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Case Report

Generalized edema associated with parvovirus B19 infection

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SUMMARY

Generalized edema is a rare presentation of human parvovirus B19 infection. The etiology of this edema is unclear, particularly because signs of heart or renal failure are often not present. We report the case of a young adult presenting with generalized edema with serological and PCR evidence of parvovirus B19 infection, and discuss the potential mechanisms of edema based on the previous literature.

1. Introduction

The human parvovirus B19 was first discovered in 1975. It belongs to the *Parvoviridae* family of small single-stranded DNA viruses.[1] Parvovirus infections are widespread and the majority of adults are immune due to past infection. In children, infection can lead to erythema infectiosum, also called fifth disease. In adults, the classic clinical symptoms are an exanthematous rash, arthralgia, and edema. However, most have only non-specific flu-like symptoms or are completely asymptomatic.

Parvovirus infection has also been associated with more serious, even life-threatening clinical manifestations. Myocarditis, hepatitis, glomerulonephritis, aplastic crisis, and chronic pure red blood cell aplasia have been described.[1–5] During pregnancy, parvovirus infection can cause anemia and generalized edema in the fetus, resulting in non-immune hydrops fetalis and spontaneous abortion.[1] Generalized edema has also been described as a rare presentation of parvovirus infection in adults.[3–5] Questions remain about the etiology of generalized edema, particularly when no signs of heart or renal failure are present. We describe the case of a young adult presenting with generalized edema with serological and PCR evidence of parvovirus infection and no signs of cardiac or renal failure, and discuss the potential mechanisms of edema.

2. Case report

The patient was a 37-year-old female with no medical history. She was admitted to our hospital with progressive generalized edema and shortness of breath. One month earlier she had experienced a period of total malaise, fever, and arthralgia. Two weeks later, bilateral edema of the legs and periorbital edema occurred spontaneously. She gained 6 kg of weight during this period.

On examination she had normal vital signs, with a blood pressure between 140/70 and 160/80 mmHg during admission. On heart auscultation a holosystolic murmur was audible (point of maximal impulse 4th intercostal space on the left side). Normal respiratory sounds were heard on both sides. Bilateral pitting edema of the lower legs and periorbital edema was present. Laboratory analysis showed a normocytic anemia (with normal folic acid and vitamin B12) and raised D-dimer and N-terminal pro-brain natriuretic peptide (NT-proBNP; 1049 ng/l). Normal C-reactive protein (CRP), leukocyte count and differential, troponin, lactate dehydrogenase, creatine kinase, thyroid stimulating hormone, kidney function (serum creatinine 89 μmol/l, estimated glomerular filtration rate (eGFR; MDRD 65.8 ml/min)) and albumin levels (38 g/l) were found. In addition, urine analysis was also normal (no leukocyturia, proteinuria, or hematuria). The fractional excretion of sodium was 0.42%. An electrocardiogram (ECG) was normal with no signs of cardiac ischemia, myocarditis, or pericarditis. Echocardiography showed normal systolic and

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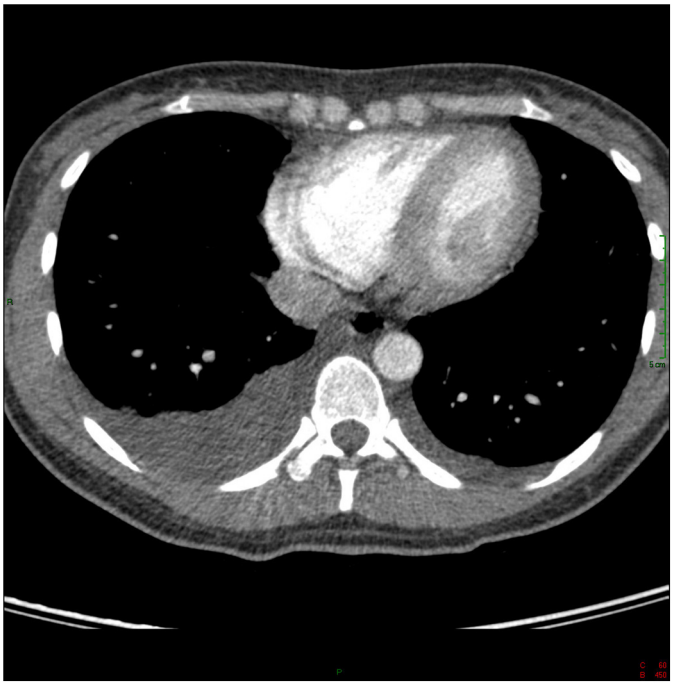

