Lupus acute cardiomyopathy is highly responsive to intravenous immunoglobulin treatment
Case series and literature review
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Abstract
Introduction: Intravenous immunoglobulin (IVIg) is currently used with considerable success for the treatment of many autoimmune diseases, including systemic lupus erythematosus (SLE). Among its various indications, IVIg has also been found to be beneficial in myocarditis, whether or not it is associated with an autoimmune disease. Nevertheless, data regarding IVIg treatment for myocarditis/cardiomyopathy in patients with SLE are sparse. The objective of this case series was to describe our experience with IVIg as a treatment for lupus myocarditis and to review the literature for IVIg for this indication.

Patient concerns: We report 5 female patients with SLE, who presented with signs of acute heart failure including pulmonary congestion and arrhythmias.

Diagnosis: Echocardiography demonstrated new reduced left ventricular ejection fraction of 20% to 30%. Two patients underwent coronary artery angiography, which demonstrated normal coronary arteries, supporting the diagnosis of myocarditis or nonischemic cardiomyopathy.

Interventions: High-dose IVIg treatment was initiated in all 5 patients.

Outcomes: Following the treatment, clinical and echocardiographic improvement in cardiac function occurred within a few days to 1 month. This dramatic improvement persisted for several years.

Conclusion: Based on our case series, we believe that IVIg has an important role in the management of lupus acute cardiomyopathy. This safe, well-tolerated optional treatment should be considered, especially in severe cases.

Abbreviations: ACR = American College of Rheumatology, ANA = antinuclear antibodies, CHF = congestive heart failure, CMR = cardiac magnetic resonance, ED = emergency department, ICU = intensive care unit, IVIg = intravenous immunoglobulin, LM = lupus myocarditis, LV = left ventricle, LVEF = left ventricular ejection fraction, SLE = systemic lupus erythematosus, WBC = white blood cell.

Keywords: acute cardiomyopathy, intravenous immunoglobulins, myocarditis, systemic lupus erythematosus

1. Introduction
Among the various treatment options for autoimmune diseases, IVIg is considered the mainstay of treatment for several conditions, especially Kawasaki disease and immune thrombocytopenic purpura. It is also used in the treatment of idiopathic inflammatory myopathies, antineutrophil cytoplasmic antibody vasculitis and autoimmune neurological conditions.[1–3]

In the last 2 decades, our group and others demonstrated the beneficial effect of IVIg treatment for SLE,[4–11] with most data supporting amelioration of severe refractory flares and hematological manifestations following this therapy.[19–15] Some report that IVIg is also effective in lupus nephritis,[16,17] in neuropsychiatric manifestations,[18–20] and during pregnancy.[21]

Cardiac involvement presents in up to 50% of SLE patients and pericarditis is the most frequent manifestation of SLE-related cardiac disease.[22] However, all other cardiac components may be involved: endocardium, myocardium, conduction tissue, and coronary arteries.[23] Lupus myocarditis (LM) is a rare but potentially fatal complication, affecting up to 10% of SLE patients.[22,24–26] It may present as an acute illness or have a chronic course with the development of cardiomyopathy.[26] The treatment of LM is generally empirical. Either oral or intravenous pulses of corticosteroids have been the mainstay of treatment, while cyclophosphamide, azathioprine, mycophenolate mofetil, and IVIg have also been used with some success.[26,27] High-dose IVIg in SLE is mainly used as an adjunctive therapy when the standard treatments are ineffective or when immunosuppressive regimen is contraindicated. However, data concerning IVIg treatment for myocarditis/cardiomyopathy in lupus are sparse.
In this communication, we retrospectively review 5 cases who developed severe myocardial dysfunction, probably as a consequence of myocarditis secondary to SLE. All experienced dramatic improvement following IVIg therapy.

