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ДИАГНОСТИКА ТРОМБОТИЧЕСКОЙ МИКРОАНГИОПАТИИ В НЕФРОБИОПТАТАХ

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DIAGNOSIS OF THROMBOTIC MICROANGIOPATHY IN KIDNEY BIOPSY SPECIMENS

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Резюме. В данном исследовании были проанализированы клинические данные и морфологические изменения в нефробиоптатах 14 пациентов с тромботической микроангиопатией (ТМА). Наиболее частыми этиологическими факторами были злокачественная гипертензия (28,6%) и послеродовый период (14,3%). Гистопатологически был выявлен спектр изменений: от острых с микротромбозом до хронических с типичным склерозом сосудов.

Ключевые слова: тромботическая микроангиопатия, биопсия почки, морфология.

Resume. This study analysed clinical and morphological data from 14 patients with thrombotic microangiopathy (TMA). The most frequent etiologies were malignant hypertension (28.6%) and postpartum (14.3%). Histopathologically, a spectrum of changes was revealed: from acute with microthrombi to chronic with typical vascular sclerosis.

Keywords: thrombotic microangiopathy, kidney biopsy, morphology.

Relevance. Thrombotic microangiopathy (TMA) is a pathological process characterised by microvascular thrombosis, vessel wall thickening, and endothelial cell swelling, resulting in thrombocytopenia, ischemic organ damage, and partially acute kidney injury. TMA represents a vast spectrum of disorders, from primary syndromes such as atypical hemolytic uremic syndrome (aHUS) and thrombotic thrombocytopenic purpura to secondary forms associated with malignant hypertension, systemic sclerosis, the postpartum period, and infection [1]. TMA has an annual incidence of 5.9-14.4 cases per million persons per year. Accurate morphological diagnosis is critical for distinguishing between primary and secondary TMA, guided targeted therapy and predicting long-term renal outcomes.

Aim: to characterise the renal histopathological features of TMA across various biopsy samples and correlate these findings with clinical data.

Objectives:

1. To identify key histopathological features of TMA (endothelial swelling, microthrombi, vascular sclerosis).
2. To classify TMA cases by etiology (postpartum TMA, malignant hypertension, systemic sclerosis, SLE, Von Willebrand Factor).
3. To correlate morphological findings with clinical presentation and disease chronicity.

4. To distinguish acute from chronic TMA changes across various biopsy samples.

Materials and Methods. Analysis of 14 kidney biopsies from patients diagnosed with TMA were obtained. Biopsies were obtained via ultrasound-guided percutaneous needle biopsy, fixed in 10% formalin, paraffin embedded and sectioned at 3μm. These sections were stained with hematoxylin and eosin (H&E), periodic acid-Schiff (PAS), Masson's trichrome, and Jones silver stain for histopathological evaluation. Slides were examined under light microscopy. Immunohistochemistry (IHC) was performed to assess immune deposits (IgA, IgG, IgM, C3, C1q). Clinical data was obtained from referral charts.

Results and their discussion. The study included 14 patients, 7 males (50%) and 7 females (50%) (M:F = 1:1). The age of patients ranged from 23 to 59 years. The mean age was 38 ± 10.3 years. It should be noted that in the age group from 21 to 30 years there were only women, and in the age group over 51 years there were only men (Fig. 1).

