ACTA MEDICA TRANSILVANICA December27(4):21-23
Online ISSN 2285-7079

Q FEVER WITH RENAL MANIFESTATIONS - CASE REPORT

LIVIA MIRELA POPA[1] COSMINA GINGĂRAȘ[2]

[1] "Lucian Blaga" University of Sibiu, [1,2]Sibiu County Clinical Emergency Hospital

Keywords:
Coxiella Burnetii, acute nephritic syndrome, macroscopic hematuria, thrombophilia

Abstract: *this article aimed at presenting the case of a young patient, who presented with altered general condition, febrile syndrome, accompanied by systematized signs and symptoms, with the onset of an acute nephritic syndrome (initially, marked by the presence of macroscopic hematuria and oliguria), later, deep venous thrombosis is associated at the level of the left common femoral vein. The evolution was favorable under specific antibiotic, anticoagulant therapy. The patient remained for further the monitoring of the infectious disease doctor, nephrologist, cardiologist.*

INTRODUCTION

Q FEVER

Coxiella burnetii is the etiological agent of Q fever or Query fever. It belongs to the Order Legionellales, Family Coxiellaceae.(1)

It is a coccobacillus with a wall similar to Gram-negative bacteria, but it uses the Gimenez staining.(2)

Coxiellosis is an endemic zoonosis worldwide (except for Antarctica and New Zealand).(2) It is transmitted mainly by inhalation of contaminated aerosols, but also by tick bite, ingestion of unpasteurized dairy products, human-to-human transmission. The source of infection is the infected animals: cattle, sheep, goats or rodents.

Occupational exposure: slaughterhouse workers, veterinarians, farmers.

Clinically. Acute infection: - 60% asymptomatic or

-The most common form of presentation is fever.

-Rapid onset with high fever, sometimes very severe retroorbital headache, myalgia, arthralgia, pneumonia, hepatitis, less often, pericarditis, myocarditis, aseptic meningitis, encephalitis, acalculous cholecystitis. The fever lasts, on average, 10 days

-Other common manifestations can be: hepatomegaly, splenomegaly, purpuric skin rash, glomerulonephritis with immune complexes.(3,4)

Chronic infection – occurs months or years after the acute infection. It can occur after symptomatic or asymptomatic infections. It is a rare form (less than 5% of acute infections).(5) The most common clinical form is endocarditis. It can also manifest under the form of vascular infections, osteomyelitis, osteoarthritis, lymphadenitis, chronic hepatitis, chronic pneumonia. (5)

ACUTE NEPHRITIC SYNDROME

It consists of the association of micro/macroscopic hematuria (usually macroscopic, with dysmorphic red blood cells and acanthocytes), hematic or hemoglobinic (and granular) cylinders, leukocyturia (inferior to hematuria) and proteinuria (over 0,5 g/24 h, but usually under 3,5 g/24 h). Clinically, it is manifested by oliguria, salt and water retention with consecutive hypervolemia, causing edema and hypertension. The rise in serum creatinine, acute (days) or rapidly progressive (weeks), is variable.(7,8) It is a medical emergency.

CASE PRESENTATION

A 41-year-old patient was admitted through the Emergency Room in the Infectious Diseases Clinic of the Sibiu County Clinical Emergency Hospital, approximately one week after the onset of a febrile syndrome, accompanied by right lumbar pain, macroscopic hematuria, dyspeptic syndrome consisting of nausea, vomiting. SARS CoV 2 PCR testing was negative.

The imaging examinations (abdominal ultrasound, native computer tomography), performed in the Emergency Room, described both kidneys with increased sizes (predominantly the right one), with marked spread of perirenal and retroperitoneal fat, spontaneously homogeneous hepatomegaly.

The presumptive diagnosis, at the time of admission, was Acute Pyelonephritis, most likely right, for which the symptoms, imaging examinations and the presence of the biological inflammatory syndrome (leukocytosis with neutrophilia (leukocytes = 18000/mm3 with neutrophils = 15910/mm3) pleaded, CRP = 74 mg/dL).

Cultures are collected: urine culture, pharyngeal, nasal exudate, sputum examination, then a broad-spectrum antibiotic was administered empirically.

The completion of biological investigations, in the Infectious Diseases Clinic, reveals the presence of a minor syndrome of nitrogen retention (but with a descending character compared to the value present at admission (serum creatinine = 1,23 mg/dl versus 1,4 mg/dl, serum urea = 48 mg/dl versus 54 mg/dl), the presence of macroscopic hematuria is confirmed, red blood cells in the urinalysis = 300 ery/µl, to which proteinuria = 100 mg/dl and leukocytes = 25 leu/µl are added, urine sediment with dysmorphic erythrocytes – frequent and eumorphic – frequent, a syndrome of hepatocytolysis is evident (GOT = 86 U/l, GPT = 108 U/l), the biological inflammatory syndrome has a marked ascending character CRP = 308 mg/dl, procalcitonin = 1 .45 ng/ml).

