TROMBOTIČNA MIKROANGIOPATIJA KAO PRVA MANIFESTACIJA DISEMINOVANE MALIGNE BOLESTI

PRIKAZ SLUČAJA

CASE REPORT

THROMBOTIC MICROANGIOPATHY AS THE FIRST MANIFESTATION OF DISSEMINATED MALIGNANT DISEASE

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SAŽETAK

Uvod: Trombotične mikroangiopatije su grupa bolesti koje karakterišu diseminovana intravaskularna tromboza, trombocitopenija i ishemijsko oštećenje organa. U ovu grupu spadaju trombotična trombocitopenijska purpura i hemolitičko-uremijski sindrom. Mada retko, jedan od uzroka trombotične mikroangiopatije mogu biti i maligne bolesti, pre svega karcinomi želuca, prostate, dojke i pluća.

Prikaz bolesnika: Prikazujemo pacijentkinju sa trombotičnom mikroangiopatijom i diseminovanom malignom bolešću nejasne etiologije.

Zaključak: Ovaj klinički entitet se naziva trombotična mikroangiopatija udružena sa tumorima. Prvi put je opisana 1970. godine, ali je do danas opisano svega nekoliko desetina slučajeva. S obzirom na veliku smrtnost, treba misliti o njemu kod pacijenata sa malignom bolešću, prisutnom mikroangiopatskom hemoliznom anemijom i trombocitopenijom.

Ključne reči: trombotična mikroangiopatija, trombotična trombocitopenijska purpura, hemolitičko-uremijski sindrom

ABSTRACT

Introduction: Thrombotic microangiopathies are a group of diseases characterized by disseminated intravascular thrombosis, thrombocytopenia and ischemic organ damage. This group includes thrombotic thrombocytopenic purpura and hemolytic-uremic syndrome. One of the causes of thrombotic microangiopathy, although rare, can also be malignant diseases, primarily cancers of the stomach, prostate, breast and lungs.

Case report: We present a patient with thrombotic microangiopathy and disseminated malignant disease of unclear etiology.

Conclusion: This clinical entity is called carcinoma-associated thrombotic microangiopathy and was first described in 1970. However, only a few dozen cases have been described to date. Considering the high mortality, it should be considered in patients with malignant disease, microangiopathic hemolytic anemia, and thrombocytopenia.

Key words: thrombotic microangiopathy, thrombotic thrombocytopenic purpura, hemolytic-uremic syndrome

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Primljeno • *Received*: November 11, 2022; **Revidirano • *Revised*:** November 28, 2022; **Prihvaćeno • *Accepted*:** December 10, 2022; ***Online first*:** December 15, 2022

DOI: 10.5937/smclk3-40946

UVOD

Trombotične mikroangiopatije (TMA) su grupa bolesti koje karakterišu diseminovana intravaskularna tromboza, trombocitopenija i ishemijsko oštećenje organa. U njih spadaju trombotična trombocitopenijska purpura (TTP) i hemolitičko-uremijski sindrom (HUS) [1].

Trombotična trombocitopenijska purpura je retka bolest, koja se ispoljava pentadom kliničkih nalaza, a to su: trombocitopenija, mikroangiopatska neimuna hemolizna anemija, oštećenje funkcije bubrega, povišena telesna temperatura i neurološki deficiti. Retko se dešava da je kod jednog pacijenta ispoljena kompletna pentada, ali trombocitopenija i mikroangiopatska hemolizna anemija predstavljaju obavezni klinički nalaz [2]. Za razliku od trombotične trombocitopenijske purpure, gde je oštećenje bubrega retka i najčešće blaga manifestacija bolesti, kod obolelih od hemolitičko-uremijskog sindroma, oštećenje bubrega je redovna pojava i sa trombocitopenijom i mikroangiopatskom hemoliznom anemijom čini kliničku trijadu HUS-a [3].

Trombotična mikroangiopatija udružena sa tumorima prvi put je opisana 1970. godine [4]. Od tada je opisano više desetina slučajeva pacijenata obolelih od karcinoma želuca, prostate, dojke, pluća, ređe i od karcinoma drugih lokalizacija i limfoma, koji su imali trombotičnu mikroangiopatiju. Klinička slika ovih pacijenata varira od tipične prezentacije TTP-a i HUS-a, koja je ređa, do atipične kliničke prezentacije pacijenata, koji imaju samo mikroangiopatsku hemoliznu anemiju i trombocitopeniju, bez ili sa minimalnim neurološkim oštećenjem ili bubrežnom insuficijencijom [5,6].

