IJHOSCR

Case Report

International Journal of Hematology-Oncology and Stem Cell Research

A Rare Case of Autoimmune Hemolytic Anemia in Pancreatic Adenocarcinoma

Soniya Abraham[1], Sana Sultana[2], Jay Parekh[3]

[1]Department of Medicine, Division of Hospital Medicine, University of Texas Health Science Center at San Antonio, San Antonio, USA
[2]Department of Medicine, Ramaiah Medical College, Bangalore, India
[3]Department of Medicine, Division of Hematology Oncology, University of Texas Health Science Center at San Antonio, San Antonio, USA

Corresponding Author: Sana Sultana, Department of Medicine, Ramaiah Medical College, Bangalore, India
E-mail:sanasultana2912@gmail.com

Received: 13, Jul, 2024
Accepted: 17, May, 2025

ABSTRACT

Autoimmune hemolytic anemia (AIHA) is the immune-mediated destruction of red blood cells leading to anemia. It is a well-known paraneoplastic syndrome in hematological malignancies, particularly lymphoproliferative disorders but rarely reported in solid tumors. In this report, we describe the case of a 79-year-old gentleman who presented with mixed AIHA, initially treated with methylprednisolone and rituximab, resulting in laboratory improvement. CT abdomen and pelvis showed a 3.6 cm pancreatic tail mass concerning for neoplasm with splenic vein thrombosis and carcinomatosis. The biopsy revealed pancreatic adenocarcinoma. Methylprednisolone was changed to prednisone and his hemoglobin remained stable throughout the hospital course. This case presents an extremely rare association between AIHA and pancreatic adenocarcinoma.

Keywords: Autoimmune hemolytic anemia; Pancreatic cancer; Paraneoplastic syndrome; Solid tumor

INTRODUCTION

Autoimmune hemolytic anemia (AIHA) is the immune-mediated destruction of red blood cells leading to anemia. It is a well-known paraneoplastic syndrome in hematological malignancies particularly lymphoproliferative disorders but rarely reported in solid tumors[1,2]. Among solid tumors, AIHA was reported to occur more commonly in patients with renal cell carcinoma and Kaposi sarcoma, with 70% of cases belonging to the warm type[1]. AIHA should be included in the differential diagnosis when evaluating anemia, particularly beyond common etiologies[3]. The hypothesized pathophysiological mechanisms of AIHA occurrence in solid tumors involves immune activation through cross reactivity between tumor and host cells and interleukin production by tumor cells, leading to autoantibody generation[4-7]. We report the case of an elderly male patient presenting with mixed AIHA in whom further investigations revealed a pancreatic adenocarcinoma with improvement in hemoglobin on treatment. This case underscores the importance of identifying AIHA as a potential paraneoplastic syndrome in solid tumors such as pancreatic cancer emphasizing the need for thorough evaluation in patients presenting with hemolytic anemia.

Case presentation

A 79-year-old male with a past medical history of type 2 diabetes mellitus, hypertension, hyperlipidemia and hypothyroidism presented with yellowing of eyes and dark urine which started three weeks prior to presentation. Review of systems revealed unintentional weight loss, alternating diarrhea and constipation. On arrival at the Emergency Department, the patient was afebrile and hemodynamically stable. The physical examination revealed scleral icterus and jaundiced skin.

His initial labs were significant for hemoglobin 5.5 g/dl, Mean Corpuscular Volume (MCV) 126 fL, Red Cell Distribution Width (RDW) 20.7%, White Blood Cell (WBC) count 4.7x1000 µL, Platelets 247x1000 µL

with high absolute reticulocyte count, Lactate Dehydrogenase (LDH) 394 U/L, haptoglobin <10 mg/dl and indirect bilirubin 6.8 mg/dl. A direct antiglobulin test was positive with anti-IgG and anti-C3 positivity. Both warm and cold autoantibodies were identified. Peripheral blood smear showed spherocytes, agglutination, and rouleaux formation (Figure 1). Lab results were overall consistent with mixed AIHA. Additional antibody testing did not show any clinically significant alloantibodies.

