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CASE REPORT Open Access

Infective endocarditis complicating rituximab in a lupus patient with lupus nephritis and dilated cardiomyopathy: case report and review of literature

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Abstract

Background Systemic lupus erythematosus is a chronic multisystem disease that has a considerable morbidity and mortality. Rituximab is used in treating some severe manifestations of systemic lupus erythematosus; however, it may expose patients to serious infections. We report a case of post rituximab infective endocarditis as the second case in literature described in patients with SLE.

Case presentation A 17-year-old male diagnosed as systemic lupus erythematosus with lupus nephritis and dilated cardiomyopathy received rituximab and underwent upper endoscopy and colonoscopy investigating iron deficiency anemia. Later on the patient developed septic shock secondary to infective endocarditis and passed away.

Conclusions Infective endocarditis is a possible complication after rituximab therapy in lupus patients with lupus nephritis and dilated cardiomyopathy. Prophylactic antibiotics may be considered in those patients in the settings of gastrointestinal endoscopies.

Keywords Infective endocarditis, Rituximab, Systemic lupus

Background

Systemic lupus erythematosus (SLE) is a disease characterized by heterogeneous multisystem organ affection that occurs in relapsing-remitting course. Rituximab (RTX) can be used in treatment of organ threatening or life-threatening manifestations [1].

Rituximab was the first anti Cluster of Differentiation 20 (CD20) monoclonal antibody to be discovered. It is currently approved for the treatment of rheumatoid arthritis and anti-neutrophil cytoplasmic antibody associated vasculitides (AAV), and is used off-label for other autoimmune diseases, like SLE. Serious infective events are recognized as possible side effects of RTX therapy, with various percentages in various diseases [2].

In this case report, we describe a rare case of infective endocarditis diagnosed after RTX use in a young adult male with SLE.

Case presentation

A 17-year-old male patient, known case of systemic lupus erythematosus for 2 years diagnosed by musculoskeletal and mucocutaneous manifestations, positive serology (positive antinuclear antibodies, positive anti-double stranded deoxyribonucleic acid (anti-dsDNA) antibodies, positive direct antiglobulin test and complement C3 and C4 consumption, and lastly lupus nephritis that was proved by histopathological assessment to be class IV. Mycophenolate was used for induction of remission and also for maintenance along with low

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dose of corticosteroids. He was also severely depressed on selective serotonin reuptake inhibitor. He suffered from persistent vomiting, diarrhea and significant weight loss with poor appetite. Vomiting and diarrhea improved after stoppage of mycophenolate. On assessment he had regular tachycardia with heart rate of 120 beats per minute, there was dyspnea on moderate exertion and paroxysmal nocturnal dyspnea but no orthopnea or lower limb edema. Echocardiography showed ejection fraction 40%, dilated left ventricular internal dimensions, impaired overall contractility, global hypokinesia, dilated left atrium, and mitral regurge, but no masses or vegetations. The echo results reflected cardiomyopathy, although the cardiac enzymes were normal, the cardiomyopathy was most likely secondary to lupus myocarditis. Laboratory assessment showed: Total leucocytic count (TLC) = 6000/mm^3, hemoglobin =7.3 g/dL, mean corpuscular volume = 74 μm^3, mean corpuscular hemoglobin = 23 pg, platelets = 496,000/mm^3, creatinine = 1.2 mg/dL, urea = 47 mg/dL, uric acid = 8 mg/dL, alanine aminotransferase = 16 mU/mL, aspartate aminotransferase = 12 mU/mL, ALP = 85 U/L, albumin = 2.1 g/dL, serum sodium = 134 mEq/L, serum potassium = 4.5 mEq/L, total calcium corrected with albumin = 9 mg/dL, serum iron = 17 µg/dL, serum total iron binding capacity = 121 µg/dL, transferrin saturation = 14%, erythrocyte sedimentation rate = 50, antinuclear antibodies = 1/160, serum complement C3 = 47 mg/dL (80–160), serum complement C4 = 15 mg/dL (15–45), 24-h urinary proteins = 5 gm/24 h.

So to control lupus nephritis and his cardiac condition, he was given pulse steroid 1 gm for three successive days and then rituximab 500 mg first dose was given and he was scheduled for rituximab 500 mg every week for 4 successive doses.

As he had microcytic hypochromic anemia with iron indices showing iron deficiency, he was prepared for upper gastrointestinal (GIT) endoscopy to exclude GIT causes, but no abnormality could be detected, so multiple biopsies were taken to exclude celiac disease.

Histopathological assessment was consistent with celiac disease (Marsh grade 3), with chronic gastritis (mild intensity). Then, he was discharged with improved general condition.

