Wegener’s granulomatosis in a 15-year-old boy

Sylva Skálová¹, Lenka Minxová¹, Miroslav Podhola²
Departments of ¹Pediatrics and ²Pathology, Medical Faculty Teaching Hospital, Charles University, Hradec Králové, Czech Republic


Wegener’s granulomatosis (WG) is an uncommon systemic vasculitis that is rarely encountered in children. A 15-year old boy presented with a one-month history of nasal obstruction, hemorrhagic rhinorrhea, malaise, fever, anorexia and weight loss, together with high values of inflammatory markers, microscopic hematuria and progressive decrease of renal functions. Renal biopsy revealed rapidly progressive crescentic glomerulonephritis with rare findings of interstitial and periglomerular granulomas. The diagnosis of WG was established and intravenous methylprednisolone and cyclophosphamide therapy followed by oral application of prednisone and azathioprine led to a complete clinical and laboratory remission of the disease. The second renal biopsy performed after 28 months of treatment did not show any activity of the process. Currently, the boy is without any clinical or laboratory signs of active disease. Since untreated WG has a fatal prognosis, early diagnosis and appropriately aggressive immunosuppressive therapy are necessary for a favorable outcome.

Key words: Wegener’s granulomatosis, rapidly progressive crescentic glomerulonephritis.
combined immunosuppressive therapy led to a complete clinical remission together with normalization of altered laboratory values within six weeks. The second renal biopsy, performed after 28 months of treatment, revealed collapse and segmental sclerosis of approximately one half of evaluated glomeruli, with no crescents and without any signs of activity of the process (Fig. 4). Currently, the boy is without any clinical or laboratory signs of active disease and has only mildly altered renal functions.

Discussion

Wegener’s granulomatosis is an uncommon autoimmune disease and is characterized by the presence of inflamed granular material in the nose and nasopharynx with granulomatous tissue containing epithelioid cells, Langhans’ cells, and foreign body giant cells, together with overall vascular disruption, sheets of released red blood cells, and numerous leukocytes in varying degrees of cytoclasia. There are inflammatory perivascular exudates and fibrin depositions in small arteries, capillaries and venules of the lungs and skin. Focal and segmental glomerulonephritis of varying severity together with necrotizing vasculitis can be encountered in the kidneys1-3. Wegener’s granulomatosis has a peak incidence in the fifth decade of life, but can occur at any age2. Any organ system can be affected by the pathologic process. The onset of WG can be slow or acute1-5, and the full spectrum of the disease may take years to evolve. While Wegener’s granulomatosis usually presents as a respiratory tract disease6, there might be central nervous system affections, ocular manifestations and migratory polyarthritis1,2.
Cutaneous manifestations might occur in 40% to 50% of patients with WG7. Patients complain of malaise, anorexia with weight loss and fever1-4. The kidneys are among the most frequently and severely affected organs in WG, with vasculitis and rapidly progressive glomerulonephritis leading to renal failure1-3,5. The detection of ANCA, in particular cytoplasmic-ANCA (c-ANCA), is considered helpful in establishing the diagnosis of WG8. However, screening for ANCA is usually not invariably positive in children with WG9. According to the American College of Rheumatology criteria from 1990, the diagnosis of WG is established by the evaluation of the characteristic clinical and pathological findings: (i) abnormal urinary sediment (red cell casts or more than 5 red blood cells per high power field); (ii) abnormal findings on the chest radiograph (nodules, cavities, or fixed infiltrates); (iii) oral ulcers or nasal discharge; and (iv) granulomatous inflammation on biopsy. The presence of two or more of these four criteria is associated with a sensitivity of 88.2% and specificity of 92.0%10. Recently, the following diagnostic criteria were proposed for WG: (i) biopsy or surrogate parameter for granulomatous inflammation in the respiratory system; (ii) biopsy-verified necrotizing vasculitis in small-to-medium sized vessels or biopsy/surrogate parameter for glomerulonephritis or positive PR3-ANCA test, and (iii) lack of eosinophilia in blood and biopsy samples11. The differential diagnosis of WG includes polyarteritis nodosa, Henoch-Schönlein purpura, Churg-Strauss syndrome and microscopic polyangiitis.

The prognosis of WG, once fatal, has significantly improved from the 18% five-month survival rate before the era of immunosuppressive agents to the current remission rate of over 75% with a regimen of cyclophosphamide and glucocorticoids3. The therapy is started with prednisone or methylprednisolone with concurrent administration of cyclophosphamide. Corticosteroids are gradually decreased after two to three months, until the patient is maintained solely on cyclophosphamide, which is given at least a full year after a clinical remission of the disease1-3,5. Azathioprine is less effective than cyclophosphamide, but may be used as an alternative or adjunct in those patients who cannot tolerate cyclophosphamide1,2. Long-term prophylactic administration of oral trimethoprim-sulfamethoxazole is highly effective for the upper respiratory tract lesions2.

The history of fever, hemorrhagic rhinorrhea, malaise and weight loss together with the high values of inflammatory markers and impairment of the renal functions were all indicative of WG in our patient. This diagnosis was further confirmed by the histologic evaluation of the renal biopsy sample, with the rare finding of granulomas in the kidney tissue. Interstitial and periglomerular granulomas are considered as infrequent lesions12. The slight positivity of p-ANCA and the absence of c-ANCA in our patient did not rule out the diagnosis of WG, as screening for p-ANCA is not always positive in WG9. The appropriate immunosuppressive therapy induced remission within six weeks. However, a close follow-up of the boy is necessary, as relapses occur in almost 50% of patients with WG, usually due to infection.

In conclusion, WG, although very rare even in adulthood, should be considered in children. An interdisciplinary approach to the care of WG patients is necessary and results in an increased survival rate13,14.

The prognosis of WG depends on early diagnosis and appropriately aggressive immunosuppressive therapy.

REFERENCES


