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One complicated case of thrombotic microangiopathy

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Abstract
HUS and TTP is syndroms,charactarized with microangiopathic hemolityc anemia, trombocytopenia, acute renal falure,severe neurological violations.Bloody diarrhea is caused with E.Coli(0157:H7).In georgia revealed other strain –E.coli(0104:H4).We prezented case when ilness started with bloody diarrhea, oliguria and neurological changing(coma, seizures.).. ADAMTS13 levels < 10% with the presence of antibody against ADAMTS13 is characteristic of most adults with TTP and these patients respond to plasma exchange. Testing for ADAMTS13 activity is appropriate in patients with suspected TTP-HUS, The combination of clinical and laboratory data, activity of ADAMTS13, and response to plasma exchange allows for better differentiation between these thrombotic microangiopathies, which itself is very important considering that both have different treatment options. Thrombotic microangiopathies are diseases characterized by thrombocytopenia, erythrocyte fragmentation, and elevated levels of LDH. Thickening of the arterioles and capillary walls with prominent endothelial swelling and detachment and subendothelial accumulation of proteins and cell debris characterize and define the pathologic lesion seen in all thrombotic microangiopathies. 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. Patient admitted in hospital after one weak from onset of clinical simptoms. Regardless of bacteriological investigations of feces, the microb does not revealed.Progress of disease was severe,with many complication:renal failure with severest neurological violations. 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.

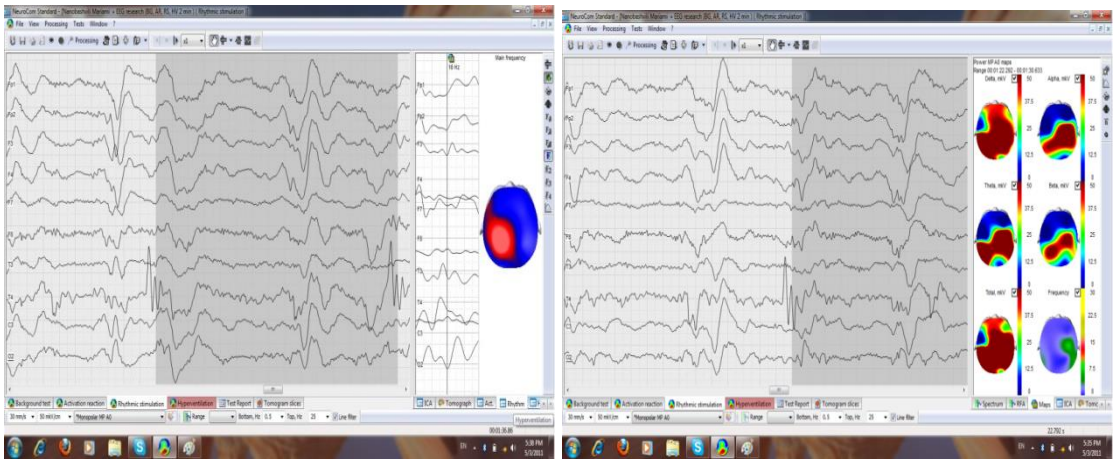
Keywords: HUS,renal replacement therapy,coma,vena cava thrombosis

Introduction
HUS and TTP is syndroms,charactarized with microangiopathic hemolityc anemia, trombocytopenia, acute renal falure,severe neurological violations.Bloody diarrhea is caused with E.Coli(0157:H7).In georgia revealed other strain –E.coli(0104:H4).We prezented case when ilness started with bloody diarrhea, oliguria and neurological changing(coma, seizures.).. ADAMTS13 levels < 10% with the presence of antibody against ADAMTS13 is characteristic of most adults with TTP and these patients respond to plasma exchange. Testing for ADAMTS13 activity is appropriate in patients with suspected TTP-HUS, The combination of clinical and laboratory data, activity of ADAMTS13, and response to plasma exchange allows for better differentiation between these thrombotic microangiopathies, which itself is very important considering that both have different treatment options. Thrombotic microangiopathies are diseases characterized by thrombocytopenia, erythrocyte fragmentation, and elevated levels of LDH. Thickening of the arterioles and capillary walls with prominent endothelial swelling and detachment and subendothelial accumulation of proteins and cell debris characterize and define the pathologic lesion seen in all thrombotic microangiopathies. 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. Patient admitted in hospital after one weak from onset of clinical simptoms.Regardless of bacteriological investigations of feces, the microb does not revealed.Progress of disease was severe,with many complication:renal failure with severest neurological violations.