Figure 1. Computed tomography image of the thorax showing bilateral pleural effusion.

diastolic function, with only mild mitral valve regurgitation and no pericardial effusion. Chest X-ray and computed tomography (CT) of the thorax demonstrated bilateral pleural effusion (Figure 1), but no pulmonary emboli or other pathology. Ultrasound imaging of the abdomen showed a dilated inferior vena cava without collapse on inspiration. No enlarged thoracic or abdominal lymph nodes were found on these imaging studies. Hypothyroidism was excluded and no autoantibodies were found with screening. Echocardiography and cardiac markers were repeated the next day and demonstrated similar results. Extensive serological tests for viral infections were performed and confirmed human parvovirus B19 infection by detection of specific IgM and IgG antibodies on the Liaison platform (DiaSorin, Saluggia, Italy). A secondary enzyme immunoassay (NovaLisa Parvovirus B19 IgM, Novatec, Germany) confirmed the positive IgM result. Also a PCR of the sample was performed, which confirmed the serological diagnosis of parvovirus B19 infection.

Our patient was treated with loop diuretics and recovered rapidly. At follow-up 3 months later, she was asymptomatic; the parvovirus IgM index had decreased significantly (from 44.3 to 6.3) and the IgG index had remained stable (from 33.4 to 37.4). Serum creatinine was slightly lower (79 μmol/l; eGFR 71 ml/min).

3. Discussion

Several case reports have been published on the occurrence of generalized edema in adults after parvovirus infection. However, the etiology of this edema remains unclear.

Edema formation is defined as an increase in interstitial volume and depends on the balance between intravascular and interstitial hydrostatic and oncotic pressure and the permeability of the vascular wall to macromolecules (e.g., albumin). Two specific forms of edema formation remain out of the scope of this overview: lymphedema due to obstruction of drainage in the lymphatic vessels in lymphoma or filariasis, and myxedema with interstitial albumin accumulation in hypothyroidism. The pathophysiology of edema formation is conceptually categorized into three groups, which relate to these three factors: an increase in capillary hydrostatic pressure, a decrease in capillary oncotic pressure, and an increase in vascular permeability ('capillary leakage'). An increased capillary hydrostatic pressure is an often hypothesized mechanism for parvovirus-induced edema formation, as most published cases have reported signs of plasma expansion.[3,4] In our patient, an increased NT-proBNP, a dilated inferior vena cava, and a decreased fractional sodium excretion were seen, suggesting volume overload. Sodium retention causing edema can be primary (due a defect in renal sodium excretion), or secondary (due to the response of normal kidneys to an actual or sensed low effective circulating volume).

Secondary causes of sodium retention are for example heart failure, liver cirrhosis, and increased capillary permeability. Parvovirus B19 infection can cause viral myocarditis[2] or high output cardiomyopathy (due to persistent anemia, as parvovirus is cytotoxic for erythroid progenitor cells). However, in our patient, echocardiography, ECG, and cardiac markers were normal and only mild anemia was present. This makes myocarditis unlikely in our patient. Previous authors have also suggested increased capillary permeability as a possible cause of parvovirus-induced generalized edema.[4] However, extensive capillary leakage is associated with the occurrence of hypotension and hemoconcentration. In our patient the opposite occurred: relatively high blood pressure, dilated inferior vena cava, elevated NT-proBNP, and anemia. This makes increased capillary permeability as a separate factor in our patient less likely.

Primary sodium retention is possible, as parvovirus B19 infection has been related to glomerular diseases causing a nephrotic syndrome.[6] In experimental nephrotic syndrome, primary sodium retention has been found to exist in combination with a normal glomerular filtration rate. This is thought to be in line with the urinary volume response to diuretics in patients, which precedes the rise in albumin levels. The condition of our patient also improved on diuretics. However, patient urine and blood samples demonstrated normal serum albumin and no evidence of proteinuria, which rules out a nephrotic syndrome. In nephrotic syndrome, pulmonary effusions are not seen, in contrast to our patient and reports in the literature.[3–5] Questions remain as to whether parvovirus B19 infection can cause a less prominent viral nephropathy, resulting only in an increase in absorption of sodium as the primary symptom, for example as a mild interstitial nephritis.

In summary, parvovirus B19 infection has been associated with a broad range of diseases causing generalized edema. As these diseases can cause severe morbidity and mortality, early recognition is important. We therefore recommend that parvovirus infection be added to the differential diagnosis of generalized edema. In the present case, primary renal sodium retention could have contributed to the fulminant generalized edema. Diuretics are key to a good prognosis.

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