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Early Identification and Treatment of Systemic Vasculitis

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Abstract: Systemic vasculitis is a group of autoimmune diseases that can affect the entire vascular system, including arteries, veins, and capillaries. Due to its wide-ranging effects, the clinical manifestations of systemic vasculitis are diverse or atypical, which can lead to misdiagnosis or delayed diagnosis. Severe cases may result in significant organ damage and even life-threatening conditions. In recent years, systemic vasculitis has gained significant attention. Numerous consensus statements and guidelines on vasculitis have been published both domestically and internationally. However, due to the complexity of its clinical presentation and the difficulty in identifying specific molecules and markers, as well as the limitations in clinical practice, there are still many challenges and difficulties in the diagnosis and treatment of systemic vasculitis. This article aims to explore several important issues in clinical practice.

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1. Introduction：

Systemic vasculitis is a rare and dangerous autoimmune disease that can affect the entire vascular system, including arteries, veins, and capillaries [1]. The disease is primarily caused by abnormal immune system attacks on the blood vessel walls, leading to inflammation and damage to the vessels. Based on the size and type of affected vessels, systemic vasculitis can be classified into various types, such as giant cell arteritis, polyarteritis nodosa, and Wegener's granulomatosis with renal involvement. The common characteristic of these diseases is the involvement of blood vessels in multiple tissues and organs, leading to systemic inflammatory reactions and symptoms [2]. Research suggests that the pathogenesis of systemic vasculitis involves various factors, including genetics, environment, and abnormal immune system function [3]. In terms of clinical manifestations, systemic vasculitis exhibits a wide range of symptoms that can affect multiple organs and systems, such as the skin, joints, lungs, and kidneys, with varying symptoms and severity. Early diagnosis and treatment are crucial for preventing disease progression and reducing complications.

In recent years, novel treatment methods for systemic vasculitis have emerged. The application of immunosuppressants, biologics, and immunomodulators has garnered significant attention and utilization [4]. Additionally, treatment targeting immune cells and factors has become a hot topic in current research [5]. Although the efficacy and safety of these treatment methods still require further research and confirmation, they provide new perspectives and approaches for the treatment and management of systemic vasculitis.

2. Classification of Systemic Vasculitis

Systemic vasculitis is a group of autoimmune diseases that involve multiple organs and systems. It can be classified based on various criteria, and the following are some common classification methods: classification based on clinical manifestations and histopathological characteristics, classification based on the size of affected vessels, and classification based on etiology [6].

2.1 Classification Based on Clinical Manifestations and Histopathological Characteristics

Based on clinical manifestations and histopathological characteristics, systemic vasculitis can be classified into anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis and systemic vasculitis [7]. ANCA-associated vasculitis includes

microscopic polyangiitis (also known as small vessel vasculitis) and renal-limited vasculitis (also known as ANCA-associated glomerulonephritis). Systemic vasculitis includes nodular polyarteritis, polyarteritis nodosa, necrotizing vasculitis, and allergic vasculitis, among others.

2.2. Classification Based on the Size of Affected Vessels

According to the size of the affected blood vessels, systemic vasculitis can be classified into large vessel vasculitis, medium vessel vasculitis, and small vessel vasculitis [8]. Among them, large vessel vasculitis affects the aorta and its branch vessels, such as giant cell arteritis and Takayasu arteritis. Medium vessel vasculitis affects medium-sized arteries and veins, such as nodular polyarteritis. Small vessel vasculitis affects small arteries, capillaries, and veins, such as ANCA-associated vasculitis and allergic vasculitis [9].

2.3. Classification Based on Etiology

Based on etiology, systemic vasculitis can be classified into primary systemic vasculitis and secondary systemic vasculitis. Primary systemic vasculitis has no clear cause and may be an autoimmune disease. Secondary systemic vasculitis is caused by factors such as infection, medication, and allergies [10]. It is important to note that due to the diverse symptoms and manifestations of systemic vasculitis, the classification may not be entirely clear and mutually exclusive. Different classification methods may overlap and intersect. Therefore, in specific clinical practice, doctors need to make comprehensive judgments and classifications based on the specific conditions of patients.

3. Early Diagnosis of Systemic Vasculitis

3.1 Early symptoms of Systemic Vasculitis

The symptoms of systemic vasculitis can vary depending on the specific type and organs involved. However, there are some common early symptoms that may indicate the presence of systemic vasculitis. These include fatigue, fever, weight loss, skin changes, joint pain, muscle pain, nerve problems, eye symptoms, sinus problems, and kidney involvement [11].