Case

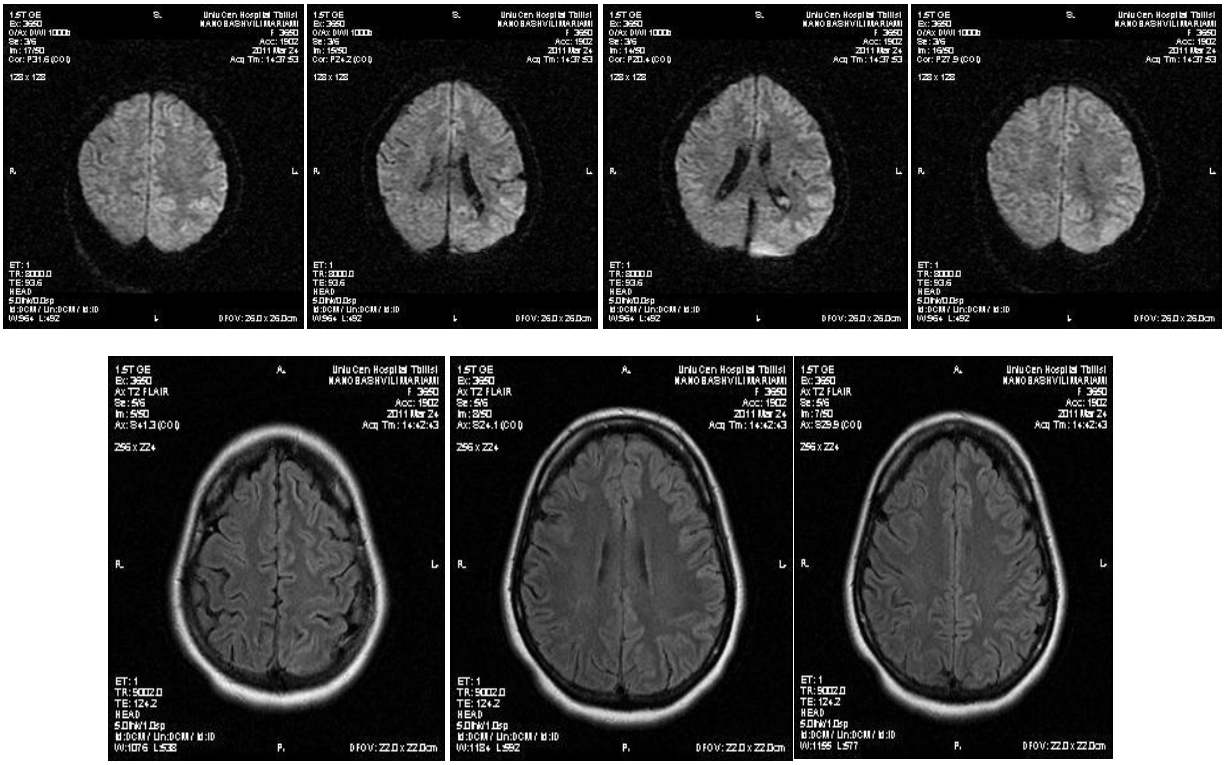
32 yars old wumen was admitted in ICU with oligoanuria,chills. Diseases started with diarrhea,vomiting, abdominal pain,oliguria,fever.Changes of awareness revealed after generelaized seizures. Patient was intubated and started artifitial ventilation. Brain CT scan revealed ventriculs dilatation,Without dislocation of midline structures. After episodes of focal seizures treatment was started with carbamazepin(400mg per day).OnEEG revealed generelaized,spike slow wave activity (pict.1)



Pict.1: EEG

MRI 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.



