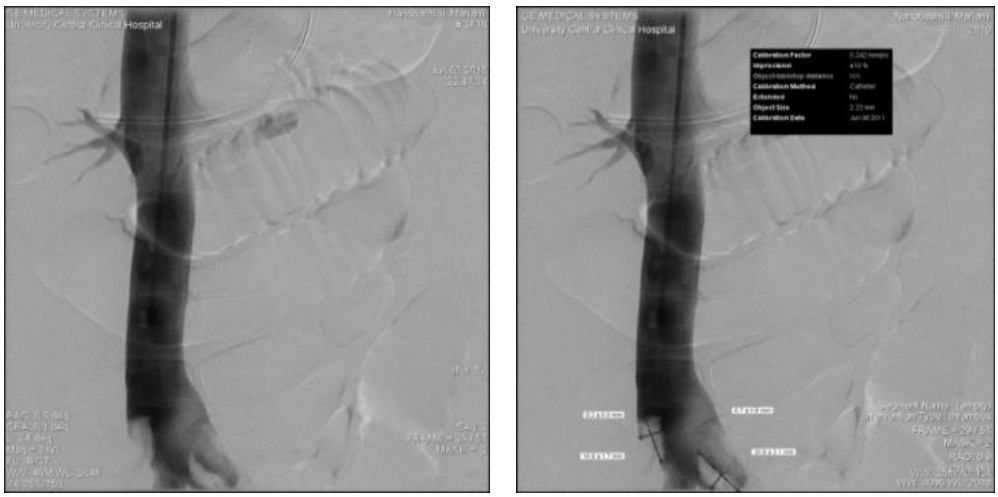


Pict9. Abdomen CT scan

Later patient state was aggravated , developed acute respiratory failure .Chest CT scan detected bilateral pneumonia.(pict 10)



Low extremity vessels ultrasonography revealed thrombus in common femoral ,deep femoral vein .Despite suitable treatment ,ventilation parametres worsened.Echocardiography revealed dilation of right chambers ,increased PASP(65mm.hg).Low extremity vessels ultrasonography revealed thrombus in left external iliac and great saphenous vein.After cavagraphy in vena cava bifurcation area detected filling defects- thrombus --8.2X16.8. and 6.7X 20.8 (pict 11).In infrarenal part of inferior vena cava was performed placement of vena cava filter(Vena Teech LP,B.Braun Medical **)**



Pict 11.Cavagraphy. Placement of filter

Regardless of suitable treatment developed severe obstructive shock

DISCUTION

D iagnosis was based on rezults of renal biopsy and morphological researches,laboratory and clinical parameters.MRI detected left side subcortical nodes ischemic damage.In lumbar aspirate by PCR method detected vires (HSV1).Patient was treated with antiviral drugs (ZOVIRAX),For treatment of sepsis was identificated source of infection(pneumonia,VAP) , .LDH level was high, Haptoglobin level was decreased ,what referred to microangipathic hemolysis .In peripheral blood smear revealed red bloos cells fragmentation ,reduction of

platelet count .D dimer and FDP level was increased . after renal biopsy,in arterial wall and in glomerulrs was found fibrin/fibrinogen deposits . Reason of renal failure was thrombic microangiopathy ,activation of platelets after endothelium damage and activation of coagulation hemostasis. In several glomerulus detected 35% necrosed tubules and remainig part of tubuls was atrophic . Patient was treated with renal replacement therapy , plasma exchange therapy. Causes of coma was thrombic microangiopathy , also accompanying reasons.For prevention of thrombosis was used anticoagulation ,nevertheless developed DVT,pulmonary embolizm , low vena cava thrombosis . Establishing the diagnosis of TTP / HUS was a 2-step process: verifying the presence of triad of microangiopathic hemolytic anemia and thrombocytopenia, Clinical differentiation of hemolytic-uremic syndrome (HUS) and TTP is often based on the presence of CNS involvement in TTP and the more severe renal involvement in HUS. Level of ADAMTS13 activity was nondeficient. Patients with TTP have either an inherited or an acquired lack of this protease activity whereas those with HUS do not have an abnormality of the enzyme.This patient despite so wide involvement of CNS , ADAMTS13 activity was not deficient.We presented the case,when the disease started with bloody diarrhea,vomiting .By fecal bacteriological analysis microbes has not been identified. Unconsciousness was manifested after hospitalization with generalized seizures.MRI was rivealed temporal and parietal cortex damage,later left ischemic damage of left subcoritical nodes,what probably was the reason of seizures. LDH and haptoglobin level was reffered microangiopathic haemolysis . In the smears of peripheral blood was observed erythrocyte fragmentation.Platelets counts was mildly decreased, FDP increased (D dimer also increased).Therefore genesis of renal failure and coma was thrombotic microangiopathy and other encompanying causes. In this patient, despite such extensive involvement of the CNS, ADAMTS13 activity was not inadequate, the treatment was effective, including plasma exchange,what suggested that the patient had HUS. The manifestation of this syndrome sometimes is atypical . The adequate assessment of clinical signs in premorbid period ,adequate exploration of organ dysfunction , using diagnostic methods after hospitalization and appropriate treatment gives the real chance to convalescence observed erythrocyte fragmentation.Platelets counts was mildly decreased ,FDP increased(D dimer also increased).Therefore genesis of renal failure and coma was thrombotic microangiopathy and other encompanying causes. In this patient, despite such extensive involvement of the CNS, ADAMTS13 activity was not inadequate, the treatment was effective, including plasma exchange,what suggested that the patient had HUS. The manifestation of this syndrome sometimes is atypical . The adequate assessment of clinical signs in premorbid period ,adequate exploration of organ dysfunction , using diagnostic methods after hospitalization and appropriate treatment gives the real chance to convalescence