Nephrology consultation is requested. At the time of

[1]Corresponding author: Livia Mirela Popa, B-dul C. Coposu, Nr. 2-4, Sibiu, România, E-mail: liviamirelapopa@yahoo.com, Phone: +40269 215050
Article received on 03.10.2022 and accepted for publication on 20.12.2022

the nephrology consultation, the patient is in a mediocre general condition, marked by significant physical asthenia, slightly dyspneic, with a diminished vesicular murmur in the lower half of the right hemithorax, with rales of stasis at this level, SaO2 in ambient air = 97%, affirmatively without episodes of hemoptysis, presenting with a dry cough, without skin eruptions, with significant leg and perimalleolar edema, bilaterally, BP = 145/70 mmHg, AV = 86/min, diuresis = 1200 ml, urine with an intensely hematuric appearance.

Investigations targeting acute nephritic syndrome are completed; immunological tests: C3, C4, Rheumatoid factor, IgA, IgM, IgG, Cryoglobulins, panel ANA, ANCA - are negative. Serum protein electrophoresis reveals mild hypoproteinemia with hypoalbuminemia.

Diuretic, parenteral oncotic and hydro-electrolytic rebalancing therapy is instituted, under which the clinical evolution was slowly favourable, diuresis over 4000 ml is obtained, with improvement of dyspnea, but with the persistence of macroscopic hematuria.

The leg edematous syndrome has a remissive character, but with the moderate persistence of the left leg edema ovelapping a high intensity pain at the level of the calf, accompanied by local heat.

Biologically, the nitrogen retention syndrome has a slightly ascending character, the onset of a hypochromic anemia is detected, the hematological investigations are continued, with evidence of the direct Coombs Test (Specific Antiglobuinic – IgG, C3) – Positive ++, LDH with much increased values compared to present value at admission = 837 U/l, D Dimers with greatly increased values = 30316 ng/ml, sputum examination, collected at admission, is positive for Enterobacter cloacae and fungi.

Cardiology consultation is requested, Venous Doppler Echocardiography of the lower limbs is performed: dilated bilateral common femoral veins, non-compressible. Intraluminal thrombus present in the left common femoral vein and spontaneous contrast in the right common femoral vein.

Diagnosis: Deep vein thrombosis of the left common femoral vein.

Transthoracic echocardiography: RV smaller than LV, LV with sizes and homogenous kinetics, LVEF = 55%, no visible transthoracic vegetations, AO normal dimensions, thin lamina of circumferential pericardial fluid.

Anticoagulant therapy is instituted, low molecular weight heparin, administered every 12 hours, in doses adapted to the patient's body weight and the degree of renal impairment.

Hematology consultation: Diagnosis: Autoimmune hemolytic anemia with warm antibodies, mild form, intra-infectious. Indications are given to initiate corticosteroid therapy, Dexamethasone 8 mg – 4 ampoules/day – 3 days, with subsequent progressive reduction and replacement with oral corticosteroid therapy.

A tumour screening is performed, paraneoplastic thrombosis is excluded.

The infectious cause of hemolytic anemia and nephritic syndrome is re-evaluated and it is decided to continue investigations with the determination of Anti Coxiella Burnetii antibodies (phase I and phase II), obtaining positive values for IgM and IgG (phase II).

The presence of deep vein thrombosis in a young man, without evidence of an oncological pathology, raises the suspicion of thrombophilia; investigations continue with the determination of the genetic profile of the risk of thrombophilia: MTHFR A1298C – heterozygous mutation, PAI -1 4G/5G – heterozygous. The risk of thrombosis increases when PAI-1 gene mutations are associated with other genetic mutations (e.g. MTHFR gene, factor V gene, prothrombin gene).

Treatment with Doxycycline 100 mg -2x100 mg/day is initiated, oral anticoagulant treatment with acenocoumarol is continued, in doses adapted to obtain a therapeutic INR result (target values = 2-3), the corticotherapy dose is reduced.

The patient is monitored periodically, biologically and clinically. At the last evaluation, the patient is in good general condition, without astheno-adynamic syndrome, without macroscopic hematuria, hemodynamically and respiratory balanced, but with the persistence of a post-thrombotic syndrome in the left lower limb. Biologically, it is without biological inflammatory syndrome, without hepatocytolysis, minimal nitrogen retention syndrome (net upward character compared to previous evaluations), without proteinuria, with microscopic hematuria (eumorphic erythrocytes).

He remains under the observation and monitoring of the infectious disease doctor and the nephrologist, continuing the specific antibiotic therapy.