Pict.2: BBrain MRI

At first creatinine, LDH and urea level was high(6.72mg/dl.198 mg/dl,3916 u/l). After renal biopsy was found 20 glomerulus,in 9 glomerulus was discovered necrotic changing(focal cortical necrosis),in 5 glomerulus ----complex replication of basement

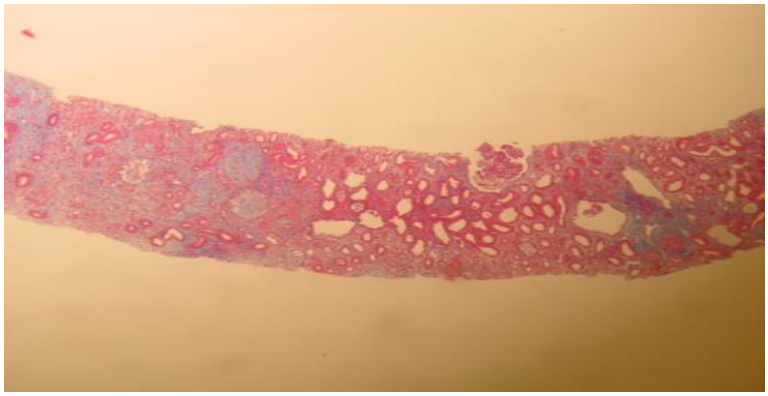
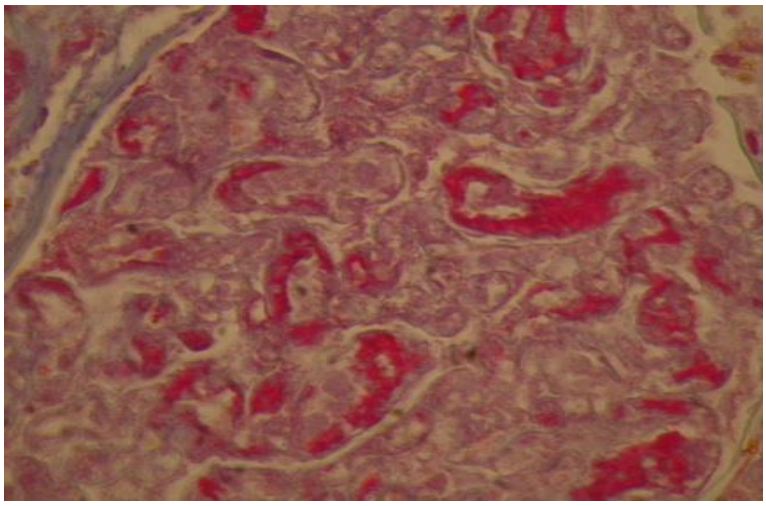
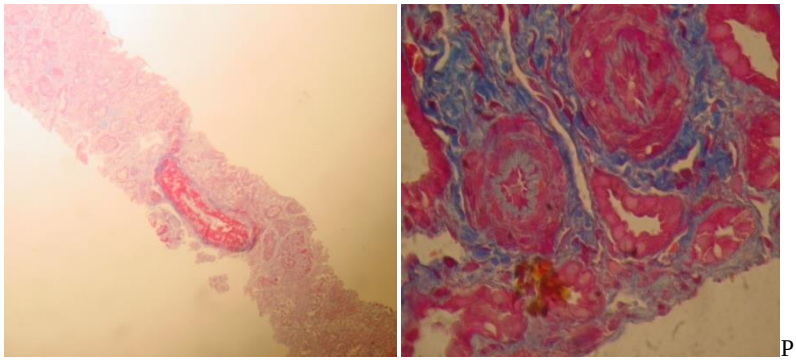


Fig.3: membrane and enlargement of mesangial matrix (pict 3, 4)



Pict.3: Renal biopsy material



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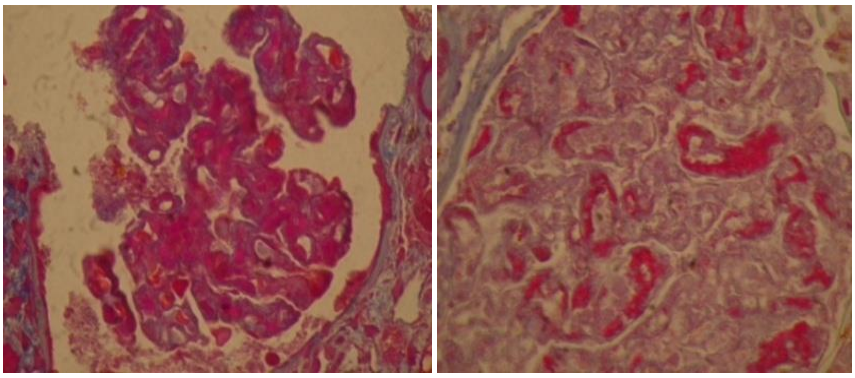
Pict.4: Renal biopsy material