Ovaj prikaz slučaja opisuje trombotičnu mikroangiopatiju kao komplikaciju diseminovane maligne bolesti nejasne etiologije.

PRIKAZ SLUČAJA

Šezdesetčetvorogodišnja pacijentkinja se inicijalno javila hematologu zbog malaksalosti, gubitka apetita, te laboratorijski verifikovane anemije i trombocitopenije. Vrednost hemoglobina u krvi kod ove pacijentkinje je bila 54 g/l, dok je vrednost trombocita bila 30 x 10^9/l. U ponovljenoj krvnoj slici, u hematološkoj ambulanti, vrednost hemoglobina je bila 53 g/l, dok je *MCV* indeks zapremine eritrocita (engl. *mean cell volume index*) iznosio 98 fl, a broj trombocita 19 x 10^9/l, uz normalan broj leukocita i urednu leukocitarnu formulu. Nakon pregleda, pacijentkinja je hospitalizovana na Klinici za hematologiju Univerzitetskog kliničkog centra Kragujevac. U ličnoj anamnezi, pacijentkinja je navela hipertenziju i dijabetes, koji je lečen oralnim antidijabeticima. Osim bledila kože i sluznica, fizikalni pregled pacijentkinje je bio uredan. Pacijentkinji je ordinirana

INTRODUCTION

Thrombotic microangiopathies (TMA) are a group of diseases characterized by disseminated intravascular thrombosis, thrombocytopenia and ischemic organ damage. This group includes thrombotic thrombocytopenic purpura (TTP) and hemolytic-uremic syndrome (HUS) [1].

Thrombotic thrombocytopenic purpura is a rare disease which manifests as a pentad of clinical findings, namely: thrombocytopenia, microangiopathic nonimmune hemolytic anemia, renal function impairment, elevated body temperature, and neurological deficits. It rarely occurs that the entire pentad manifests in one patient, however, thrombocytopenia and microangiopathic hemolytic anemia are always a part of the clinical finding [2]. As opposed to thrombotic thrombocytopenic purpura, wherein kidney damage is a rare and most frequently mild manifestation of disease, in patients suffering from hemolytic-uremic syndrome, kidney damage is a regular occurrence and, together with thrombocytopenia and microangiopathic hemolytic anemia, it makes up the HUS clinical triad [3].

Carcinoma-associated thrombotic microangiopathy was first described in 1970 [4]. Since then, a few dozen cases have been described wherein patients suffering from gastric, prostate, breast, and pulmonary cancer, and less frequently from carcinomas of other localization and lymphomas, also had thrombotic microangiopathy. The clinical presentation of these patients varies – from typical TTP and HUS presentation, which is rarer, to atypical clinical patient presentation, wherein patients only have microangiopathic hemolytic anemia and thrombocytopenia, without or with minimal neurological damage or renal insufficiency [5,6].

This case report describes thrombotic microangiopathy as a complication of disseminated malignant disease of unclear etiology.