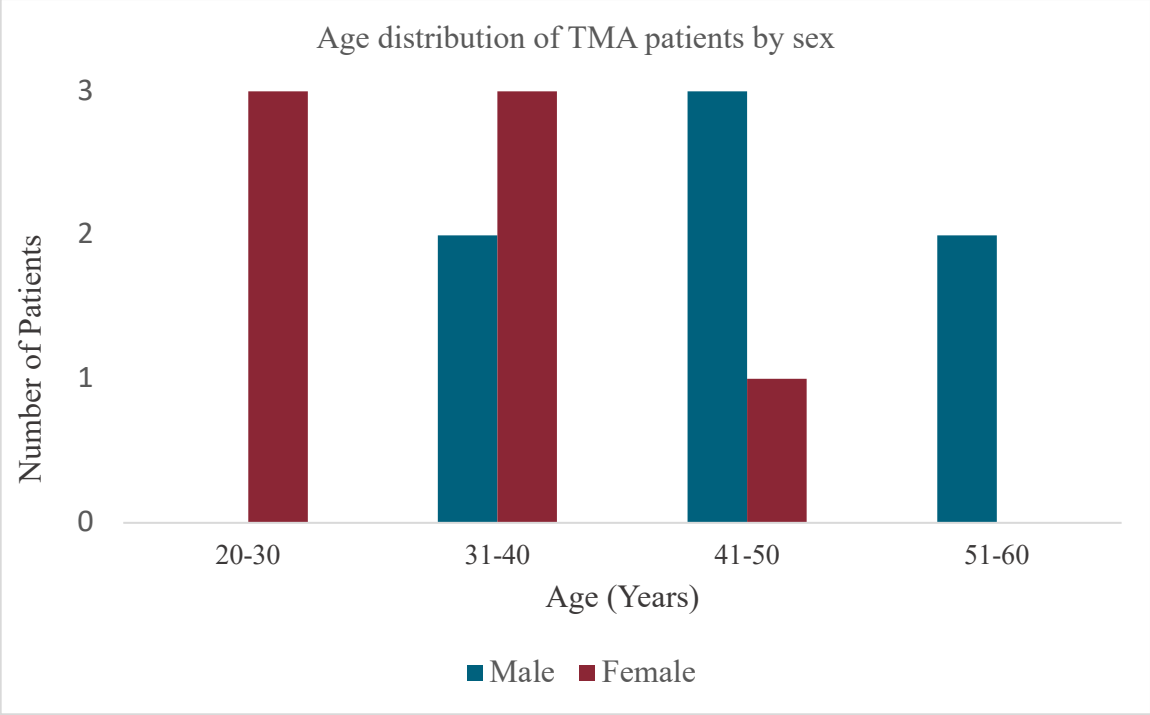

Fig. 1 – Age distribution of TMA patients by sex (n=14)

Whilst examining histopathology, all cases exhibited features consistent with TMA, such as endothelial swelling, microthrombi, focal segmental glomerulosclerosis, and vascular sclerosis. However, clinical presentations and features did vary (table 1).

Tbl. 1. Key histopathological findings across kidney biopsy specimens (n=14)

Feature	Present in Cases	Percentage
Endothelial Injury	10/14	71.4%
Microthrombi	9/14	64.3%
Interstitial Fibrosis	12/14	85.7%
Vascular Sclerosis	11/14	78.6%
Tubular Atrophy	10/14	71.4%
Focal Segmental Glomerulosclerosis	8/14	57.1%

Six main etiological groups were identified. Four patients (28.6%) presented with malignant hypertension (BP up to 200/120 mmHg). Histopathology revealed characteristics suggesting malignant due to fibrointimal proliferation (fig. 2), arteriolar hyalinosis, and variable glomerular ischemia with segmental sclerosis. The findings in this study are consistent with a recent systematic review that reported 95.2% of malignant hypertension patients also had renal TMA after biopsy was performed [1].

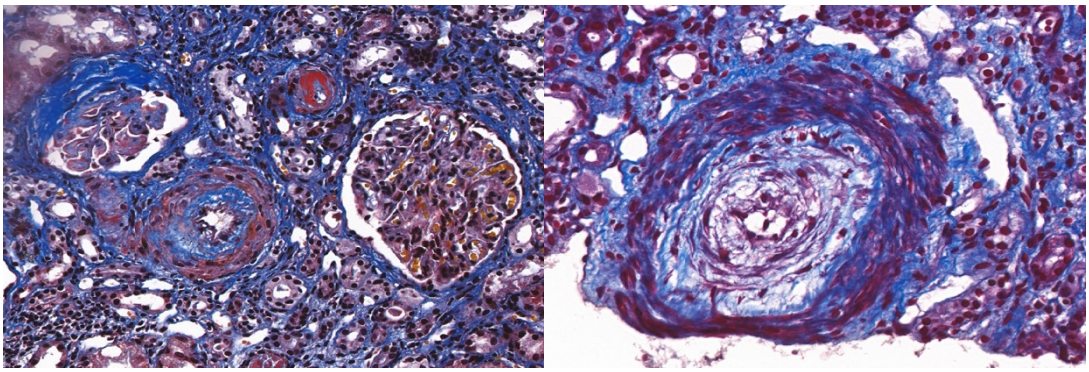

Fig. 2 – Fibrointimal proliferation of vessels – Masson-trichrome (x200)

Two female patients (14.3%) presented with postpartum TMA and complications included placental disruption, aHUS, and disseminated intravascular coagulation syndrome. Histopathology revealed acute changes such as the presence of microthrombi in vessels (fig. 3), acute tubular necrosis, and glomerular necrosis. The increased vulnerability for TMAs in postpartum cases is possibly due to the presence of ‘gravid endothelium’ altering microvasculature that results in the promotion of thrombosis [2].