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)



Pict.5: Renal biopsy material

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)

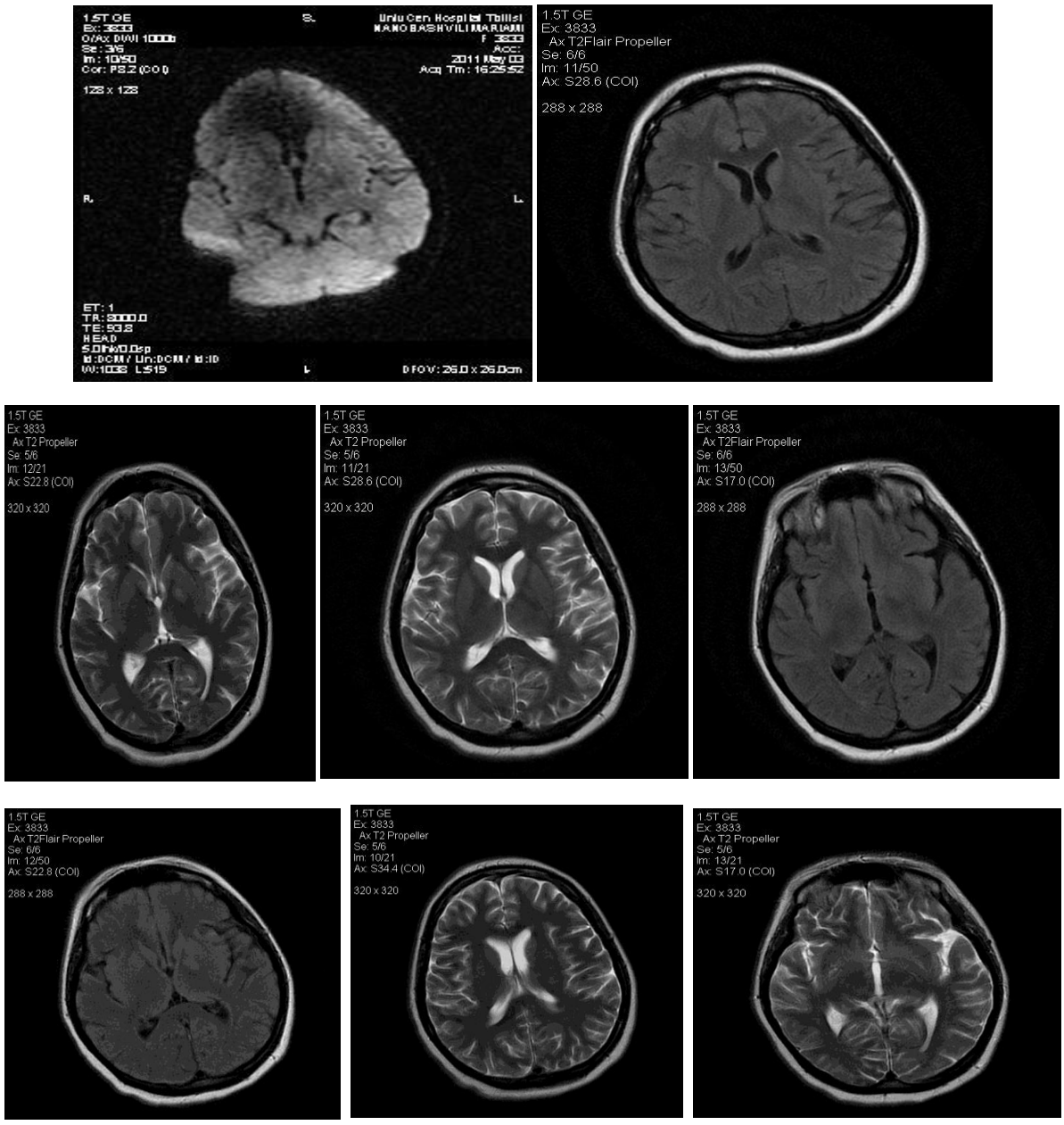
Antinuclear antibody was not found.In peripheral blood revealed leicocytosis: white blood cell count--41000/mm^3, anisocytosis,shisocytosis,poikilocytosis,Neutrophils count 31.4mg/d l