One week after discharge, the patient presented to the emergency room with fever, tachycardia and toxic facies. By examination, there were vasculitic lesions over hands and feet (Fig. 1). The patient was shocked with high sepsis parameters (high erythrocyte sedimentation rate, C-reactive protein, TLC, liver enzymes, and creatinine), cardiovascular support started with norepinephrine infusion with intravenous fluids and broad spectrum antibiotics, but the conscious level deteriorated, so the patient was intubated and mechanically ventilated. Echocardiography was done and showed vegetations over the mitral valve (Fig. 2). So, the case was diagnosed as infective endocarditis. First set of blood cultures was withdrawn and came back later as negative, and in spite of maximal ventilatory and cardiovascular support, the clinical state deteriorated rapidly and the patient, unfortunately, passed away.

Discussion

In this case, we reported a male patient, 17 years old who received RTX presenting with infective endocarditis after gastrointestinal endoscopy.

SLE patients have a higher risk of infective endocarditis especially those with pre-existing heart disease, chronic kidney disease, recent steroid pulse therapy or recent invasive dental procedure [3].

Our patient did not receive antibiotic prophylaxis based on the recommendations of the American Society

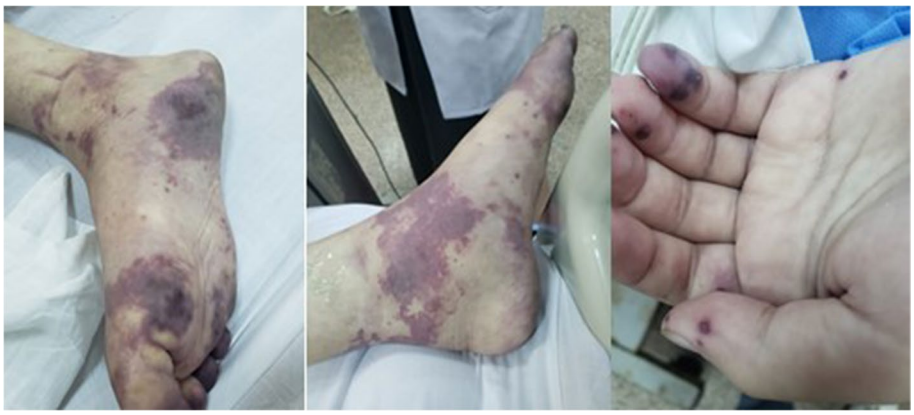

Fig. 1 Vasculitic lesions over hands and feet

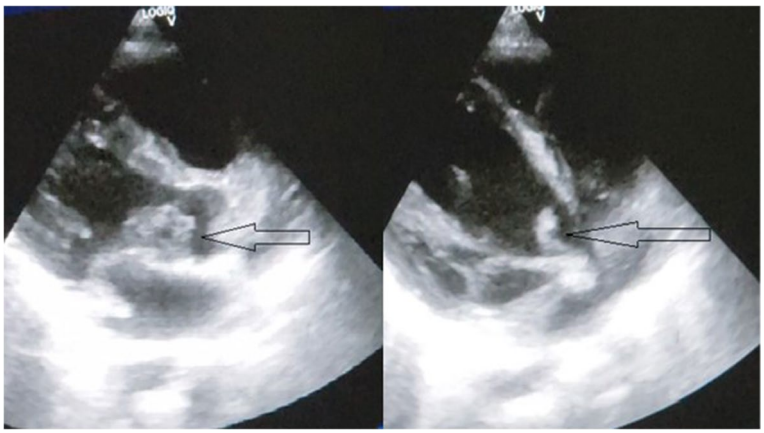

Fig. 2 Echocardiography images showing vegetations over the mitral valve

of Gastrointestinal Endoscopies which stated clearly that in patient with immunocompromised state and normal neutrophil count, as our patient, it is no recommended to give antibiotic prophylaxis, as a method of preventing infections other than infective endocarditis, as there is no evidence to support this practice. To prevent infective endocarditis, the same guidelines recommend using antibiotic prophylaxis only when the endoscopies involve risky procedures for bacteremia like esophageal dilatation, sclerotherapy, or maneuvers that manipulate the common bile duct, or when the patient has a predisposing cardiac condition, namely; prosthetic cardiac valves, history of previous infective endocarditis, cardiac transplant recipients who develop cardiac valvulopathy, and patients with some of congenital heart diseases. But when there is no predisposing cardiac condition and the patient is going for upper endoscopy, with or without biopsy, or colonoscopy, it is not recommended to give antibiotic prophylaxis, as transient bacteremia of usual daily activities may exceed that of such procedures [4].

On the contrary, our management of the case puts an alert regarding those recommendations, and highlights the need to further investigate the role of antibiotic prophylaxis in cases of immunosuppressed states.

Our case also describes a rare complication post Rituximab treatment in SLE patients.

