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Transient Aplastic Crisis Associated with Parvovirus B19 Infection in a Patient with Pernicious Anemia and Hemolysis

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Abstract

Introduction: Parvovirus B19 is a human erythrovirus that causes variable clinical manifestations depending on the host's immunological and hematological status. In patients with underlying hematological disorders, it can trigger transient aplastic crisis. **Case Description:** A 68-year-old man with a history of type 2 diabetes mellitus, chronic gastritis, and anemia under investigation presented with progressive fatigue, anorexia, and weight loss. Physical examination revealed cutaneous-mucosal pallor and pancytopenia with severe vitamin B12 deficiency, direct hyperbilirubinemia, and haptoglobin < 8mg/dL. Blood smear showed marked anisocytosis with macrocytic predominance and hypersegmented neutrophils. Investigation confirmed chronic gastritis by endoscopy and positive anti-parietal cell antibodies and IgM/IgG for Parvovirus B19. Intramuscular vitamin B12 supplementation resulted in gradual anemia improvement and complete pancytopenia resolution. **Discussion:** This case illustrates the importance of early recognition of Parvovirus B19 infection as a cause of transient aplastic crisis in patients with underlying pernicious anemia. Appropriate clinical suspicion can prevent unnecessary invasive procedures, as aplasia is transient and responds to supportive measures.

Keywords

Aplastic Crisis, Parvovirus B19, Pernicious Anemia, Hemolysis

1. Introduction

Parvovirus B19 is a single-stranded DNA virus belonging to the Parvoviridae family, with specific tropism for erythroid progenitor cells [1]. This ubiquitous human pathogen causes a broad spectrum of clinical manifestations that vary significantly

according to age, immunological, and hematological status of the host [2] [3].

In immunocompetent children, infection typically manifests as erythema infectiosum (fifth disease), characterized by facial exanthema with a "slapped cheek" appearance [4]. In adults, manifestations are often oligosymptomatic or include arthralgia and constitutional symptoms [5]. However, in patients with underlying hematological disorders, particularly those with chronic hemolytic anemia, bone marrow failure syndromes, or nutritional deficiencies, Parvovirus B19 infection can precipitate episodes of transient aplastic crisis [6] [7].

Pernicious anemia, characterized by vitamin B12 deficiency secondary to autoimmune gastritis and intrinsic factor deficiency, constitutes a risk factor for the development of severe hematological complications during viral infections [8]. The combination of cobalamin deficiency with Parvovirus B19 infection can result in severe pancytopenia, creating significant diagnostic and therapeutic challenges [9].

We present the case of a 68-year-old patient with pernicious anemia who developed transient aplastic crisis associated with Parvovirus B19 infection, emphasizing the importance of early recognition of this association to avoid unnecessary invasive diagnostic interventions.

2. Case Report

2.1. Patient Information and Clinical Presentation

A 68-year-old Caucasian male with relevant medical history of type 2 diabetes mellitus on metformin therapy, chronic gastritis treated with esomeprazole, and anemia under investigation in Internal Medicine consultation. He had been on oral iron supplementation for several months without significant improvement of hematological parameters.

The patient presented to the Emergency Department with progressive fatigue lasting several weeks, marked anorexia, and unquantified weight loss. He denied fever, night sweats, pain complaints, or visible bleeding. Physical examination showed hemodynamic stability with evident cutaneous-mucosal pallor. No lymphadenopathy or organomegaly was palpated.

2.2. Diagnostic Investigation

Initial laboratory studies revealed:

1) Hemoglobin: 4.2 g/dL (NV: 14 g/dL - 18 g/dL).
2) Leukocytes: 2800/μL (NV: 4000/μL - 11,000/μL).
3) Neutrophils: 1400/μL (NV: 2000/μL - 7500/μL).
4) Platelets: 85,000/μL (NV: 150,000/μL - 400,000/μL).
5) MCV: 115 fL (NV: 82 fL - 98 fL).
6) Reticulocytes: 0.5% (NV: 0.5% - 2.5%), corrected reticulocyte index: 0.06.

Biochemical profile demonstrated:

1) Vitamin B12: <50 pg/mL (NV: 300 pg/mL - 900 pg/mL).
2) Folic acid: 3.2 ng/mL (NV: 3 ng/mL - 20 ng/mL).