Secondary coagulation hemostasis was changed: decreased antithrombin III, increased soluble fibrin-monomer complex (sched.2)

Sched.2: Tests of coagulation hemostasis

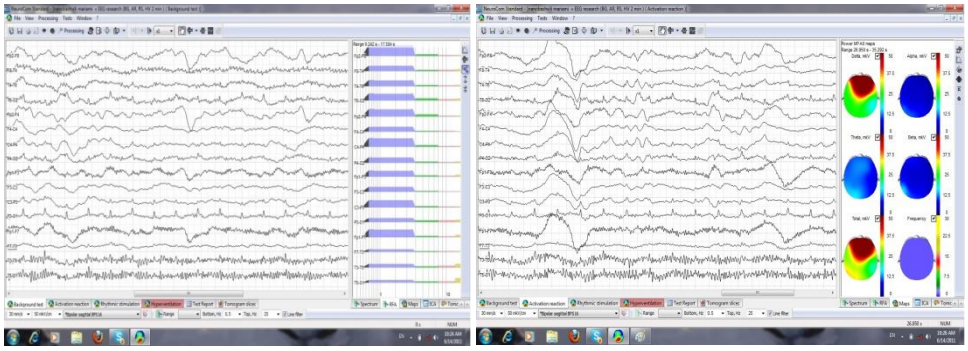
FDP --21mg%	AT-III----70%
D-dimer 9000 ng/ml(<500ng/ml)	

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



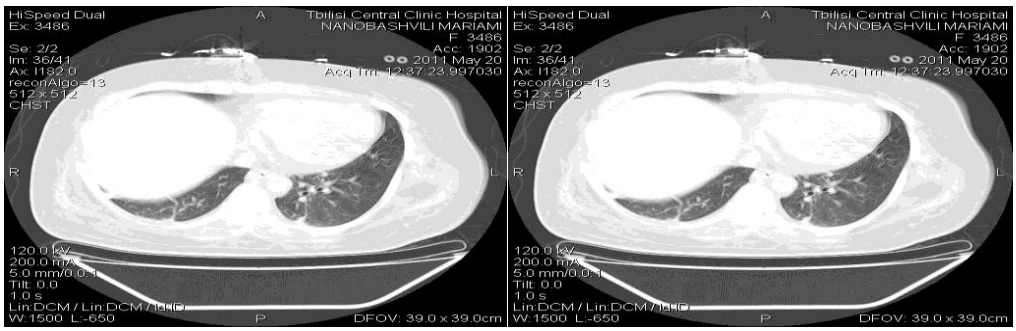
Pict.6: Brain MRI

EEG—detected low ammplitude waves,without specific pathological activity (pict7)



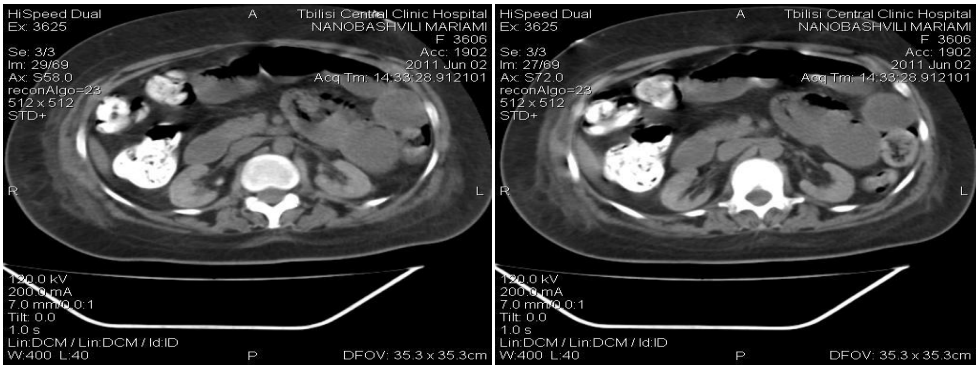
Pict. 7: EEG

After 35 day from hospitalization neurological state improved, awareness was adequate,without cognitive violations.lasted renal replacement therapy. Chest Ct scan (pict8) detected improument of lung radiological findings.



