03

ATYPICAL HEMOLYTIC UREMIC SYNDROME DIAGNOSIS AND TREATMENT

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Atypical hemolytic uremic syndrome (aHUS), more commonly known as complement-related HUS is a kind of thrombotic microangiopathy (TMA) characterized by inherited pathogenic variants in complement genes or acquired autoantibodies against complement factors, predominantly involving kidney [1]. Activation of the alternative complement pathway (AP), which occurs due to dysfunction in complement regulatory proteins or, less commonly, activation of mutations in the complement proteins themselves, constitutes the pathogenesis of aHUS and enables endothelial damage [2]. It may also present as secondary aHUS triggered by COVID-19, Shiga toxin-producing Escherichia coli, or other identifiable conditions [1]. As a triad for the diagnosis of aHUS; thrombocytopenia, microangiopathic hemolytic anemia (MAHA), and acute kidney injury are used, however, there is no universally accepted diagnostic criterion and it is considered inadequate because it is established without even histological findings in the kidney [1]. Complement factor H (CFH), complement factor I (CFI), membrane cofactor protein (MCP, CD46), thrombomodulin, complement factor B (CFB), and complement 3(C3) mutations are the mutations that play a dominant role in the pathogenesis of aHUS [2,3]. In 30% to 40% of patients who respond to complement inhibition, these mutations are not detectable or have genetic variants of unknown significance [2]. In a patient presenting with TMA findings, thrombotic thrombocytopenic purpura (TTP) must be excluded by showing that ADAMTS13 activity is above 10%. Short-acting C5 blockade (eculizumab) should be initiated without delay in those with ADMTS13 levels above 10% and those with severe oliguric acute renal failure [1]. Stool sampling should be done in individuals with diarrhea to detect Shiga toxin and/or microorganisms that produce Shiga toxin. Ravulizumab is a long-acting C5 inhibitor that is considered safe and effective in both treatment-naive adult and pediatric patients and in pediatric patients who have previously received complement inhibition [4]. Ravulizumab's half-life is four times longer than eculizumab (~51.8 days vs. ~11 days) and offers a reduced dosing frequency of up to 4-8 weeks instead of every 2-3 weeks [5]. All patients receiving complement inhibitors should be included in the vaccination program for Neisseria meningitis, Streptococcus pneumonia, and Haemophilus influenza type b, and early signs of infection should be carefully monitored and necessary parenteral antibiotic therapy should be started without delay. Although plasma exchange (PEX) treatment can provide partial benefit, especially in those with CFH, C3, and thrombomodulin gene variants, it has now been replaced by complement inhibitors where available. PEX treatment response is insufficient in CFI variants and does not provide additional benefits to complement inhibitors in MCP (CD46) deficiency [6]. Kidney transplantation treatment is associated with a high risk of recurrence, especially in patients with CFH mutations. However, the post-transplant relapse rate decreased with eculizumab treatment[7]. Iptacopan is an orally available, highly potent proximal complement inhibitor that specifically binds to CFB, the primary driver of the disease, thereby inhibiting AP [8]. Other treatments are being investigated, including alternative pathway-blocking agents and lectin pathway inhibitors.

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04

INNOVATIONS IN AL AMYLOIDOSIS MANAGEMENT

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Introduction: Immunoglobulin light chain (AL) amyloidosis is the most common type of systemic amyloidosis. AL amyloidosis is considered a plasma cell disorder caused by generally small and slowly proliferating clone of plasma cells in bone marrow that produces nonfunctional immunoglobulins. **Diagnosis:** Considering diagnosis of systemic amyloidosis is to evaluate for the presence of monoclonal paraprotein with electrophoresis and immunofixation of both serum and urine, serum kappa and lambda free light chain (FLC) levels, 24-hour urine protein. If testing confirms presence of a monoclonal immunoglobulin or abnormal FLC ratio, then tissue biopsy necessary for diagnosis should be performed. If amyloid is detected in the biopsy, the type of amyloid must be determined for a complete diagnosis. **Staging:** The most frequently used staging system is the Mayo 2012 model, which assigns a score of 1 for troponin T (≥0.025 μg/L), N-terminal probrain natriuretic peptide (NT-pro BNP; ≥1800ng/L) or BNP ≥400 ng/L, and a difference in serum FLCs (dFLC ≥180 mg/Land is believed to be superior at identifying very high risk individuals (1). An alternative model with high prediction performance is the European 2015 modification of the Mayo 2004 model assigning a score of 1 for troponin T (≥0.035 μg/L), NT-proBNP (≥ 332ng/L) and for stage 3 patients uses the absence or presence of ≥1800 ng/L criteria for IIIA, IIIB designation, respectively (2). Induction Therapy for Newly Diagnosed AL Amyloidosis: Many clinical studies investigated the role of bortezomib-based regimens, which were eventually accepted as the standart of care, the most commonly used regimen is combination of CyBorD. With the completion of the phase III Andromeda trial, the treatment paradigm has started to the addition of daratumumab together with CyBorD in the upfront setting. For patients who are eligible for autologous stem cell transplantation (ASCT), recommended beginning with induction therapy with daratumumab-CyBorD for two to four cycles and then evaluate the response. In patients who achieve a hematological very good partial response (VGPR) or better, forego ASCT and associated treatment-related morbidity and mortality in favor of completion of daratumumab-CyborD induction, followed by daratumumab maintenance for a total of 2 years. **Autologous Stem Cell Transplantation:**