The patient received one unit of packed red blood cells (PRBC) and was started on intravenous methylprednisolone (80 mg every 6 hours) and rituximab infusion (375 mg/m2) with improvement in hemoglobin and resolution of hemolysis.

Further investigations were done to evaluate the underlying etiology of hemolytic anemia. No prior history of blood transfusions or new medications was noted. Serological tests for HIV, Hepatitis C, Hepatitis B, Epstein Barr Virus and Mycoplasma were found to be negative. Cold agglutinin titer, cryoglobulin, antinuclear antibody and anticardiolipin antibody were negative. No evidence for monoclonal gammopathy was detected on serum protein electrophoresis and flow cytometry. Computed tomography (CT) of the chest did not show any evidence of thymoma or lymphoma. CT abdomen and pelvis showed 3.6 cm pancreatic tail mass concerning for neoplasm with splenic vein thrombosis and peritoneal carcinomatosis. A biopsy of pancreatic tail mass revealed moderate to poorly differentiated adenocarcinoma. CA-19 9 was elevated to 8251 U/mL. Methylprednisolone was changed to prednisone and his hemoglobin remained stable throughout the hospital course. He was discharged home with the plan to receive rituximab weekly for three more weeks and prednisone with slow taper outpatient. He was referred to an Oncologist for further management of pancreatic adenocarcinoma. The patient consulted with the oncologist and chose to transition to hospice care.

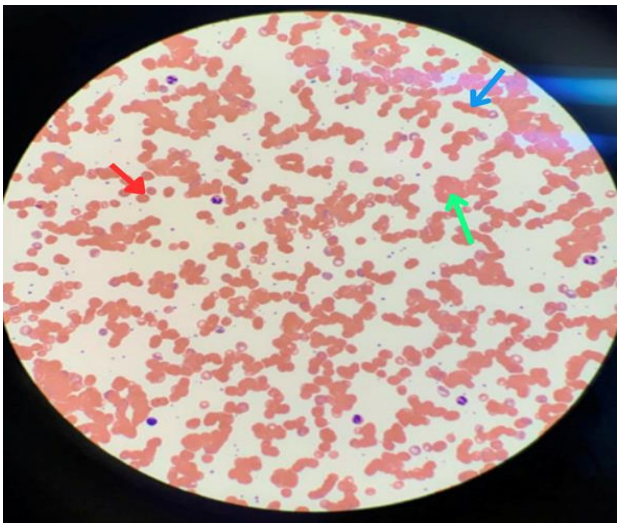

Figure 1. Peripheral smear showing Spherocytes (red arrow), Agglutination (green arrow) and Rouleaux formation (blue arrow)

DISCUSSION

This case presents an extremely rare association between AIHA and pancreatic adenocarcinoma. In the context of pancreatic adenocarcinoma, it is crucial to differentiate AIHA from other causes of anemia, including anemia of chronic disease and direct tumor effects. Linking AIHA to solid tumors requires the exclusion of more common causes, including autoimmune/infectious etiologies and medications[3]. The exact pathogenesis of AIHA and carcinoma has not been understood clearly but postulated mechanisms involve the release of inflammatory mediators, particularly interleukins by tumor cells and immune cross-reactivity between tumor and host cells [4, 5]. Tumor cells may provoke the immune system to produce autoantibodies that target and destroy red blood cells, leading to hemolytic anemia [6,7]. In pancreatic adenocarcinoma, the inflammatory microenvironment may support adaptive immune responses such as B cell activation, differentiation and production of autoantibodies against self-antigens, as observed in studies where autoantibodies reacted with intracellular proteins F-actin and HSPD1[8]. Similar autoimmune activity can contribute to hemolysis observed in AIHA.