CASE REPORT

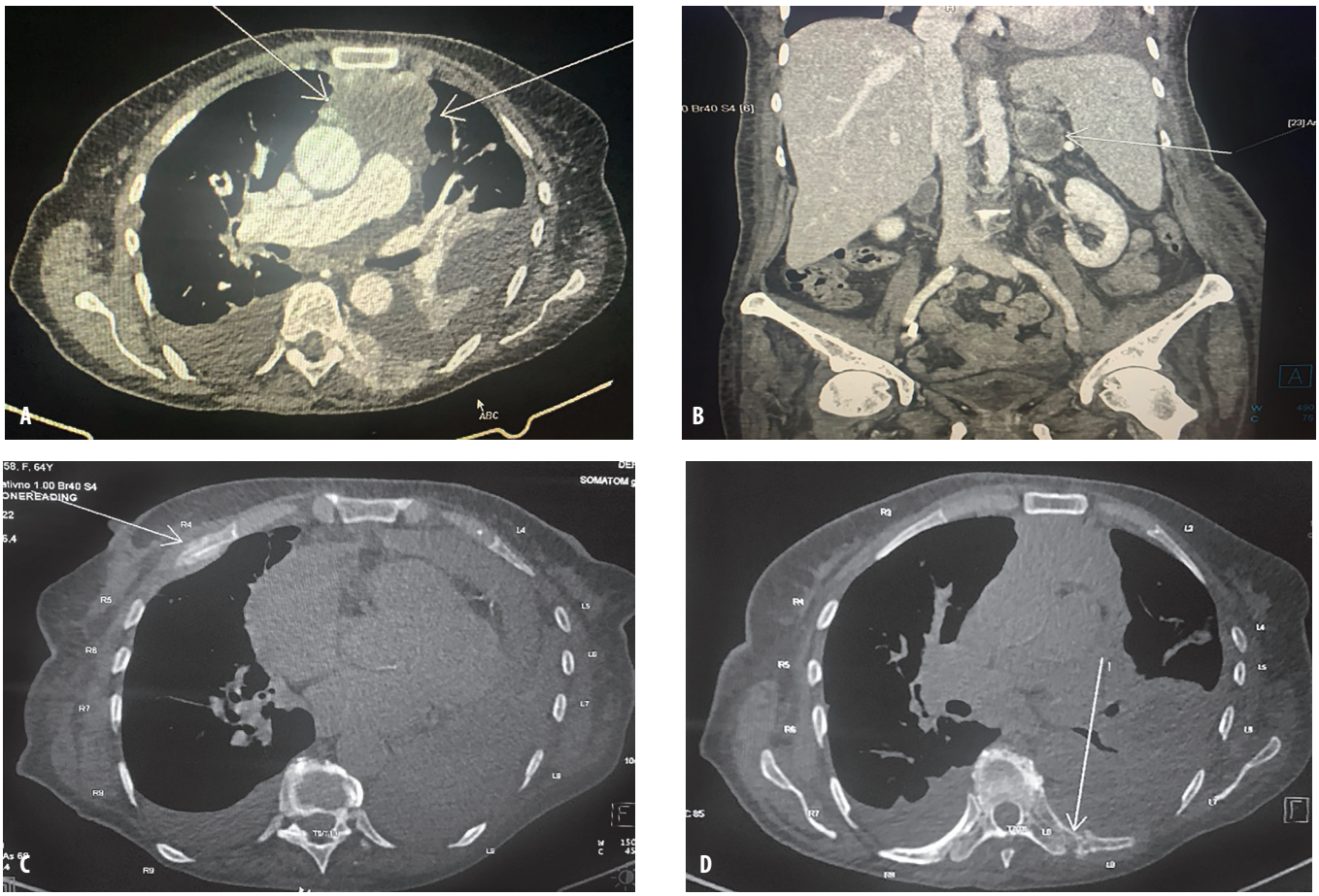
A sixty-four-year-old patient was initially referred to a hematologist due to malaise and weakness, loss of appetite, and anemia and thrombocytopenia, which was verified by laboratory tests. The hemoglobin blood level in this patient was 54 g/l, while the platelet count was 30 x 10^9/l. A repeated blood test, performed in the hematology laboratory, yielded a hemoglobin level of 53 g/l, an MCV index (mean cell volume index) of 98 fl, and a platelet count of 19 x 10^9/l, while the leukocyte count and differential were normal. After the examination, the patient was admitted to the Clinic of Hematology of the University Clinical Center of Kragujevac. In her personal history, the patient reported hypertension and diabetes, for which she was taking oral antidiabetics.

transfuzija dve doze deplazmatisanih eritrocita, nakon koje je hemoglobin pacijentkinje iznosio 74 g/l.

Urađene su dodatne laboratorijske pretrage. Vrednost laktat dehidrogenaze je iznosila 5.965 IU/l (normalna vrednost: do 241 IU/l); vrednost ukupnog bilirubina je bila 70,7 µmol/l (normalna vrednost: 2 – 21 µmol/l); vrednost direktnog bilirubina je bila 7,9 µmol/l (normalna vrednost: 1 – 5 µmol/l); broj retikulocita je iznosio 10,5% (normalna vrednost: do 2%); vrednost haptoglobina je bila 0,1 g/l (normalna vrednost: 0,5 – 2,2 g/l). U analizama hemostaze, utvrđena je povišena vrednost D-dimera od 1.298 ng/ml (normalna vrednost: do 240 ng/ml), kao i blago produženo protrombinsko vreme od 14,5 s (normalna vrednost: 11 – 13,5 s). Ostali parametri hemostaze, uključujući i antitrombin 3, bili su u referentnom opsegu. Analizom tumor markera, dobijene su nemerljivo visoke vrednosti *CA* (engl. *cancer antigen*) 19-9 i *CA* 72-4. Započeta je hitna terapijska izmena plazme (TIP), ukupno dva volumena plazme pacijentkinje dnevno, uz primenu pronizona u dozi od 2 mg/kg. Nakon četiri dana tera-

