

ВИПАДКИ З ПРАКТИКИDOI: 10.21802/artm.2023.4.28.230
UDC 616-071+616.5**CLINICAL CASE OF HEREDITARY HEMORRHAGIC ANGIOMATOSIS IN DERMATOLOGICAL PATIENT**

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Abstract. Osler-Weber-Rendu syndrome or hereditary hemorrhagic angiomatosis is a rare non-skin-specific inherited disorder in an autosomal dominant pattern, that affects more than a million people worldwide, males and females equally. It is caused by a mutation in genes, which encodes the endoglin – a protein that is responsible for the strength of the vascular wall. As a result, microaneurysms are formed everywhere and they can cause hemorrhage, systemic emboli, or heart failure.

Clinically this angiomatosis manifests in childhood. In approximately 90% of affected individuals, due to the formation of small, fragile vascular malformations (telangiectases) in the mucous membranes lining the inside of the nose, the first apparent symptom is recurrent nosebleeds. Gastrointestinal or frequent uterine bleeding (hemorrhaging), which affects about 25-30% of patients, usually does not present until the third decade of life, or later and often leads to chronically low levels of iron in the blood and eventually to anemia. After 12 years old affection of skin and mucosal membrane vessels causes the formation of esthetic problems: multiple telangiectasias distort the appearance of a person.

The diagnosis confirmation does not require complex research manipulations, nevertheless, sometimes it is difficult to differentiate from the multiple spider-like nevi in chronic liver diseases, multiple senile angiomas, Von Willebrand disease, or CREST syndrome.

The use of dermoscopy is not crucial, however, we can use it as a complementary tool for diagnosis verification.

Case presentation. We present a clinical case of Osler-Weber-Rendu syndrome to draw the attention of all specialties doctors, as it is not an aesthetic problem, but a serious, sometimes life-threatening, systemic disease.

A 46-year-old woman applied to a cosmetology clinic with multiple red vascular elements scattered over the entire surface of the body, causing a visible cosmetic defect. Despite the presence of manifestations of the disease in the anamnesis (frequent nosebleeds, persistent iron-deficiency anemia, excessive uterine bleeding that caused extubation), dermatologists were the first to diagnose this syndrome at such a late age.

Objectively numerous spiderweb-like red lesions with different sizes and shapes cover the whole body, even the lips and tongue. Dermoscopic signs are expanded vascular loops and lacune, grouped dots, and clods on a pink background. No pigmented components are visible.

Conclusion. Management of such a patient is complex: the patient should be under the close supervision of a family doctor and other organ-specific specialists, who determine appropriate tactics of management. Continuously strengthening the vascular wall, trauma avoidance, and non-using the contraindicated in this disorder medications are the basis. As this syndrome is a hereditary disease, only symptomatic treatment can be offered to the patient. To improve quality of life and prevent life-threatening complications various surgical techniques and laser therapy are applied nowadays. However, target therapy affecting the vascular endothelial growth factor is the modern approach.

It is also critical to undergo an appropriate diagnostic screening (Dopplerography, contrast echocardiography, computer tomography, or magnetic resonance angiography) for the timely detection of aneurysms of vessels as well as the prevention of internal bleeding that can lead to serious disability or even mortality.

Keywords: Osler-Weber-Rendu syndrome, clinical presentation, case report, esthetic problem, management.

Background. Hereditary hemorrhagic angiomatosis or Osler-Weber-Rendu syndrome is a rare inherited non-skin-specific disorder, that leads to a different degree of patient disability, impacts the quality of life, and shortens its expectancy. Nowadays, it affects more than a million people worldwide, with a prevalence of 1.5 -2 persons per 100000 in wide geographic variability. The ratio among Afro-Caribbean residents is higher, but we do not know the exact number in Ukraine. This disease occurs

among males and females equally and most people do not know they have it, therefore, the number of people suffering from this condition may be higher [1].

The type of inheritance of the syndrome is autosomal dominant – 80% of patients (mostly women) have mutations in ENG or activin A receptor-like type 1 (ACVRL1) genes, which encode endoglin, a protein of endothelial cells that binds transforming growth factor β and is responsible for the strength of the vascular wall.