Additionally, different types of systemic vasculitis may present with specific early symptoms. For instance, Giant cell arteritis (temporal arteritis) may cause headaches, scalp tenderness, jaw pain, vision changes (such as double vision or sudden loss of vision), and flu-like symptoms [12]. Takayasu arteritis may lead to weak or absent pulses in the arms or legs, high blood pressure, chest pain, and visual disturbances [13]. Polyarteritis nodosa may manifest as abdominal pain, muscle aches, weakness, skin ulcers or nodules, and nerve involvement resulting in sensory changes or weakness [14]. Wegener's granulomatosis (granulomatosis with polyangiitis) may involve symptoms like sinus inflammation, nosebleeds, cough, chest pain, shortness of breath, joint pain, and skin rashes [15]. Churg-Strauss syndrome (eosinophilic granulomatosis with polyangiitis) may present with asthma-like symptoms, nasal polyps, eosinophilia (elevated eosinophil count in the blood), skin rash, and peripheral neuropathy [16]. Microscopic polyangiitis may involve kidney involvement (glomerulonephritis), lung problems (cough, shortness of breath), skin rash, joint pain, and peripheral neuropathy [17].

However, it's important to recognize that while the symptoms mentioned are commonly associated with systemic vasculitis, they can also be present in other medical conditions. Therefore, obtaining an accurate diagnosis, especially in the early stages, requires a comprehensive medical evaluation. Seeking proper medical assessment is crucial to differentiate systemic vasculitis from other potential causes.

3.2 Early Diagnosis of Systemic Vasculitis

The key to diagnosing systemic vasculitis lies in understanding its diverse manifestations. The disease may have a chronic course with gradual deterioration or sudden onset. Some symptoms may appear like other diseases, which increases the difficulty of diagnosis. To diagnose systemic vasculitis, comprehensive examinations are usually required, including physical examination, blood tests, imaging tests, and tissue examination [18].

Physical examination mainly involves identifying symptoms such as pain, erythema, congestion, and swelling. Blood tests are performed to check for anemia, leukopenia, thrombocytopenia, and other symptoms. Imaging tests, such as CT scans, MRI scans, and X-rays, can detect organ damage caused by vasculitis [19]. Tissue examination includes pathological examination or biopsy, which can determine the extent of vascular damage. Physical examination can reveal some disease-related signs, such as arthritis, skin lesions, and ocular inflammation. Blood tests can detect inflammatory markers in patients, such as elevated C-reactive protein and erythrocyte sedimentation rate, as well as the production of certain autoimmune antibodies. Among them, autoantibody testing plays an important role in the diagnosis and classification of systemic vasculitis. Positive serum ANCA (anti-neutrophil cytoplasmic antibody) indicates small vessel vasculitis; positive anti-GBM antibody suggests Goodpasture's syndrome; positive anti-Scl70 antibody suggests scleroderma, etc.

Imaging tests can show changes in blood vessels, such as stenosis and wall thickening caused by vasculitis [20].

Despite the availability of some diagnostic methods, early diagnosis of systemic vasculitis remains a challenging task. Systemic vasculitis is a group of complex autoimmune diseases with diverse clinical presentations, and early symptoms are often atypical, making timely diagnosis difficult. Furthermore, systemic vasculitis lacks specific markers [21-22], which further complicates early diagnosis. As different types of systemic vasculitis have different clinical manifestations and courses, the diagnosis of early cases requires heightened awareness and comprehensive analysis by doctors. In recent years, many studies have focused on exploring reliable biomarkers and imaging techniques to assist in early diagnosis and treatment of systemic vasculitis. Additionally, the involvement of various immune cells and factors in the pathogenesis of systemic vasculitis has led to the exploration of novel molecular markers and molecular targeted therapies, providing new possibilities and insights for early diagnosis and treatment [23].

In personalized medicine, the analysis of patients' genetic and molecular features and the discovery of promising biomarkers are crucial for the treatment of systemic vasculitis. However, currently, there is limited data on systemic vasculitis. Genetic studies have mainly included genome-wide association studies (GWAS) [24-25], which have made significant discoveries in the pathogenesis of systemic vasculitis, and exome sequencing studies have identified monogenic vasculitis [26]. Although many studies have involved novel biomarkers in systemic vasculitis, these biomarkers are rarely used in the routine clinical practice of managing systemic vasculitis patients. Currently, there are no algorithms using biomarkers for treatment decision-making in systemic vasculitis.

4. Treatment of Systemic Vasculitis

Systemic vasculitis is an autoimmune disease, and the main goals of treatment are to alleviate symptoms, prevent organ damage, reduce inflammation levels, and improve patients' quality of life [27]. The primary methods for treating systemic vasculitis include medication, surgical intervention, and rehabilitation therapy. Medication therapy for systemic vasculitis mainly involves immunosuppressants, glucocorticoids, and cytokine inhibitors [28]. These medications can alleviate inflammation, control the autoimmune response, and prevent organ damage. However, the use of these medications requires attention to side effects and appropriate drug administration, as they may affect the normal functioning of the immune system and increase the risk of adverse reactions such as infections, liver and kidney impairment, and malignancies.