Apart from pallor of the skin and mucosa, the patient's physical exam was normal. A transfusion of two doses of deplasmatized erythrocytes was administered to the patient, upon which her hemoglobin level was 74 g/l.

Additional laboratory tests were performed. The value of lactate dehydrogenase was 5,965 IU/l (normal value: up to 241 IU/l); the level of total bilirubin was 70.7 µmol/l (normal value: 2 – 21 µmol/l); the level of direct bilirubin was 7.9 µmol/l (normal value: 1 – 5 µmol/l); the reticulocyte count was 10.5% (normal value: up to 2%); the level of haptoglobin was 0.1 g/l (normal value: 0.5 – 2.2 g/l). In the hemostasis analysis, an elevated D-dimer level of 1,298 ng/ml was registered (normal value: up to 240 ng/ml), as well as slightly prolonged prothrombin time of 14.5 s (normal value: 11 – 13.5 s). Other parameters of hemostasis, including antithrombin 3, were within the reference range. Tumor marker analyses revealed immeasurably high values of cancer antigen (CA) 19-9 and CA 72-4. Emergency therapeutic plasma exchange (TPE) was initiated, a total of two patient plasma volumes a day, with the application of 2 mg/kg of



Slika 1. Multislajsna kompjuterizovana tomografija grudnog koša, abdomena i male karlice (engl. *multi-slice computed tomography – MSCT*)
A) Konglomerati limfnih nodusa u medijastinumu; B) Metastatska promena u levoj nadbubrežnoj žlezdi; C) Metastatska promena u prednjem okrajku četvrtog rebra desno; D) Metastatske promene u zadnjem okrajku osmog rebra levo

Figure 1. Multi-slice computed tomography (MSCT) of the thorax, abdomen, and lesser pelvis
A) Conglomerate masses of lymph nodes in the mediastinum; B) Metastatic lesion in the left adrenal gland; C) Metastatic lesion on the anterior end of the fourth right rib; D) Metastatic lesions on the posterior end of the eighth left rib

pije, vrednost hemoglobina je porasla na 87 g/l, dok je broj trombocita dostigao 45 x 10^9/l, ali zbog razvoja respiratorne insuficijencije nije bilo moguće uraditi gastroduodenoskopiju. Pacijentkinji su ordinirani kiseonik, preko oronazalne maske, i bronhodilatatori.

Urađena je multislajsna kompjuterizovana tomografija grudnog koša, abdomena i male karlice, na kojoj je uočeno sledeće: više konglomerata patoloških limfnih nodusa u medijastinumu (najveći je bio promera 60 x 46 mm), intraperikardni izliv – promera 22 mm, sekundarni depoziti u jetri (najveći je bio promera 13 mm), te sekundarni depozit na levom nadbubregu – promera 29 x 28 mm. Kada su u pitanju koštane strukture, uočeni su sekundarni depoziti na četvrtom rebru desno i osmom rebru levo, kao i gasne inkluzije u pršljenovima T8 i L2. Sluznica želuca nije opisana, iz tehničkih razloga (Slika 1).

Nakon sedam dana od početka bolesti, nastavljena je TIP i kortikosteroidna terapija. Vrednost hemoglobina je u tom trenutku iznosila 88 g/l, broj trombocita je bio 49 x 10^9/l, vrednost laktak dehidrogenaze je bila 1.720 IU/l, dok je vrednost ukupnog bilirubina iznosila 32,2 μmol/l, a direktnog bilirubina 5,2 μmol/l. Osmog dana od početka terapije, došlo je do respiratornog pogoršanja kod pacijentkinje i smrtnog ishoda.