Vascular dysplasia develops, manifested by the absence of muscle and elastic membranes in the vascular wall. The vascular wall consists only of endothelial cells surrounded by connective tissue. Therefore, microaneurysms are formed, which are easily damaged and lead to hemorrhages. It develops in the skin, mucosal membranes, lungs, liver, and central nervous system. Consequently, it can cause such life-threatening conditions as systemic emboli or heart failure [2].

Clinical presentation of this syndrome can vary, but the classic clinical triad includes multiple mucocutaneous telangiectases, positive family history, and epistaxis that begins during childhood or adolescence at a mean age of 12 years [3].

Our article aims to draw the attention of dermatologists, cosmetologists, family doctors, and doctors of other specialties to such a case of rare dermatoses as hereditary hemorrhagic angiomatosis, its clinical findings for preventing diagnostic errors, and inadequate treatment.

Case presentation. We present a clinical case of Osler-Weber-Rendu syndrome in a dermatological patient and wish to emphasize the seriousness of such rare dermatosis. It is not a dermatological or esthetic problem; however, the skin presentations can be the first signs of systemic disease. Misdiagnosing or untimely recognition may cause a fatal outcome for the patient.

A 46-year-old woman complained of the presence of multiple red lesions on the skin, which have become more frequent in the last 10 years; subjectively do not disturb; and it causes an apparent cosmetic defect. This patient presented to the cosmetology clinic with the desire to remove some significant elements.

From her medical history, it is known that she has been suffering from this since childhood. In the history of frequent nosebleeds at the age of 5-10 years, at the age of 15-18, the first telangiectasias appeared on the back and right palm. After 30 years, the number of spider veins and frequent uterine bleeding began to increase sharply (in 2015, the uterus was extubated). For several years a hematologist observed the anemia.

Objectively: there are countless red elements in the form of spots and small nodules distributed in the trunk, arms and legs, scalp, and face. Even oral mucosa (tongue, lips) is involved. Thin spiderweb-like purple-red lesions blanch with diascopy. The size varies from 0.1 to 0.8 cm in diameter. (Fig. 1, 2A, B).



Fig. 1. Numerous telangiectasias on the trunk, with different shapes and sizes.



Fig. 2. Telangiectasias on the hands (A) and legs (B).

On dermoscopy: bright red vascular formations represented by expanded vascular loops and lacunae on the

red background. Grouped dots and clod represent the vessels. There are no pigmented structures. (Fig 3-5).



Fig.3. Dermoscopy. Clustered clods and dots vessels on pink background.



Fig.4. Grouped dots, clods, and curved vessels.



Fig.5. Elevated elements, clods on pink background.
The general blood test was notable for the Hb level of 80 g/l (baseline level, 120-150g/l) and ferritin of 8 ng/ml

(normal range is 12-263 ng/ml). Findings of coagulation, biochemical analysis of blood, tests for hepatitis, and serological reactions were within the normal range. Ultrasound examination of the abdominal cavity organs reveals moderate splenomegaly, chronic cholecystopancreatitis, and nephrolithiasis.

During the interpretation of the obtained results, we established that anemia of the second degree and splenomegaly are the consequences of internal bleeding; a dermoscopic picture indicates hemangiomas.

Clinically, Rendu-Osler-Weber syndrome is very similar to multiple spider-like nevi in chronic liver diseases, multiple senile angiomas, and CREST syndrome. Therefore, we should differentiate it correctly. A detailed anamnesis, a correct assessment of the clinical status, and the results of additional examination methods are the key to the indisputable confirmation of the dermatosis. Although at such a late age, dermatologists diagnosed this hereditary disease for the first time.

Unfortunately, we do not have a magical healing agent for this patient. The problem is complex as such patients should be continuously observed by the family doctor and follow certain recommendations. This patient was referred to a vascular surgeon and is currently being treated by a laser technology specialist.

A few basic tips should be highlighted in the management of hereditary hemorrhagic angiomatosis:

- Treatment consists of surgical resection, embolization, electrocoagulation, or laser therapy and it is indicated for arterio-venous malformations causing hemorrhage.

Modern approach - target therapy - using drugs that target VEGF (vascular endothelial growth factor) and the angiogenic pathway with the use of bevacizumab (anti-VEGF antibody). Several exciting high-throughput screenings and preclinical studies have identified new molecular targets directly related to the signaling pathways affected by the disease. These include FKBP12, PI3-kinase and angiopoietin-2 [4].