3) Total bilirubin: 3.8 mg/dL (NV: 0.2 mg/dL - 1.2 mg/dL).

4) Direct bilirubin: 2.1 mg/dL (NV: 0 mg/dL - 0.3 mg/dL).

5) Haptoglobin: <8 mg/dL (NV: 30 mg/dL - 200 mg/dL).

6) LDH: 890 U/L (NV: 135 U/L - 225 U/L).

7) Erythrocyte sedimentation rate: 50 mm/1st hour.

Peripheral blood smear revealed marked anisocytosis with macrocytic predominance, erythrocyte dysmorphism, and hypersegmented neutrophils, findings compatible with megaloblastic anemia.

Additional serological investigation demonstrated:

1) Anti-parietal cell antibodies: positive (titer 1:160).

2) Anti-intrinsic factor antibodies: positive.

3) IgM Parvovirus B19: positive.

4) IgG Parvovirus B19: positive.

Upper gastrointestinal endoscopy, performed previously, had documented signs of chronic atrophic gastritis compatible with autoimmune gastritis.

2.3. Therapeutic Intervention

Supportive therapy was initiated with intramuscular vitamin B12 supplementation (1000 μg daily for 7 days, followed by weekly administration). Blood transfusions were not administered, given the patient's stable hemodynamic status, opting for rigorous clinical surveillance.

2.4. Follow-Up and Results

Clinical evolution was favorable, with gradual symptom improvement and progressive recovery of hematological parameters. Laboratory control at 2 weeks showed:

1) Hemoglobin: 7.8 g/dL.

2) Leukocytes: 4200/μL.

3) Platelets: 180,000/μL.

4) Reticulocytes: 8.5%.

At 4 weeks, complete normalization of the hemogram and pancytopenia resolution was verified. The patient continues outpatient follow-up with regular vitamin B12 supplementation, remaining asymptomatic.

3. Discussion

This case illustrates a complex clinical presentation that combines underlying pernicious anemia with transient aplastic crisis induced by Parvovirus B19. The coexistence of these two nosological entities creates significant diagnostic challenges and emphasizes the importance of adequate clinical suspicion [10] [11].

Parvovirus B19 has specific tropism for erythroid progenitor cells through binding to P antigen, expressed on the surface of erythrocyte precursors [12]. Under normal conditions, infection rarely causes significant hematological manifestations in immunocompetent individuals. However, in patients with underlying hemato-

logical disorders, particularly those with hemolytic anemia or severe nutritional deficiencies, transient suppression of erythropoiesis may occur, resulting in aplastic crisis [13] [14].

Pernicious anemia, characterized by severe vitamin B12 deficiency secondary to autoimmune gastritis, predisposes patients to hematological complications during viral infections [15]. Cobalamin deficiency compromises DNA synthesis in hematopoietic cells, resulting in ineffective erythropoiesis and progressive pancytopenia [16]. When associated with Parvovirus B19 infection, this hematological vulnerability is exacerbated by direct viral suppression of bone marrow [17].

Laboratory findings in our case are consistent with this complex pathophysiology. Initial pancytopenia reflected both vitamin B12 deficiency and viral bone marrow suppression. The presence of hyperbilirubinemia and decreased haptoglobin suggested concomitant hemolysis, probably related to ineffective erythropoiesis characteristic of cobalamin deficiency [18]. Hypersegmented neutrophils in blood smear constitute a pathognomonic sign of megaloblastic anemia [19]. In the context of megaloblastic anemia, biochemical markers of hemolysis (elevated LDH, low haptoglobin, increased bilirubin) are commonly observed due to the destruction of erythroid precursors within the bone marrow (intramedullary hemolysis). However, the reticulocyte index remains low because reticulocyte maturation and release are impaired by vitamin B12 deficiency, limiting bone marrow compensation for the anemia.