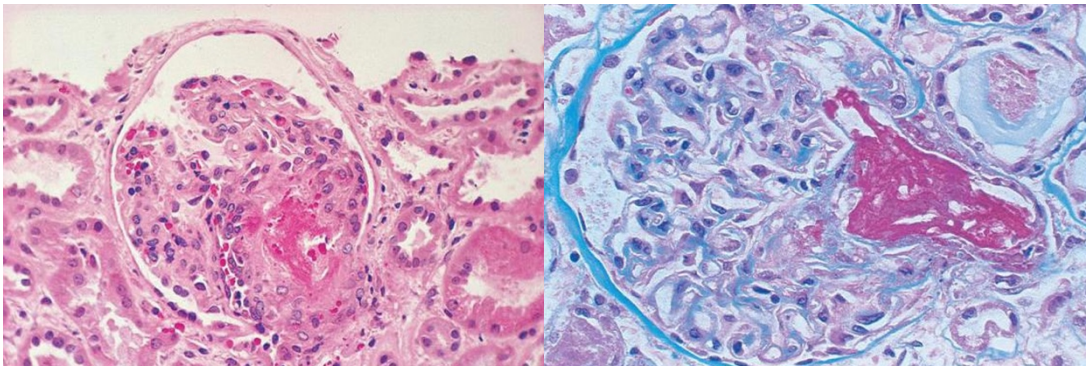

Fig. 3 – Microthrombi in arterioles: A – Masson-trichrome (x400); B – H&E (x200)

Two patients (14.3%) presented with systemic sclerosis. Kidney involvement in systemic sclerosis primarily manifests as Scleroderma Renal Crisis (SRC), a medical emergency marked by a sudden onset of severe high blood pressure and acute kidney failure. However, patients with kidney disfunction usually show tissue fibrosis and vasculopathy at renal biopsy [3]. Two of the cases showed chronic TMA changed with significant vascular sclerosis (fig. 4) and interstitial fibrosis (up to 40%).

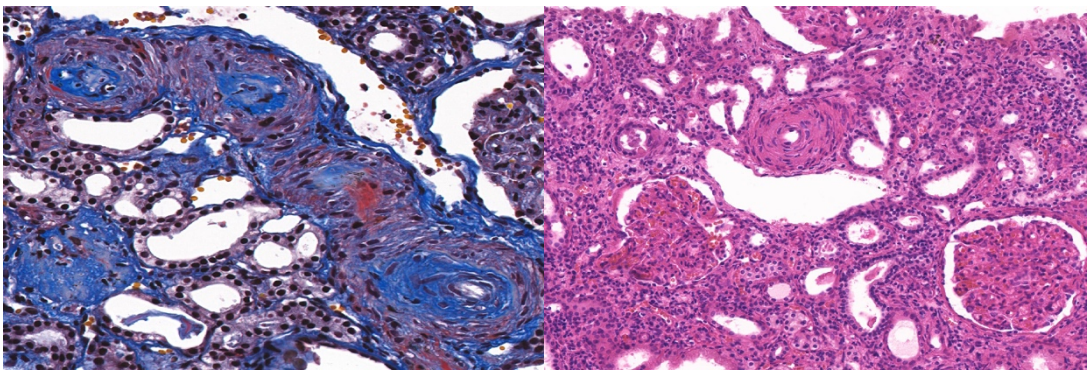

Fig. 4 – "Onion-skin" sclerosis of the arterial and arteriole walls: A – H&E (x100); B – Masson-trichrome (x300)