The association of AIHA as a paraneoplastic syndrome in pancreatic adenocarcinoma has been sparingly described in the literature. Puthenparambil et al. described 52 cases of AIHA occurring as a paraneoplastic syndrome in solid tumors, of which one case was linked to pancreatic cancer. AIHA was

more commonly associated with lung cancer, kidney tumors and Kaposi sarcoma, frequently occurring in metastatic cases[1]. Hariz et al. reported a case of AIHA in the setting of pancreatic adenocarcinoma with liver metastasis[6]. Koike et al also reported a similar case of AIHA followed by demyelinating neuropathy in the setting of pancreatic cancer [7]. In a study of 1038 solid tumor patients, only 14 patients presented with autoimmune paraneoplastic syndromes, of which 14% were associated with AIHA. Autoimmune phenomena was more commonly observed in prostate and ovarian carcinoma patients. These syndromes commonly occurred metachronously between 6 months to 6 years after diagnosis or rarely, synchronously as in our case [9].

The first line treatment for AIHA is mainly corticosteroids, such as prednisone. Rituximab, Mycophenolate, Azathioprine and Intravenous Immunoglobulin are also used to treat AIHA. Treatment of underlying tumors along with corticosteroids remains the cornerstone therapy to date[3,5]. Hariz et al. reported an improvement in hemoglobin following chemotherapy initiation without significant response to corticosteroids[6]. Koike et al. also reported refractoriness to corticosteroids but improvement of labs following splenectomy in a patient who was later diagnosed with pancreatic adenocarcinoma[7]. Rituximab, a CD20 monoclonal antibody is preferred over splenectomy as second line treatment in cancer patients with an immunocompromised status[10-12]. Tumor control via chemotherapy or radiation, has also shown to alleviate hemolysis in carcinoma patients with AIHA[2].

CONCLUSION

AIHA occurs rarely in solid tumor patients, especially in pancreatic cancers. In order to make this challenging association, physicians must first exclude etiologies that occur more frequently in cancer patients. Due to the limited number of cases described, treatment strategies have not been well defined but include treating the underlying cancer as well as use of corticosteroids.

REFERENCES

1. Puthenparambil J, Lechner K, Kornek G. Autoimmune hemolytic anemia as a paraneoplastic phenomenon in solid tumors: A critical analysis of 52 cases reported in the literature. Wien Klin Wochenschr. 2010;122(7-8):229-36.
2. Spira MA, Lynch EC. Autoimmune hemolytic anemia and carcinoma: an unusual association. Am J Med. 1979;67(5):753-8.
3. Fattizzo B, Giannotta JA, Serpenti F, et al. Difficult Cases of Autoimmune Hemolytic Anemia: A Challenge for the Internal Medicine Specialist. J Clin Med. 2020;9(12):3858.
4. Visco C, Barcellini W, Maura F, et al. Autoimmune cytopenias in chronic lymphocytic leukemia. Am J Hematol. 2014;89(11):1055-62.
5. Isotani S, Horiuchi A, Koja M, et al. Autoimmune hemolytic anemia associated with renal urothelial cancer: A case report and literature review. BMC Urol. 2015;15:75.
6. Hariz A, Hamdi MS, Boukhris I, et al. Autoimmune haemolytic anaemia in pancreatic adenocarcinoma: a potential paraneoplastic presentation. BMJ Case Rep. 2019;12(7):e229807.
7. Koike H, Yoshida H, Ito T, et al. Demyelinating neuropathy and autoimmune hemolytic anemia in a patient with pancreatic cancer. Intern Med. 2013;52(15):1737-1740.
8. Yao M, Preall J, Yeh JT, et al. Plasma cells in human pancreatic ductal adenocarcinoma secrete antibodies against self-antigens. JCI Insight. 2023;8(21):e172449.
9. Nenova IS, Valcheva MY, Beleva EA, et al. Autoimmune Phenomena in Patients with Solid Tumors. Folia Med (Plovdiv). 2016;58(3):195-199.
10. Zanella A, Barcellini W. Treatment of autoimmune hemolytic anemias. Haematologica. 2014;99(10):1547-54.
11. Lechner K, Jäger U. How I treat autoimmune hemolytic anemias in adults. Blood. 2010;116(11):1831-8.
12. Barcellini W. Immune Hemolysis: Diagnosis and Treatment Recommendations. Semin Hematol. 2015;52(4):304-12.