Positive serology for IgM and IgG anti-Parvovirus B19 confirmed recent infection or viral reactivation. Simultaneous detection of both antibodies may indicate acute infection in seroconversion phase or reactivation in a previously exposed patient [20]. No myelogram or PCR for parvovirus B19 was performed (as this study would have to be performed in an external laboratory, making it impossible to obtain results in a timely manner), so the diagnosis was supported by positive serology (IgM and IgG), clinical and laboratory findings strongly suggestive of megaloblastic anemia associated with acute viral infection, and exclusion of peripheral causes for pancytopenia.

The absence of typical clinical manifestations of Parvovirus B19 infection, such as exanthema or arthralgia, is not uncommon in adults, particularly in patients with significant comorbidities [21].

Conservative therapeutic approach with intensive vitamin B12 supplementation proved effective, avoiding the need for bone marrow biopsy or other invasive interventions. This strategy is based on recognition that aplastic crisis associated with Parvovirus B19 is typically transient and self-limited [22] [23]. The robust reticulocyte response observed at 2 weeks confirmed erythropoiesis recovery and resolution of viral bone marrow suppression.

Recent literature (2021-2024) documents an epidemic resurgence of Parvovirus B19-related aplastic crises in adults, with heterogeneous clinical characteristics and variable severity. A paradigmatic case published in 2025 described an immunocompetent adult in the fifth decade of life who developed severe aplastic anemia (Hb < 5 g/dL, pancytopenia) following mechanical valve replacement, with a viral load >

100 million genomic equivalent copies/mL, presenting profound reticulocytopenia (RPI < 0.002) and marked hemolysis indicated by LDH > 500 U/L, requiring rigorous differential diagnosis with prosthetic mechanical hemolysis and responding favorably to intravenous immunoglobulin (IVIG) 1.5 g/kg - 2.0 g/kg combined with erythropoiesis-stimulating agents.[24] The CDC reported in 2024 a 3.6-fold increase in the incidence of aplastic crises in patients with sickle cell disease compared to the previous 13 years, attributing this phenomenon to post-COVID-19 pandemic "immunity debt" [25] [26]. Moreover, a 2022 report documented the fourth worldwide case of severe aplastic anemia in a previously healthy and immunocompetent young adult (22 years old) without underlying hemoglobinopathy, emphasizing that B19-related aplastic crises—traditionally considered exclusive to patients with chronic hematologic diseases—can occur in individuals without obvious predisposing factors [27].

These recent cases highlight the need to maintain a high index of diagnostic suspicion in adults with acute pancytopenia associated with paradoxical reticulocytopenia, particularly in the post-pandemic epidemiological context characterized by increased viral circulation and expanded population susceptibility.

4. Conclusions

The clinical importance of this case lies in demonstrating that Parvovirus B19 infection should be considered in the differential diagnosis of pancytopenia in patients with pernicious anemia, particularly when there is acute deterioration of hematological parameters. Early recognition of this association can prevent unnecessary invasive diagnostic procedures, as aplasia is transient and responds adequately to supportive measures [28] [29].

Additionally, this case emphasizes the vulnerability of patients with severe nutritional deficiencies to hematological complications during viral infections. Nutritional status optimization, particularly timely correction of vitamin deficiencies, may reduce the risk of severe aplastic episodes in patients exposed to bone marrow suppressive viral agents.

This report is limited by the fact that it is a single case, which limits the generalizability of the findings. Potential confounding factors include chronic use of metformin (which can reduce B12 absorption) and a proton pump inhibitor (esomeprazole, a possible factor in micronutrient malabsorption), as well as the lack of invasive studies (bone marrow biopsy) and the use of only serology to diagnose Parvovirus B19 infection.

5. Key Points

1) Parvovirus B19 infection can trigger transient aplastic crisis in patients with underlying pernicious anemia, exacerbating pre-existing pancytopenia.

2) The combination of severe vitamin B12 deficiency with viral bone marrow suppression creates a complex hematological picture requiring adequate clinical recognition.

3) Suspicion of Parvovirus B19 infection in patients with acute pancytopenia deterioration can prevent unnecessary invasive procedures, as aplasia is typically transient.

4) Intensive vitamin B12 supplementation constitutes first-line therapy, being sufficient to promote hematological recovery in most cases.

5) Rigorous clinical monitoring and serial follow-up of hematological parameters are essential to document aplastic crisis resolution and guide therapeutic decisions.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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