One patient (7.1%) was diagnosed with systemic lupus erythematosus (SLE), showing a "full house" IHC pattern (IgG, IgA, IgM, C3, C1q all +++). This patient presented with an elevated level of proteinuria, along with the presence of microthrombi in glomerular capillaries (fig. 5). Endothelial swelling and a significant reduction of tubular epithelium were also noted. One patient (7.1%) had minimal change disease with elevated von Willebrand Factor (VWF) and isolated microthrombi. Increased plasma levels of VWF in many cardiovascular, neoplastic, metabolic (e.g. diabetes), and connective tissue diseases are presumed to arise from adverse changes to the endothelium and may predict an increased risk of thrombosis [3]. Higher levels of VWF are more common among people that have had ischemic stroke (from blood-clotting) for the first time [3].

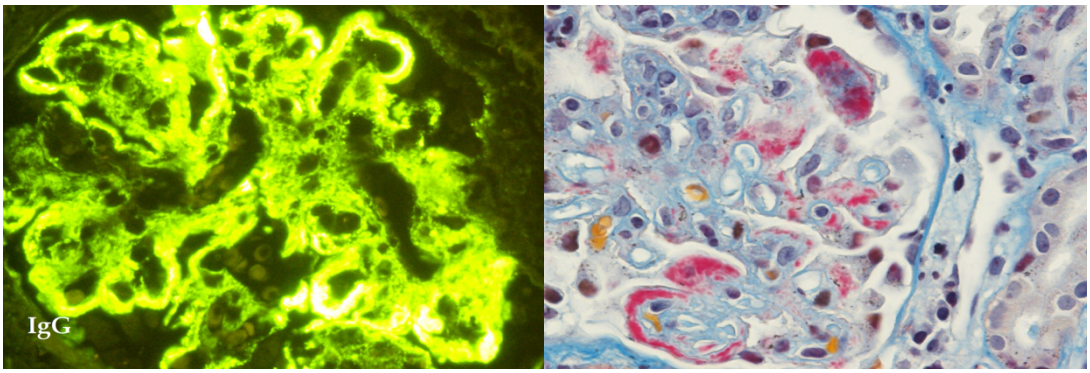

Fig. 5 – SLE: A – Microthrombi in glomerular capillaries, Masson-trichrome (x400; B – Expression of IgG in a glomerulus, Immunofluorescence (x400)

A notable finding in this study was the spectrum of chronicity observed across TMA etiologies. Acute TMA (postpartum, drugs-induced) was characterized by prominent microthrombi, marked endothelial swelling, widespread tubular necrosis, and minimal interstitial fibrosis (less than 10%). Chronic TMA (malignant hypertension, systemic sclerosis) was characterized by fibrointimal proliferation, arteriolar hyalinosis, established interstitial fibrosis (ranging from 20-80%), and irreversible changes (table 2). The degree of interstitial fibrosis correlated with clinical outcomes: patients with acute changes presented with rapid-onset anuria but retained potential for recovery, whereas those with chronic changes had progressive CKD with limited reversibility.

Tbl. 2. Comparison of acute and chronic histopathological features in TMA

Feature	Acute TMA	Chronic TMA
Predominant Etiology	Postpartum, Drug-Induced	Malignant Hypertension, Systemic Sclerosis
Microthrombi	Prominent	Absent
Endothelial Injury	Present	Present, but less than Acute
Tubular Necrosis	Widespread	Selective
Interstitial Fibrosis	Minimal (Less than 10%)	Ranging from 20-80%
Vascular Sclerosis	Slight	Prominent
Prognosis	Potentially Reversible	Irreversible

Conclusions:

1. TMA represents a heterogeneous group of disorders with diverse etiologies (postpartum TMA, malignant hypertension, systemic sclerosis, SLE, drug-induced), all sharing common histopathological features.

2. Histopathology demonstrates a spectrum of chronicity – from acute reversible changes (microthrombi, endothelial swelling, tubular necrosis) to chronic irreversible damage (fibrointimal proliferation, arteriolar hyalinosis, interstitial fibrosis).

3. The degree of chronic changes on biopsy (interstitial fibrosis, tubular atrophy, vascular sclerosis) correlates with clinical outcomes and predicts potential for renal recovery versus progression to end-stage renal disease.

4. Detailed morphological analysis is essential for distinguishing primary TMA from secondary forms, guided targeted therapy and determining prognosis.

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