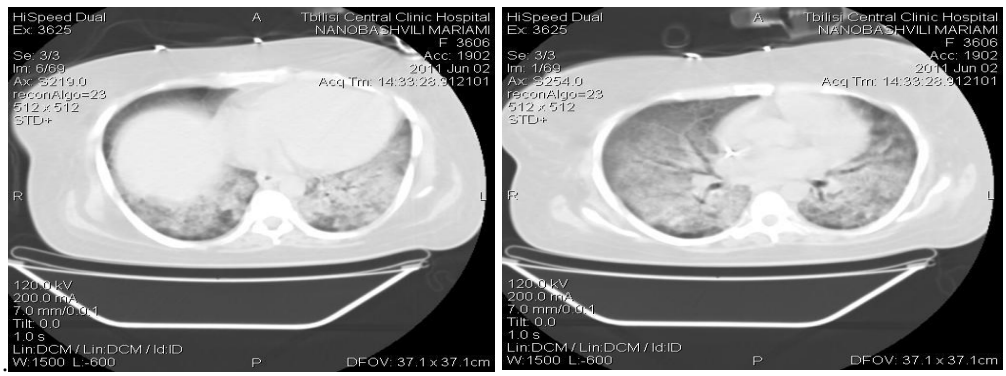
Pict. 8: Chest CT scan

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)



Pict. 9: Abdomen CT scan

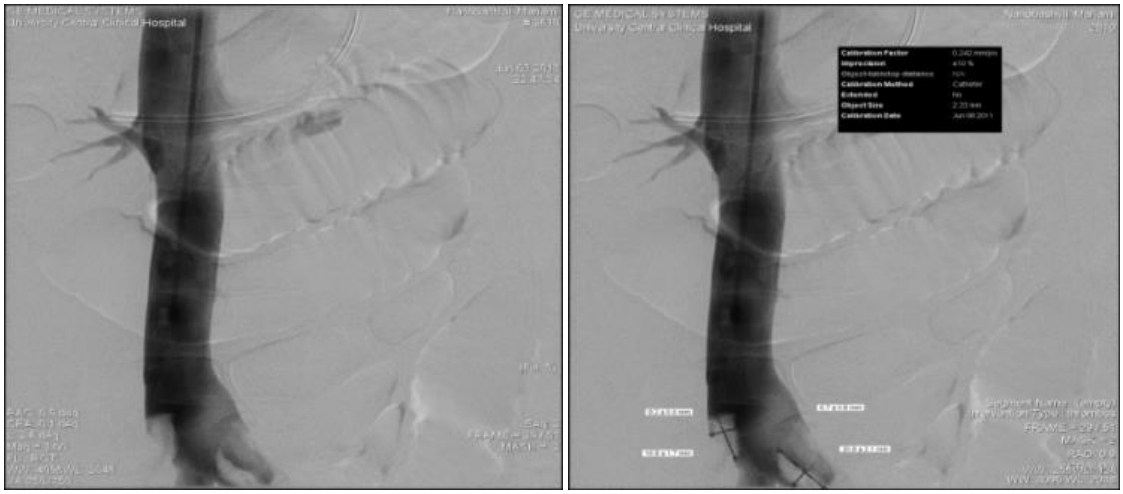
Later patient state was aggravated, developed acute respiratory failure.Chest CT scan detected bilateral pneumonia.(pict 10)



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.

Discussion

desease started with bloody diarrhea, vomiting.After 7 day from onset patient was admitted in hospital.Identification of microb was not possible with Feces bacteriological analysis. D iagnosis was based on rezults of renal biopsy and morphological researches,laboratory and clinical parameters. unconciousness and right side hemiparesis revealed after seazures.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, excluding systemic/secondary conditions that would cause this changings. In HUS, an antecedent history of diarrheal illness was presented. 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. Among other causes, disseminated intravascular coagulation could also cause microangiopathic hemolytic anemia and thrombocytopenia, but it was distinguished by laboratory results.

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

Conclusion

The manifestation of this syndrome sometimes is atypical. We presented the case,when the disease started with bloody diarrhea,vomiting.By fecal bacteriological analysis microbes has not been identified. 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

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