REFERENCES

I. Diagnosis and treatment of thrombotic microangiopathy Gemma L Thompson [1,2], David Kavanagh [1,2,✉] Int J Lab Hematol 2022 Sep 8;44(Suppl1):101–113. doi: 10.1111/ijlh.13954Clinical Evaluation and

II. Management of Thrombotic Microangiopathy Joshua Leisring, Sergey V. Brodsky, Samir V. Parikh : 23 August 2023 https://doi.org/10.1002/art.42681

III. Brocklebank V, Wood KM, Kavanagh D. Thrombotic microangiopathy and the kidney. Clin J Am Soc Nephrol. 2018;13(2):300-317. [DOI] [PMC free article] [PubMed] [Google Scholar]

IV. Moake JL. Thrombotic microangiopathies. N Engl J Med. 2002;347(8):589-600. [DOI] [PubMed] [Google Scholar]

V. Scully M, Yarranton H, Liesner R, et al. Regional UK TTP registry: correlation with laboratory ADAMTS 13 analysis and clinical features. Br J Haematol. 2008;142(5):819-826. [DOI] [PubMed] [Google Scholar]

VI. Alwan F, Vendramin C, Vanhoorelbeke K, et al. Presenting ADAMTS13 antibody and antigen levels predict prognosis in immune-mediated thrombotic thrombocytopenic purpura. Blood. 2017;130(4):466-471. [DOI] [PubMed] [Google Scholar

VII. Atypical Hemolytic-Uremic Syndrome: A Case Report and Literature ReviewArsalan Rafiq,[A,B,C,D,E,F] Hassan Tariq,[A,B,C,E,F] Naeem Abbas,[E,F] and Roopalekha Shenoy[A,E], Am J Case Rep. 2015; 16: 109–114.Published online 2015 Feb 24. doi: 10.12659/AJCR.892907

VIII. Anti-Factor H Autoantibody–Associated Hemolytic Uremic Syndrome: Review of Literature of the Autoimmune Form of HUS. Marie-Agnes Dragon-Durey,Caroline Blanc,Nature reviews Nephrology8,622-633,November2012 doi:10.1038/neph. 2012.

IX. Platelet count and prothrombin time help distinguish thrombotic thrombocytopenic purpura-hemolytic uremic syndrome from DIC in adults.PARK IA-AM j Clin Pathol-01-MAR-2010;133(3):460-5

X. Therapeutic plasma exchange in patients with TTP-HUS :the 10 year experience of a single center.Kirn -Hematology -01-MAR-2011;16(2):73-9

XI. Atypical hemolytic uremic syndrome and thrombotic thrombocytopenic purpura: clinically differentiating the thrombotic microangiopathies. Nester CM, Thomas CP. Eur J Intern Med. 2013;24(6):486–91. [PubMed]

XII. Diagnostic criteria for atypical hemolytic uremic syndrome proposed by the Joint Committee of the Japanese Society of Nephrology and the Japan Pediatric Society. Clin Exp Nephrol. 2014;18(1):4–[PubMed]

XIII. Neurological involvement in children with E. coli O104:H4-induced hemolytic uremic syndrome. Bauer A, Loos S, Wehrmann C, et al. Pediatr Nephrol 2014; 29:1607.

XIV. Thrombotic microangiopathy(TTP and HUS):advances in differentiation and diagnosis.Schneide M-Clin Lab SCI-oi-oct-2007;20(4):216-20

XV. Interventions for hemolytic-uremic syndrome and thrombotic-thrombocytopenic purpura,a systematic review of randomized contolled trials.Michaelem-AM j Kidney dis-01-Feb-2009;53(2):259-72

XVI. A Case Report and Literature Review of Eculizumab Withdrawal in Atypical HemolyticUremic Syndrome. Borja Quiroga ,Alberto de Lorenzo ,Cristina Vega ,Fernando de Alvaro, Am J Case Rep, 2016; 17: 950-956

XVII. Acute neurological involvement in diarrhea-associated hemolytic uremic syndrome. Nathanson S, Kwon T, Elmaleh M, et al. Clin J Am Soc Nephrol 2010; 5:1218.

XVIII. Atypical hemolytic uremic syndrome-Kavanagh D-Curr opin hematol-01-Sep-2010;15(5):432-8

XIX. Is there a shared pathophysiology for TTP and HUS?-Desch K-j.AM Soc Nephrol-01 sep-2007;18(9):2457-60

XX. HUS and atypical HUS**. Blood.** 2017 May 25; 129(21): 2847–2856.

XXI. oh CH, Alhamdi Y, Abrams ST. Current pathological and laboratory considerations in the diagnosis of disseminated intravascular coagulation. Ann Lab Med. 2016;36(6):505-512. [PMC free article] [PubMed] [Google Scholar]

XXII. Nester CM, Barbour T, de Cordoba SR, et al. Atypical aHUS: State of the art. Mol Immunol. 2015;67(1):31-42. [PubMed] [Google Scholar]

XXIII. Kielstein JT, Beutel G, Fleig S, et al. ; Collaborators of the DGfN STEC-HUS registry. Best supportive care and therapeutic plasma exchange with or without eculizumab in Shiga-toxin-producing E. coli O104:H4 induced haemolytic-uraemic syndrome: an analysis of the German STEC-HUS registry. Nephrol Dial Transplant. 2012;27(10):3807-3815.[PubMed] [Google Scholar]

XXIV. Scully M, Goodship T. How I treat thrombotic thrombocytopenic purpura and atypical haemolytic uraemic syndrome. Br J Haematol. 2014;164(6):759-766. [PMCfree article] [PubMed] [Google Scholar]