DISKUSIJA

Patofiziološki mehanizam nastanka trombotične trombocitopenijske purpure jeste smanjena aktivnost metaloproteinaze ADAMTS13, čiji je najčešći uzrok postojanje antitela na ovu metaloproteinazu, a značajno ređe, njen urođeni deficit. S obzirom da je funkcija ADAMTS13 metaloproteinaze sečenje velikih multimera fon Vilebrandovog faktora na manje fragmente, i s obzirom na to da veliki multimeri fon Vilebrandovog faktora imaju veliki trombogeni potencijal, smanjena aktivnosti ove metaloproteinaze dovodi do diseminovane intravaskularne tromboze organa. Hipoperfuzija zahvaćenih organa dovodi do njihovog oštećenja, broj trombocita se smanjuje, jer se oni troše prilikom diseminovane tromboze, a hemolitička anemija nastaje kao posledica mehaničkog oštećenja eritrocita prilikom prolaska kroz sužene trombozirane krvne sudove [7]. Uzrok nastanka HUS-a su najčeće crevne infekcije, uzrokovane sojevima bakterija *Escherichia coli* i *Shigella dysenteriae*, koje produkuju *Shiga* toksin i tako oštećuju endotel krvnih sudova dovodeći do diseminovane intravaskularne tromboze. U ređim slučajevima, atipična forma HUS-a je uzrokovana oštećenjem endotela usled neadekvatne aktivacije komplementa [3].

Mehanizam nastanka trombotične mikroangiopatije udružene sa tumorima je raznolik, a nekada i više faktora može uticati na njen nastanak. S obzirom da

prednisone. After four days of treatment, the hemoglobin level rose to 87 g/l, while the platelet count reached 45 x 10^9/l. However, due to the development of respiratory insufficiency, it was not possible to perform gastroduodenoscopy. Oxygen, via oronasal mask, as well as bronchodilators, were administered to the patient.

Multislice computed tomography of the thorax, abdomen and lesser pelvis was performed, which revealed the following: multiple conglomerate masses of pathological lymph nodes in the mediastinum (the largest measuring 60 x 46 mm), intrapericardial effusion – measuring 22 mm in diameter, secondary deposits in the liver (the largest measuring 13 mm), and a secondary deposit on the left adrenal – measuring 29 x 28 mm. As far as skeletal structures are concerned, secondary deposits on the fourth right rib and the eighth left rib were detected, as well as gas inclusions in the T8 and L2 vertebrae. The gastric mucosa was not described, for technical reasons (Figure 1).

Seven days after the onset of disease, TPE and corticosteroid therapy were continued. At that point, the level of hemoglobin was 88 g/l, the platelet count was 49 x 10^9/l, the lactate dehydrogenase level was 1,720 IU/l, the value of total bilirubin was 32.2 μmol/l, while the value of direct bilirubin was 5.2 μmol/l. On the eighth day of treatment, respiratory failure occurred resulting in the lethal outcome.

DISCUSSION

The pathophysiological mechanism of the development of thrombotic thrombocytopenic purpura is the decreased activity of metalloproteinase ADAMTS13, whose most common cause is the existence of antibodies against this metalloproteinase, and, much less commonly, its congenital deficit. Since the function of ADAMTS13 is cleaving large von Willebrand factor multimers into smaller fragments, and since large von Willebrand factor multimers have great thrombogenic potential, a reduced activity of this metalloproteinase leads to disseminated intravascular organ thrombosis. Hypoperfusion of the affected organs leads to their damage, the platelet count decreases, as they are spent during disseminated thrombosis, while hemolytic anemia develops as the result of mechanical erythrocyte damage occurring during their passage through thrombosed and narrowed blood vessels [7]. The cause of HUS development are most commonly intestinal infections caused by strains of *Escherichia coli* and *Shigella dysenteriae*, which produce the *Shiga* toxin, thus damaging the endothelium of blood vessels, which leads to disseminated intravascular thrombosis. Less commonly, the atypical form of HUS is caused by endothelial damage due to deficient complement activation [3].

se najčešće javlja kod adenokarcinoma koji produkuju mucin, jedan od potencijalnih patofizioloških mehanizama nastanka ove trombotične mikroangiopatije jeste direktno toksično dejstvo mucina na endotel krvnih sudova [4]. Primećena je veća incidencija trombotične mikroangiopatije kod pacijenata koji su imali metastaze u koštanoj srži. Karcinomi u koštanoj srži direktno prodiru u krvne sudove i dovode do sekundarne mijelofibroze, koja takođe oštećuje endotel krvnih sudova, što za posledicu ima oslobađanje velikih multimera fon Vilebrandovog faktora [8,9]. Takođe, kod nekih pacijenata dolazi do stvaranja autoantitela na ADAMTS13 metaloproteinazu, kao i kod primarnog TTP-a [5].