2. Cases

2.1. Patient 1

The details of this case of a 59-year-old female patient were described elsewhere. The patient presented to the Emergency Department (ED) with rectal bleeding. She had been diagnosed a few years earlier as having SLE, presenting with 4 of 11 American College of Rheumatology (ACR) criteria, including arthritis, pleuritis, high antinuclear antibodies (ANA) titers (1:1280), and elevated anti-dsDNA antibody titers. She was successfully treated with a few courses of IVIg and steroids for secondary myelofibrosis. Two months before admission, the patient had begun to receive 40 mg prednisone daily, which was continued throughout her admission. Upon admission, the patient was tachycardic, her blood pressure was 90/40 mm Hg, hemoglobin was 3.0 g/dL, white blood cell (WBC) count was 15.9 × 10^9/L, and platelet count was 587 × 10^9/L. Both prothrombin time and partial thromboplastin time were within normal ranges and an electrocardiogram was unremarkable. Gastric suction demonstrated “coffee ground” appearance of the gastric contents. Angiography of the mesenteric vessels demonstrated a bleeding gastroduodenal artery. Consequently, embolization of the bleeding vessel, in addition to transfusion of 4 units of packed red blood cells were instrumental in stabilizing the patient’s condition and achieving a hemoglobin of 9.6 g/dL.

Two days later, she developed a slow ventricular tachycardia and subsequently a ventricular fibrillation. After a successful resuscitation, she was transferred to the intensive care unit (ICU), where ST segment elevations were found in leads II, III, aVF, and V1–V6. Echocardiography demonstrated severe left ventricular dysfunction, with an akinesia that involved most of the left ventricle (LV) except for the basal segments. Estimated left ventricular ejection fraction (LVEF) was 20%. Creatine phosphokinase was 884 U/L (normal: 20–200 U/L) and its MB fraction was 147 U/L (normal: 5–25 U/L). A coronary angiography demonstrated normal coronary arteries. Hence, the differential diagnosis included acute myocardial infarction, either due to a thromboembolic event or vasculitis, vs myocarditis secondary to SLE. The patient refused to undergo cardiac biopsy. Therefore, the diagnosis of myocarditis was not proven histologically. The patient had no clinical signs of skeletal myositis. Of note, although she had arthralgia, anti-dsDNA, and antiphospholipid antibodies were negative during this hospitalization. Additionally, her ANA titer was 1:640, erythrocyte sedimentation rate was 90 mm/h, and the antibody titers to SS-A, SS-B and RNP, and levels of C3 and C4, were within normal ranges. Three days later, the patient was treated with nitrates, histamine receptor blockers, angiotensin-converting enzyme inhibitors, thiamine and her regular dose of prednisone (40 mg/day). In addition, high dose IVIg treatment was instituted: she received 0.5 g/kg IVIg per day for 4 consecutive days. Neither anticoagulants nor antiaggregates were added, because of the threat of recurrent massive gastrointestinal bleeding. Two days after IVIg treatment was initiated, an echocardiography revealed no significant change; whereas, 1 week afterwards, the estimated LVEF increased to 40%. The echocardiographic changes were associated with the patient’s subjective feeling of improvement, as well as objective signs such as normalization of blood pressure and complete normalization of her electrocardiogram (without the appearance of Q waves). There was no change in the ANA titer, while the erythrocyte sedimentation rate decreased to 70 mm/h.

The patient was discharged 2 days later, and follow-up echocardiography 1 month later demonstrated normal LV function, with an estimated ejection fraction of 53%. No clinical or echocardiographic evidence of cardiomyopathy was found during the next 2 years.

2.2. Patient 2

A 34-year-old woman was hospitalized in the Department of Internal Medicine because of fever. SLE had been diagnosed 5 years previously, when she presented with 6 of the 11 ACR criteria (arthritis, malar rash, oral ulcers, direct Coombs’ positive autoimmune hemolytic anemia, high titer of ANA (1:1280) and elevated anti-dsDNA antibody titers). She had been treated regularly with 10 mg/day of prednisone and 200 mg hydroxychloroquine twice daily.

On admission, the patient was tachycardic, her blood pressure was 110/70 mm Hg, and her temperature was 38°C. Hemoglobin was 9.5 g/dL, WBC count was 11.3 × 10^9/L, platelet count was 190 × 10^9/L. Her electrocardiogram was unremarkable. On the fourth day of hospitalization, the patient developed progressive dyspnea. Bibasilar pulmonary crackles were present on auscultation. An emergency echocardiography demonstrated moderate to severe LV dysfunction, with widespread akinesia of the LV except for the basal segments, with an estimated ejection fraction of 25%. Based on our previous experience, we initiated high dose IVIg therapy. The patient received 1 g/kg IVIg for 2 consecutive days with rapid improvement in cardiac function. After 3 days, her LVEF improved remarkably to 55%. No evidence of cardiomyopathy was found during the next 3 years.