One reported case was the only precedent to our case; a 54-year-old female whose successful treatment of cerebral lupus with rituximab was complicated by the development of streptococcus intermedius endocarditis, on valves damaged by Libman-Sacks endocarditis more than 20 years previously. Echo showed no vegetations but blood culture yielded growth of streptococcus viridans, the patient received antibiotics with good response. The authors recommended antibiotic prophylaxis in cases of SLE receiving RTX with evidence of valvular damage in echo [5]. But again our case had no previous cardiac damage or predisposing cardiac condition.

In one systematic review, including 188 SLE patients who received RTX, 171 (91%) patients showed a significant improvement in one or more of the systemic SLE manifestations but adverse events were reported in 44 (23%) patients; the most frequent were infections (19%), only one of those was endocarditis by Streptococcus Viridans [6].

Another retrospective cohort studied serious infectious events after RTX in two hundred twenty-one patients with autoimmune diseases (corresponding to 276 RTX courses). There were only three cases (Table 1) of endocarditis, none of them was SLE [7].

Another study of safety of rituximab in rheumatoid arthritis (RA) patients with a history of severe or recurrent bacterial infection showed one case of endocarditis among 30 patients with RA who received RTX. The case was that of 67-year-old female, with disease duration of 6 years. Rheumatoid factor and anti-cyclic citrullinated peptide were positive. She was on 7 mg prednisolone/day with no other immunomodulators. The patient suffered from septicemia and endocarditis, and after 48 months, she received RTX with no subsequent infection detected. The same study showed that rituximab therapy was well tolerated in 24 (80%) of 30 patients with RA and a history of severe or recurrent bacterial infection. So, the authors concluded that rituximab therapy may be safe regarding the recurrence of infections, but with strict follow-up [8].

Another 5-year observational study that included 989 patients with RA who received RTX showed that 341 significant infections occurred in 197 patients (19.9%) only. In that study only one case of fungal endocarditis

Table 1 Three cases of endocarditis post RTX therapy [7]

Patient	5	75	145
Gender	F	F	F
Age	76	63	85
Diagnosis	Systemic vasculitis	Other (IgG4-related disease)	Systemic vasculitis
Time since RTX initiation (months)	4.4	12.9	10.2
Infection	Endocarditis, spondylitis	Endocarditis	Endocarditis
Microorganism	Staphylococcus aureus	Staphylococcus epidermidis	MRSA
Treatment	Cloxacillin, rifampicin; levofloxacin, rifampicin	Daptomycin, gentamicin	Daptomycin, gentamicin
Death attributed to infection	No	No	No

was detected in a 29-year-old male, with the time from RTX infusion to death about 4 months [9].

Another study that observed patients with RA receiving RTX for 9.5 years with special focus on adverse events concluded that rituximab was generally well tolerated with no evidence of an increased safety risk or increased reporting rates of any types of adverse events with prolonged exposure to rituximab during the 9.5 years of observation, including 3194 patients. As regarding infections, the most commonly reported infections (> 5% patients) in rituximab patients were upper respiratory tract infections, nasopharyngitis, urinary tract infections, bronchitis, sinusitis, diarrhea, influenza, and gastroenteritis, while the most frequent serious infections was lower respiratory tract infection, predominantly pneumonia (2%), but not endocarditis. Serious opportunistic infections were rare, with seven events reported in the whole population, none of which was endocarditis or bacteremia [10].

Conclusions

Infective endocarditis is a possible but rare complication after rituximab therapy in patients with systemic lupus erythematosus. To the best of our knowledge, our case is the second case published with this complication post RTX. Prophylactic antibiotics may be considered in patients of autoimmune diseases receiving immunosuppressive therapy in the settings of gastrointestinal endoscopies, more research is needed to cover this evidence-deficient area so that the respective guidelines could be changed.

Abbreviations

AAV	Anti-neutrophil cytoplasmic antibody associated vasculitides
Anti-dsDNA	Anti-double stranded deoxyribonucleic acid
C3	Complement 3
C4	Complement 4
CD20	Cluster of Differentiation 20
GIT	Gastrointestinal tract
RA	Rheumatoid arthritis
RTX	Rituximab
SLE	Systemic lupus erythematosus
TLC	Total leucocytic count

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Authors' contributions

M. A. S. was the responsible resident, wrote the discussion, final version of the manuscript. R. F. Y. was the responsible resident, wrote the case presentation, and approved the final version of the manuscript. H. I. E. G. was the senior consultant and approved the final version of the manuscript. The author(s) read and approved the final manuscript.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request, anonymously.

Declarations

Ethics approval and consent to participate

The parents of the deceased patient gave their consent to participate.

Consent for publication

The parents of the deceased patient gave their consent to publish this paper.

Competing interests

The authors declare that they have no competing interests.

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