Hemoterpija takođe može biti uzrok nastanka trombotične mikroangiopatije udružene sa tumorima, i to pre svega direktnim toksičnim doznozavisnim dejstvom na endotel krvnih sudova, a ređe akutnom imunom reakcijom. Primer doznozavisnog toksičnog dejstva jeste gemcitabinom indukovani HUS, koji ima incidenciju od 0,015% do 0,31% pacijenata lečenih gemcitabinom. Medijana kumulativne doze gemcita-

The mechanism of the development of carcinoma-associated thrombotic microangiopathy is variable, and sometimes multiple factors can contribute to its occurrence. As it most commonly occurs in mucin-producing adenocarcinomas, one of the potential pathophysiological mechanisms of the development of this type of thrombotic microangiopathy is the direct toxic effect of mucin on the blood vessel endothelium [4]. A higher incidence of thrombotic microangiopathy in patients with metastases in bone marrow has been observed. Carcinomas in bone marrow directly penetrate blood vessels leading to secondary myelofibrosis, which also damages the endothelium of blood vessels, which, in turn, results in the release of large von Willebrand factor multimers [8,9]. Also, in some patients, the production of autoantibodies against ADAMTS13 metalloproteinase occurs, as in primary TTP [5].

Chemotherapy can also be the cause of the development of carcinoma-associated thrombotic microangiopathy, primarily through the direct toxic dose-dependent effect on the blood vessel endothelium, and

Tabela 1. Diferencijalna dijagnoza trombotičnih mikroangiopatija (TMA) i procedure potrebne za njihovu dijagnostiku [1]

Table 1. Differential diagnosis of thrombotic microangiopathies (TMA) and the procedures necessary for their diagnosis [1]

Diferencijalna dijagnoza trombotičnih mikroangiopatija (TMA) / *Differential diagnosis of thrombotic microangiopathies (TMA)*	**Dijagnostički testovi / *Diagnostic tests***
Primarne trombotične mikroangiopatije (TMA) / *Primary thrombotic microangiopathies (TMA)*	
Trombotična trombocitopenijska purpura (TTP) / *Thrombotic thrombocytopenic purpura (TTP)*	
Kongenitalna TTP / *Congenital TTP*	Mutacije gena za ADAMTS13 metaloproteinazu / *ADAMTS13 gene mutations*
Stečena TTP / *Acquired TTP*	Aktivnost ADAMTS13 metaloproteinaze, nivo inhibitora na ADAMTS13 / *ADAMTS13 metalloproteinase activity, the level of ADAMTS13 inhibitor*
Hemolitičko-uremijski sindrom (HUS) / *Hemolytic-uremic syndrome (HUS)*	
Tipični HUS / *Typical HUS*	Kultura stolice (Shigella, Salmonella), detekcija Shiga toksina / *Coproculture (Shigella, Salmonella), Shiga toxin detection*
Atipični HUS / *Atypical HUS*	Mutacije gena za regulatorne proteine sistema komplementa / *Mutations in genes of the complement system regulatory proteins*
Sekundarne trombotične mikroangiopatije (TMA) / *Secondary thrombotic microangiopathies (TMA)*	
TMA udružena sa malignom hipertenzijom / *TMA associated with malignant hypertension*	Merenje krvnog pritiska, otkrivanje sekundarnih uzroka hipertenzije (endokrini, renalni) / *Measuring blood pressure, discovering secondary causes of hypertension (endocrine, renal)*
TMA udružena sa trudnoćom (preeklampsija, ekplampsija, HELLP sindrom) / *TMA associated with pregnancy (preeclampsia, eclampsia, HELLP syndrome)*	Test na trudnoću, nivo enzima jetre, kvantifikovanje proteinurije, merenje krvnog pritiska / *Pregnancy test, determining the levels of liver enzymes, quantification of proteinuria, blood pressure measuring*
TMA uzrokovana lekovima / *Drug-induced TMA*	Prekidanje suspektnog leka / *Discontinuation of the suspect drug*
TMA uzrokovana infekcijom / *Infection-induced TMA*	Virusološko i bakteriološko testiranje / *Virological and bacteriological testing*
TMA udružena sa tumorima / *Carcinoma-associated TMA*	Radiološka i patohistološka dijagnostika / *Radiological and pathohistological diagnostics*
TMA udružena sa autoimunim bolestima / *TMA associated with autoimmune diseases*	Serološki markeri autoimunih bolesti, klinički znaci i dijagnostički kriterijumi / *Serological markers of autoimmune diseases, clinical signs and diagnostic criteria*

