Short Communication

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ABO Discrepancy Revealing Cold Agglutinin Syndrome in Pancreatic Neoplasm: Literature Review Regarding a Case

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ABSTRACT

Paraneoplastic syndromes (PNS) are rare in patients with solid tumours. This paper describes a case involving the rare occurrence of cold agglutinin syndrome (CAS) in conjunction with pancreatic head neoplasia (Santos IL, et al. [1]).

Abbreviations: PRBC: Packed Red Blood Cells; PNS: Paraneoplastic Syndromes; CAS: Cold Agglutinin Syndrome; AIHA: Autoimmune Haemolytic Anaemia; DAT: Direct Antiglobulin Test; IAS: Irregular Antibody Screening

Introduction

CAS is characterized by spontaneous erythrocyte agglutination associated with accelerated destruction of red blood cells by the immune system. CAS is generally associated with autoimmune diseases and lymphoproliferative neoplasms and is very rare in solid tumors. The diagnosis of autoimmune haemolytic anaemia (AIHA) is based on clinical or laboratory evidence of hemolytic anemia and the detection of autoantibodies, specifically IgM, with a positive C3 direct antiglobulin test (DAT) and the presence of circulating cold agglutinins in the serum. Due to the excess of circulating free antibodies, an ABO blood group discrepancy may be observed.

Material & Methods

Clinical Case

A 64-year-old woman was admitted for surgery due to a pancreatic neoplasia. Reserve of packed red blood cells (PRBC) was requested. Blood samples were tested by the Sephadex® gel column agglutination method (Johnson ST, et al. [2]).

Results/ Observations

The initial sample at room temperature showed discrepancies in the ABO blood group classification (Figure 1). The irregular antibody screening (IAS) and autologous control were positive (Figure 2). The identification of the irregular antibody with a standard cell panel and autologous RBC determined its reactivity with all the red blood cells tested. The agglutinin titer was 1024 (data not shown). The DAT screening was positive for anti-IgM, -C3c, and -C3d (Figure 3). Despite the laboratory findings, the patient did not present any clinical manifestations of CAS. Preheating a new sample and further testing at 37°C revealed blood group A RhD positive (Figure 4). IAS was negative, and DAT was reactive only with anti-C3d (Figure 5). Using the same

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heating method at 37°C, compatible RBCs were found (Figure 6). The tumor was considered inoperable. The patient progressed without treatment and specific clinical symptoms of CAS, despite worsening anemia (Hb=6.8g/dL) and of the immunohematological profile. He died 7 months after diagnosis.

