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Case Report

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Autoimmune hemolytic anemia associated with clear cell renal carcinoma: a case report

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ABSTRACT

Autoimmune hemolytic anemia (AIHA) is hemolytic anemia characterized by auto-antibodies against erythrocytes. It is commonly induced by hematological neoplasms such as malignant lymphoma; however urological cancers are rarely seen in this area. We present a case of clear cell renal carcinoma that responded to right partial nephrectomy, presenting with Coombs-positive warm AIHA. A 34-year-old male patient presented with fatigue lasting for 1 week, and icterus. His hemoglobin level was 6.8 g/dL, indirect bilirubin was 9.3 mg/dL, lactate dehydrogenase (LDH) 1031 U/L and both direct and indirect Coombs tests were positive. In the abdominal computed tomography, there was a 6 cm diameter mass lesion of heterogeneous density in the middle part of the right kidney. Corticosteroid treatment was started and then partial nephrectomy was performed. After surgical resection, the hemoglobin level gradually returned to normal. We detected warm AIHA associated with clear cell renal cancer. We are reporting on clear cell renal cancer that responded to corticosteroids and partial nephrectomy, presenting with severe AIHA at the hematology clinic. Clear cell renal cancer should be considered in the differential diagnosis for warm AIHA, and nephrectomy might offer a treatment option for renal cell carcinoma associated AIHA.

Keywords: Autoimmune hemolytic anemia, clear cell renal carcinoma, partial nephrectomy, paraneoplastic syndrome

INTRODUCTION

Paraneoplastic syndromes (PNSs) have been recognized as a variety of symptoms associated with certain cancers but not directly attributable to tumor invasion or compression. PNSs are linked to tumor secretion of functional peptides and hormones or to immune cross-reactivity between tumor and normal host tissues. These syndromes can affect various organ systems, including the neurological, hematological, endocrinological, dermatological, and rheumatological systems. Autoimmune hemolytic anemia can be seen as a paraneoplastic syndrome. It has been reported that treatment of the underlying tumor usually improves such conditions.[1,2]

CASE

A 34-year-old male patient presented with complaints of weakness, yellowing of the eyes and skin for 1 week. On physical examination, the sclera and skin were distinctly yellow. Hemoglobin level was 6.8 g/dl (normal, 13.5-16.5 g/dl), mean erythrocyte volume (MCV) was 105.8 fL, leukocyte counts was 7.85 x 10^3/ul and platelet count was 430 x 10^3/µl. Absolute reticulocyte count was high as 6.97%. Prothrombin time and activated partial thromboplastin time were within normal time intervals. The serum haptoglobin level was normal, at 1.36 mg/dl. While lactate dehydrogenase level increased to 1031 U/L (normal, 0-450 U/L), serum total bilirubin level increased significantly to 10.3 mg/dl (normal, 0.0-1.1 mg/dl), and the direct bilirubin level was slightly elevated 1 mg/dl (normal, 0.0-0.4 mg/dl). The patient's iron level was 169 µg/dl (50-178 µg/dl), total iron binding capacity was 153 µg/dl (173-285 µg/dl), transferrin was 52% (16-45), ferritin level was 287.12 ng/ml, folate level was 2,7 ng/ml (3.1-19.9 ng/ml), and B12 level was 225 pg/ml (187-883 pg/ml). It was observed that B12 level was normal and folate level was low. Serum immunoglobulin (Ig) levels were normal and no abnormal band was detected in electrophoresis. While the direct Coombs test was positive for IgG and complement C3, the indirect Coombs test was also positive. The other tests to exclude other autoimmune diseases; anti-nuclear antibodies, antibodies against double-stranded DNA, and anti-phospholipid antibodies were all negative. Crossmatch compatible blood transfusion was given to the patient. The patient's weight was 80 kg. Therefore, oral corticosteroid therapy 80 mg/day (1 mg/kg) was administered after the diagnosis was made, resulting in limited improvement.

Abdominal, thorax and neck computed tomography scans were requested in order to diagnose the underlying malignant lymphomas. On the abdominal computed tomography, there was a 6 cm diameter mass lesion of heterogeneous density in the middle part of the right kidney and it was confirmed by magnetic resonance imaging. Right partial nephrectomy was planned as the surgical treatment and clear cell renal carcinoma was reported through the pathology result. After right partial nephrectomy, hemoglobin levels and reticulocyte count gradually returned to normal. Full body computerized tomography scans with neck, abdomen and thorax were taken 6 months after the operation for surveillance. There were no findings that reveals malignancy other than the serous collection area in the operation area. The direct Coombs test was positive for IgG and complement C3, while the indirect Coombs test was negative.

DISCUSSION

AIHA is a disease caused by auto-antibodies against erythrocytes. Most cases of AIHA are idiopathic, but AIHA may be secondary to some malignancies. These immune-mediated hematological diseases are uncommon but can be seen as a typical PNS. In the literature, AIHA as a PNS has been diagnosed with a variety of multiple tumors, including hematological neoplasms such as malignant lymphoma, squamous cell carcinoma, adenocarcinoma, renal cell carcinoma, small cell carcinoma, and seminoma. However, renal malignancy is rarely associated with hematological PNS.[3,4]

AIHA developing secondary to the paraneoplastic process of the renal tumor has been reported to be associated with severe anemia, which can lead to serious morbidity and even mortality.[5] In this respect, accurate diagnosis of AIHA as PNS and initiation of treatment as soon as possible is vital. The diagnosis of paraneoplastic AIHA should be made after exclusion of metastases, infections, metabolic processes, and vascular changes. The pathogenesis of these PNSs includes the release of substances with endocrine and metabolic activity by tumor cells or induction of the release of inflammatory mediators, particularly cytokines such as interleukin (IL).[3] Steroids represent the main treatment for idiopathic AIHA. Although other immunosuppressants such as azathioprine, mycophenolate mofetil, monoclonal antibodies rituximab and intravenous immunoglobulins have also been used successfully, steroid-resistant cases may also require splenectomy. Control of carcinoma by tumor excision, corticosteroids, other immunosuppressant agents and chemotherapy may improve hematological abnormalities. In fact, most reports about kidney tumors seem to be identified with nephrectomy as an effective treatment.[6,7]

In our case, we performed partial nephrectomy to completely control AIHA that partially responded to corticosteroid treatment and for primary treatment of renal cancer. Surgical treatment improved the hemolytic status and corticosteroid treatment was discontinued with a controlled taper. There was no recurrence. There was no finding in favor of metastasis in the control tomography. This demonstrates the importance of surgery in conjunction with steroid therapy for the control of AIHA.

In addition, the fact that the patient's direct Coombs test is still positive may be attributed to the metastasis due to clear cell kidney cancer or the received erythrocyte replacement. Continuation of corticosteroids or use of immunosuppressant agents such as rituximab were not considered due to normal Hg and reticulocyte levels. The patient is under close follow-up.

CONCLUSION

We report a rare case of AIHA as a PNS associated with clear cell renal cancer. As a PNS, hemolytic anemia is diagnosed by excluding other causes such as primary hematological changes, metastasis, and vascular processes. Hemolytic anemia might be considered as a PNS in patients presenting with AIHA and may be associated with the cases of clear renal cell cancer. It should be kept in mind that surgical intervention is considered together with steroid administration in these patients.

ETHICAL DECLARATIONS

Informed Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written permission is available for review by the editor of this journal.

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