DISCUSSIONS

Infection with Coxiella burnetii and the resulting disease, Q fever, is considered a zoonosis, infected animals being the primary sources of infection.

Urban epidemics related to the proximity of farms, where Coxiella spores are carried by the wind, have also been described. The infectious dose is very small: 1-10 viable Coxiella cells. There are differences between strains isolated in various parts of the world.(9)

Our patient denies any contact with potentially infected animals or the ingestion of contaminated milk, he does not know if there are animal farms in the vicinity of the house (at the time of the onset of the disease, the patient had been living in England for several months).

In the specialized literature, hematuria is described as a common syndrome in Coxiella burnetii infection. The reported cases, in which a renal biopsy was also performed, described glomerulonephritis by immune complexes in approximately 25% of cases, the majority of cases of glomerulonephritis being associated with endocarditis.(10)

The primary manifestation of the infection differs from one area to another, in Canada pneumonia is more common, while in France liver damage is more common.(2)

It has been suggested that these differences may reflect the route of infection, the ingestion of contaminated milk causing hepatitis and inhalation of contaminated aerosols causing pneumonia. Endocarditis has been described as a frequent association, especially in cases of chronic Coxiella infection, and usually occurs in patients with prior valvular heart disease, immunosuppression, or chronic renal failure.

In our case, endocarditis was not diagnosed. Instead, hepatitis and hemolytic anemia were present.

It should be noted that in 50% of cases the presence of a hepato-splenomegaly was highlighted. In our case too, hepato and splenomegaly was confirmed, and biologically, hepatocytolosis was observed.(10)

In the literature, the presence of a reactive thrombocytosis is described, with the presence of a number of at least 1 million platelets, a more frequent manifestation during the convalescence period. This thrombocytosis can cause deep vein thrombophlebitis.(10)

Our patient developed this vascular complication, which has been attributed to the presence of thrombophilia, since, biologically, the presence of reactive thrombocytosis was not found.

Sometimes, the diagnosis can be delayed, due to the initial symptoms that are non-specific, practically at the beginning of the disease, several pathologies from the infectious sphere can be considered. The association of hemolytic anemia,

accompanied by kidney and liver damage, directed us towards serological screening by determining phase I and II antibodies for Coxiella burnetii.

The current therapy is based on the ESC 2016 recommendations and consists in the administration of Doxycycline (200 mg/day) x 14 days, in acute Q fever, and macrolides, trimethoprim-sulfamethoxazole, fluoroquinolones are included as treatment alternatives. Trimethoprim-sulfamethoxazole is recommended for pregnant women.(3)

In the case of chronic Q fever (which also includes endocarditis): doxycillin+hydroxychloroquine x18 months (24 months for prosthetic heart valve postendocarditis). Serological testing will be done every 3 months during two years, after stopping the antibiotic treatment.(3)

CONCLUSIONS

Given the presence, especially of sheep, of ticks in our geographical area, this zoonosis is underdiagnosed,

The particularity of this case consists in the fact that, in evolution, there was also renal damage (the presence of glomerulonephritis), this association not being described in the specialized literature, as the most frequent association,

The negative impact on the general condition is given by the presence of deep venous thrombosis (in an important vein), in the conditions of the association of thrombophilia, a pre-existing pathology unknown to the patient.

REFERENCES

1. Eldin C, Mélenotte C, Mediannikov O, et al. From Q fever to Coxiella burnetii infection: a paradigm change. Clin Microbiol Rev. 2017 Jan;30(1):115-90.
2. Boarbi S, Fretin D, Morihttps M. Coxiella burnetii, agent de la fièvre Q. Canadian Journal of Microbiology. 2016;26(2).
3. Diagnosis and Management of Q Fever — United States, 2013 Recommendations from CDC and the Q Fever Working Group, Recommendations and Reports. 2013;62(3).
4. Ceaușu E. et al. Tratat de Boli Infecțioase, vol II. Editura Medicală. București; 2020.
5. Hartzell JD, Wood-Morris RN, Martinez LJ, et al. Q fever: epidemiology, diagnosis, and treatment. Mayo Clin Proc. 2008 May;83(5):574-9.
6. Ceaușu E. et al. Tratat de Boli Infecțioase, vol I. Editura Medicală. București; 2018.
7. Mircescu G et.al. Glomerulopatiile. Editura medicală. București; 2016.
8. Covic A, et.al. Nefrologie. Principii teoretice și practice. Casa Editorială Demiurg. Iași; 2011.
9. Bennett JE. Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases; 2020.
10. Walker D, Raoult D, Brouqui P, Marrie T. Boli Ricketsiale. Harrison. Principiile Medicinei Interne. 14th ed. Editura Teora; 2001.