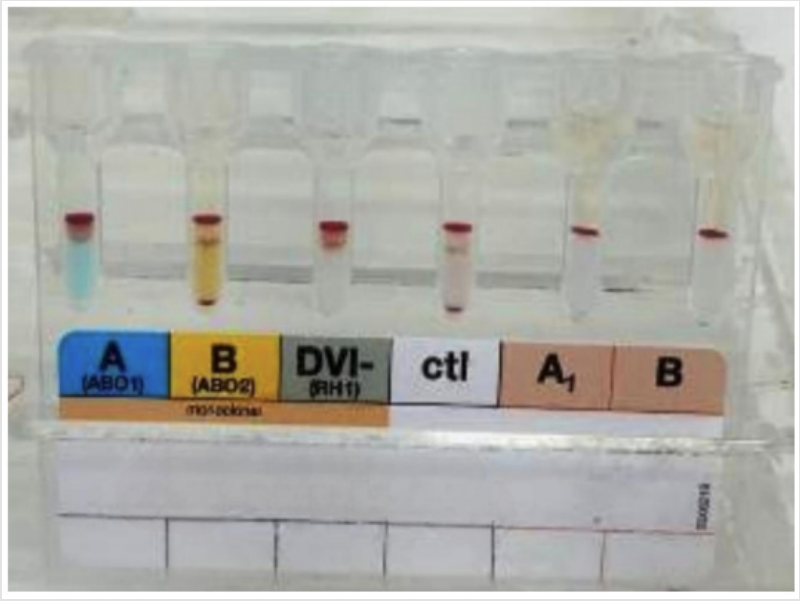

Figure 1: ABO classification and RhD test at room temperature by the Sephadex® gel column agglutination method. The direct classification of red blood cells, positive (4+/4) with anti-A and anti-B monoclonal reagents (wells 1 and 2, from left to right), was incompatible with the presence of natural anti-A and anti-B agglutinins (4+/4) in the reverse classification (wells 5 and 6). The reactive result (4+/4) of red blood cells with the anti-RhD reagent (well 3) was also invalidated by positivity (4+/4) with the negative control of the reagent (well 4).

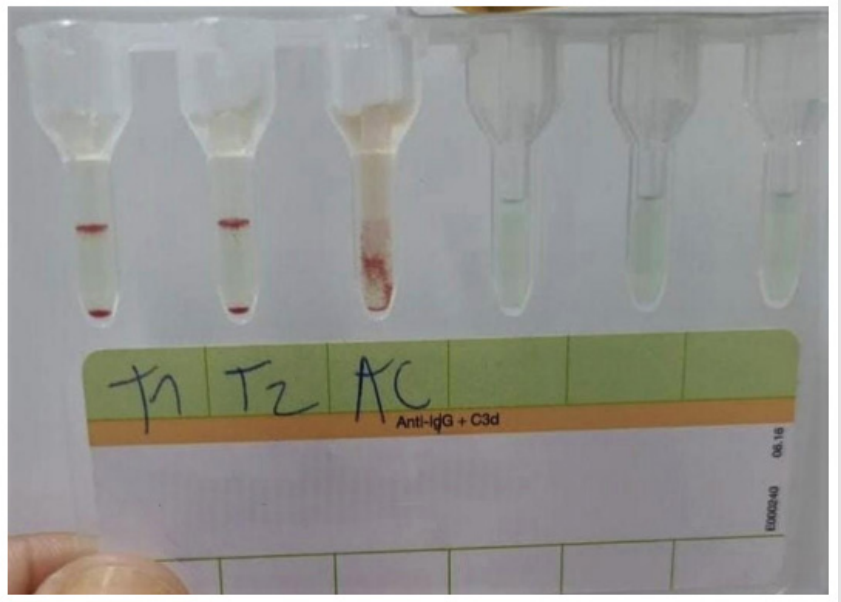

Figure 2: Irregular antibody screening (wells 1 and 2) and autologous control (well 3) by the Sephadex® gel column agglutination method in microcards containing polyclonal human antiglobulin (anti-IgG and anti-C3d). From left to right, wells 1 and 2 displayed unexpected antibodies in the patient's serum. Well 3 (3+/4) showed the presence of antibodies fixed to the patient's RBC (autoantibodies).

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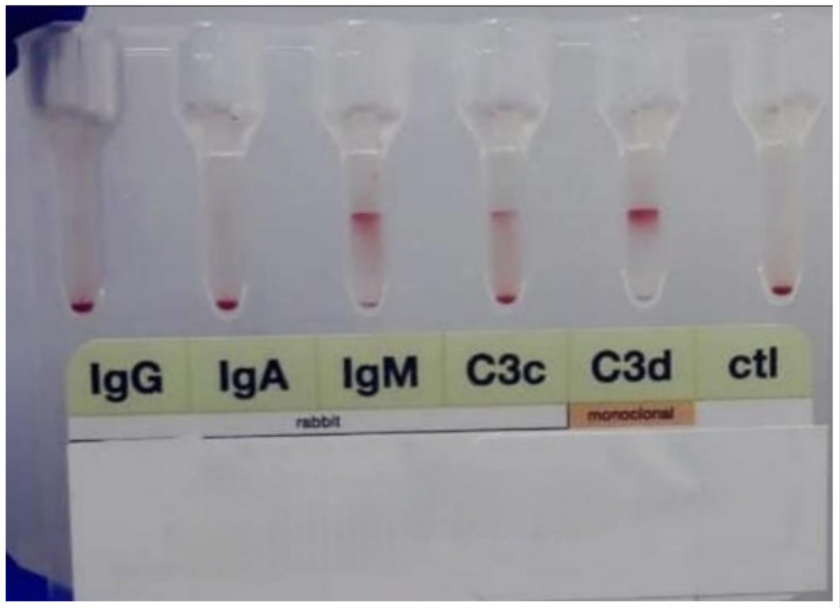