Immunosuppressants are commonly used medications in the treatment of systemic vasculitis, including cyclophosphamide, methotrexate, and azathioprine [29]. They work by suppressing the activity of the immune system to alleviate inflammation and control the autoimmune response. However, the use of immunosuppressants requires caution due to side effects such as bone marrow suppression, infections, and liver and kidney impairment, necessitating regular monitoring. Glucocorticoids are another commonly used medication for treating systemic vasculitis [30]. They relieve symptoms by suppressing the inflammatory response. However, long-term use of glucocorticoids can lead to side effects such as osteoporosis, hypertension, and diabetes. Therefore, when using glucocorticoids, attention should be paid to dosage and duration, and efforts should be made to minimize the risk of side effects. Cytokine inhibitors are a class of medications that have been developed in recent years, including biologics and small molecule drugs [31]. They interfere with the inflammatory response and autoimmune reaction by inhibiting specific cytokines. However, the use of cytokine inhibitors also requires attention to side effects such as infections and liver and kidney impairment, requiring regular monitoring. When using medication to treat systemic vasculitis, it is important to administer drugs appropriately, monitor adverse reactions, and minimize the risk of side effects. Additionally, factors such as patient age, disease condition, and treatment efficacy should be considered when selecting the appropriate medication treatment plan.

For certain cases of systemic vasculitis patients, surgical intervention may be necessary. Especially when patients experience organ damage, surgical treatment can help repair or alleviate the affected organs [32], thereby improving symptoms and quality of life. For example, patients with severe kidney damage may require kidney transplantation or hemodialysis as surgical treatments to replace kidney function [33]. In cases of intestinal obstruction or perforation caused by vasculitis, treatments such as intestinal resection surgery may be necessary [34]. In addition, in cases of localized purulent infection or necrosis, surgical treatment may also be necessary. However, during surgery, it is important to consider the patient's immune status and the risk of infection before and after the procedure. Certain drug treatments may affect the patient's immune status, so it may be necessary to stop or adjust the corresponding

medication before surgery. Additionally, close monitoring of the patient's recovery is needed after surgery to promptly detect and manage potential complications such as infections.

Rehabilitation therapy can help restore the impaired physical function, improve quality of life, and psychological well-being of patients with systemic vasculitis. Rehabilitation treatments can include physical therapy, exercise therapy, nutritional adjustments, and psychological therapy, among others [35]. Physical therapy involves using physical methods such as heat therapy, cold therapy, massage, and physiotherapy to alleviate pain, enhance muscle strength, and promote blood circulation. Exercise therapy helps patients maintain physical flexibility and muscle strength, thereby improving their overall adaptability and immune function. Nutritional adjustments assist patients in maintaining a healthy state by ensuring adequate intake of nutrients. Psychological therapy helps patients address emotional issues, alleviate anxiety and depression, and enhance their psychological resilience and coping abilities [36]. Additionally, social and family support are integral components of rehabilitation therapy, as they help patients establish positive interpersonal relationships and a supportive family environment, thereby boosting their confidence and overall well-being. Overall, rehabilitation therapy is an essential part of the comprehensive treatment of systemic vasculitis, aiding in the recovery of physical function, improvement of psychological well-being, and enhancement of overall quality of life, enabling better management of the disease.

Meanwhile, a range of emerging imaging modalities with the potential to monitor vasculitis are also emerging. The combination of positron emission tomography with computed tomography or magnetic resonance imaging for structural and molecular imaging is rapidly advancing and may soon provide reliable long-term monitoring of vasculitis inflammation [37]. Furthermore, the emergence of radiotracers that assess macrophage activation and immune checkpoint activity represents an exciting new area for imaging vasculitis [38]. These advancements will allow for more precise imaging of disease activity soon, enabling clinicians to provide more targeted and personalized patient management.

The key to prevention and treatment of systemic vasculitis lies in early detection and intervention. Patients with autoimmune diseases such as rheumatoid arthritis, systemic lupus erythematosus, should undergo regular check-ups to detect early lesions and symptoms. Additionally, lifestyle adjustments should be considered, such as maintaining a healthy diet and engaging in moderate exercise to promote immune strength and overall health. Overall, systemic vasculitis is a highly complex disease that requires comprehensive treatment. It is important for patients to actively cooperate with their healthcare provider's treatment plan while paying attention to diet and exercise to enhance immune strength. If the condition improves, regular check-ups are still necessary to ensure disease remission.

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