- To strengthen the vascular wall - vasoconstrictors and estrogens are recommended.
- Taking anticoagulants and non-steroidal anti-inflammatory, cytostatic, and anabolic hormones should be avoided.
- Anemia should be adequately controlled.
- The use of dermoscopy is not crucial, however, it reveals a vascular pattern of lesions and can be used as a complementary tool for the diagnosis.
- Abdominal color Doppler sonography, computer tomography, and magnetic resonance angiography are helpful for central nervous system screening and for pulmonary, hepatic, and pelvic AVM detection [5].

Conclusions. Rendu-Osler-Weber disease is a rare genetic disease with an autosomal dominant type of inheritance that affects the blood vessels of the whole body due to dysplasia and leads to bleeding. The prognosis is variable and depends on the severity of the symptoms. In general, it is favorable as long as these bleedings are controlled. Manifesting by multiple telangiectasias on the skin and mucous membranes (mouth, nose, eyes, genitals) causes significant cosmetic discomfort and distress in the patient's daily lives. Frequent and heavy bleeding leads to

the development of chronic iron deficiency anemia. In 90% of patients, the symptoms of the disease may be hidden until the age of 30–40 years. The diagnosis is based on 4 criteria: bleeding, telangiectasia, visceral elements, and hereditary anamnesis. Treatment depends on the manifestations of the disease.

Timely recognition of this disease's symptoms can ensure monitoring of potential complications from cerebral and pulmonary visceral arteriovenous malformations, which is a source of serious morbidity and mortality.

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КЛІНІЧНИЙ ВИПАДОК СПАДКОВОГО ГЕМОРАГІЧНОГО АНГІОМАТОЗУ У ДЕРМАТОЛОГІЧНОГО ПАЦІЄНТА

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Резюме. Синдром Ослера-Вебера-Рендю - рідкісне неспецифічне для шкіри спадкове захворювання, спричинене мутацією в генах, що кодують ендоглін — білок, який відповідає за міцність судинної стінки. У результаті такого захворювання будь-де утворюються мікроаневризми, які можуть викликати крововилив, системну емболію чи навіть серцеву недостатність. Клінічно зазначений ангіоматоз проявляється у дитячому віці. Після 12 років ураження судин шкіри та слизових оболонок призводить до формування естетичних проблем, а саме: утворення множинних телеангіектазій, які спотворюють зовнішність пацієнта.

Хоча для підтвердження діагнозу синдром Ослера-Вебера-Рендю не потрібне застосування складних діагностичних маніпуляцій, проте іноді це захворювання важко диференціювати від множинних павукподібних невусів при хронічних захворюваннях печінки, множинних старечих ангіом або CREST-синдрому. У такому випадку застосування дермоскопії не має вирішального значення, однак її можна використовувати як додатковий метод діагностики.

Ми презентуємо клінічний випадок з метою привернення уваги лікарів всіх спеціальностей до синдрому Ослера-Вебера-Рендю як такого, який є не тільки естетичною проблемою для пацієнтів, а й серйозним системним захворюванням, що може загрожувати життю.

Опис випадку. 46-річна жінка звернулася в косметологічну клініку зі скаргами на такий помітний косметичний дефект як множинні червоні судинні елементи, що розсіяні по всій поверхні тіла. Дерматологи, незважаючи на наявні прояви захворювання в анамнезі (часті носові кровотечі, персистуюча анемія, важкі маткові кровотечі, що спричинили екстубацію), вперше у такому пізньому віці діагностували цей синдром.

Висновки. Ведення такого пацієнта є комплексним: пацієнт повинен бути під пильним наглядом сімейного лікаря; безперервно укріплювати судинну стінку і пам'ятати про медикаменти, що є протипоказані при даній мальформації. Важливо періодично проходити відповідне діагностичне обстеження (доплерографію, комп'ютерну томографію чи магнітно-резонансну ангіографію) для своєчасного виявлення аневризму судин і запобігання внутрішній кровотечі або навіть і смерті.

Ключові слова: синдром Ослера-Вебера-Рендю, клінічний випадок, опис випадку, естетична проблема, тактика ведення пацієнта.

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