Figure 3: Direct antiglobulin test screening with Sephadex® gel column agglutination method in microcards containing polyclonal human antiglobulin (anti- IgG, -IgA, -IgM and -C3d) from rabbit source and monoclonal anti-C3d. The IgM autoantibody (well 3) had fixed the C3c and C3d fractions (wells 4 and 5) of the complement cascade to the patient's RBCs.

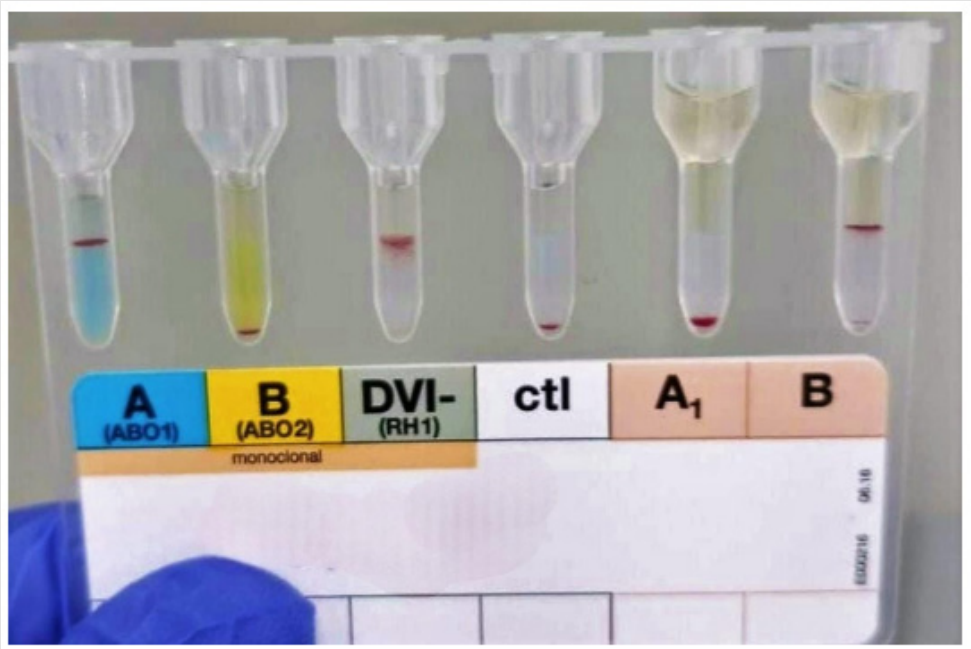

Figure 4: ABO classification at 37°C. After collecting a new sample and keeping it at 37°C from collection until the laboratory results were read, the compatibility between direct and reverse classification allowed the patient to be identified as A RhD+.