bina, koja je dovodila do HUS-a, iznosila je 20 g/m^2 [10]. Osim ovog toksičnog dejstva gemcitabina, opisani su slučajevi HUS-a i nakon prve ili druge doze ovog leka, za šta se smatra da su odgovorni sledeći faktori: neadekvatna aktivacija komplementa i oštećenje endotela posredovano komplementom [11]. Incidencija HUS-a izazvanog direktnim toksičnim dejstvom mitomicina C na endotel je još i veća i iznosi od 2% do 15% [12,13], a ovakvo dejstvo zabeleženo je još i kod bleomicina, cisplatina, 5-fluorouracila, citozin arabinozida, i drugih lekova [12]. Sumarni prikaz uzroka nastanka trombotičnih mikroangiopatija i procedura koje su potrebne za njihovu dijagnostiku dat je u Tabeli 1.

S obzirom na visoke vrednosti tumor markera *CA* 19-9, specifičnog za gastrointestinalne tumore, i *CA* 72-4, visoko specifičnog za karcinom želuca, naša pacijentkinja je verovatno bolovala od karcinoma želuca. Međutim, s obzirom na inicijalno niski broj trombocita i razvoj respiratorne insuficijencije, nije bilo moguće sprovesti gastroduodenoskopiju. Takođe, periferne limfne žlezde nisu bile uvećane niti dostupne za biopsiju. U prilog dijagnozi karcinoma želuca govori i činjenica da je najveći procenat obolelih od trombotične mikroangiopatije udružene sa tumorima upravo imao karcinom želuca (26,2% svih obolelih od trombotične mikroangiopatije udružene sa tumorima) [6].

S obzirom na veliku smrtnost od trombotične mikroangiopatije udružene sa tumorima, od skoro 50%, od suštinskog značaja je da se na vreme prepozna i primeni terapija u vidu terapijske izmene plazme, kortikosteroidne terapije i naravno kauzalnog lečenja maligne bolesti [6].

Sukob interesa: Nije prijavljen.

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less commonly, through acute immune reaction. An example of the dose-dependent toxic effect is gemcitabine-induced HUS, whose incidence is between 0.015% and 0.31% of patients treated with gemcitabine. The median cumulative dose of gemcitabine which lead to HUS, was 20 g/m^2 [10]. In addition to this toxic effect of gemcitabine, cases of toxic effects of gemcitabine have been described after the first or second dose of this drug. The following factors are considered to be responsible for this: deficient complement activation and complement mediated endothelial damage [11]. The incidence of HUS induced by the direct toxic effect of mitomycin C on the endothelium is even higher, and ranges between 2% and 15% [12,13], and such an effect has been registered also in bleomycin, cisplatin, 5-fluorouracil, cytosine arabinoside, and other drugs [12]. The causes of the development of thrombotic microangiopathy as well as the necessary procedures for their diagnosis are presented in Table 1.

Bearing in mind the high levels of tumor marker CA 19-9, which is associated with gastrointestinal tumors, and of CA 72-4, which is highly associated with gastric cancer, our patient was probably suffering from gastric cancer, however, due to the initially low platelet count and the development of respiratory insufficiency, it was not possible to perform gastroduodenoscopy. Also, peripheral lymph nides were nether enlarged nor accessible for biopsy. The fact that the highest percentage of patients with carcinoma-associated thrombotic microangiopathy suffer from gastric carcinoma (26.2% of all patients suffering from carcinoma-associated thrombotic microangiopathy) speaks in favor of the diagnosis of gastric cancer in this patient [6].

Due to the high mortality from carcinoma-associated thrombotic microangiopathy, which is nearly 50%, it is essential to recognize it on time and initiate treatment in the form of therapeutic plasma exchange, corticosteroid therapy, and of course causal treatment of the malignant disease [6].

Conflict of interest: None declared.

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