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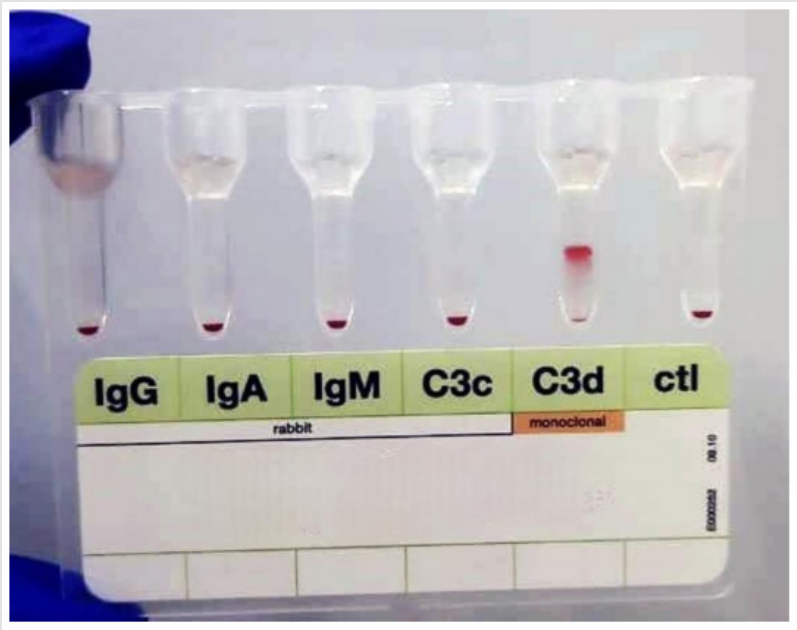

Figure 5: Direct antiglobulin test screening with preheated sample. The autoantibody reacted only against anti-C3d antiglobulin.

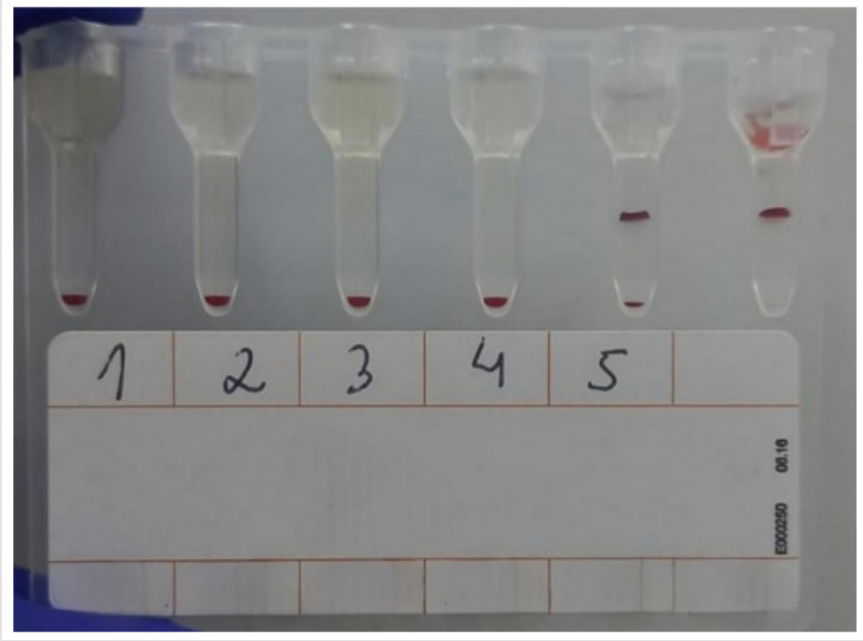

Figure 6: Compatibility test between packed red blood cells (PRBC) and the preheating sample. PRBC from different donors proved to be compatible (wells 1-4 from left to right).

Discussion/Conclusion

PNS is a rare phenomenon in patients with solid tumors, defined as clinical or laboratory alterations not directly related to tumor growth, but rather to the ectopic production of biological substances or immune reactions associated with the neoplasm. Ovarian dermoid cysts (benign) and lymphomas are directly associated with AIHA. In a literature review (1945-2009), Puthenparambil J, et al. [3] (Puthenparambil J, Lechner K & Kornek G) observed 53 cases of AIHA associated with non-hematological solid neoplasms, and among them, only one case was associated with pancreatic neoplasm. The majority of AIHA occurred 6 months before or after cancer diagnosis. There was no association between the type of AIHA and the site of the neoplasm, and complete remission was achieved by treating the underlying neoplasm. It is noteworthy that none of the patients with cold antibodies (1/3 of them) presented any symptoms related to CAS. The present case is noteworthy due to the rarity in the relevant literature of the association of CAS and pancreatic neoplasia.

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