2.3. Patient 3

A 51-year-old woman with a common variable immunodeficiency syndrome associated with SLE and antiphospholipid syndrome was hospitalized in the Department of Internal Medicine due to dyspnea. She was diagnosed 4 years previously with SLE based on 4 of the 11 criteria (serositis, arthritis, positive ANA and positive anti-dsDNA antibodies with low C3 and C4 levels). She was treated regularly with IVIg (0.4 g/kg once a month). Upon admission, the patient was tachycardic, her blood pressure was 95/70 mm Hg. Hemoglobin was 11.0 g/dL, WBC count was 15.9 × 10^9/L, and platelet count was 222 × 10^9/L. An electrocardiogram demonstrated atrial fibrillation with left bundle branch block. Echocardiography demonstrated moderate global LV dysfunction, with an estimated ejection fraction of 30%. Coronary angiography demonstrated normal coronary arteries. Based on our experience with IVIg therapy and due to her common variable immunodeficiency syndrome, we decided not to treat this patient with immunosuppressive therapy, but rather with high dose IVIg. The patient was given 0.4 g/kg IVIg per day for 5 consecutive days. After 2 weeks, her LVEF increased to 40%. One month after treatment, LVEF was 55%. The patient’s clinical condition paralleled the echocardiographic improvement. No clinical or echocardiographic characteristics of cardiomyopathy were noted during the next 4 years of follow-up.
2.4. Patient 4

This 36-year-old woman with a past medical history of SLE and antiphospholipid syndrome was diagnosed 16 years earlier by presenting with 4 of the 11 ACR criteria\[^{[29]}\], including: arthritis, photosensitivity, high titer of anticardiolipin antibodies, anti-dsDNA antibodies and ANA (1:640). She had been treated with mycophenolate mofetil and warfarin due to recurrent thromboembolic events (3 events of deep vein thrombosis and an incident of pulmonary embolism). Additionally, she had a history of depression and 1 suicide attempt and was being treated with tricyclic antidepressants.

She was initially admitted with fever, chills, and a rash on her chest and neck, and was discharged once her symptoms subsided. Several days later she returned to the ED and was noted to have a superficial chest vein distention. She was diagnosed with a left jugular vein thrombosis and treatment was immediately begun with low molecular weight heparin. She was subsequently discharged home.

On her third admission, she complained of abdominal pain and fever. An abdominal CT demonstrated retroperitoneal inflammation, pressure on the right ureter, and mild hydronephrosis. Blood and urine cultures were negative. Chest X-ray was unremarkable. Empiric antibiotics were initiated but were discontinued several days later when a herpetic rash developed around her lips. At that point, acyclovir and glucocorticoids were administered.

Twelve days into her admission, the patient developed shortness of breath. A follow-up CT scan showed improvement in the retroperitoneal inflammation and hydronephrosis yet signs of heart failure were evident. Echocardiography demonstrated severe LV failure with severe mitral regurgitation and pulmonary hypertension. Troponin C levels were elevated. With a probable diagnosis of myocarditis secondary to SLE, the patient was transferred to the ICU.

During her prolonged stay in the ICU, the patient was treated with high doses of methylprednisolone, followed by broad spectrum antibiotics for fever and sepsis. Blood cultures were positive for ESBL Klebsiella and MRSA. In addition, she required mechanical ventilation during 10 days for presumed acute respiratory distress syndrome, as well as hemodialysis due to severe renal failure with volume overload. Eventually, her fever subsided and she was extubated, after which she was transferred back to the internal medicine department.

On her arrival in the department, she was dyspneic with O₂ saturation of 85% on room air, with generalized edema and proximal muscle weakness. A ventilation/perfusion lung scan demonstrated low probability of pulmonary embolism. Repeat echocardiography showed severe LV failure with severe pulmonary hypertension. Of note, in addition to her declining physical condition, the patient was inclined to psychotic outbursts and unruly behavior, which were attributed at the time to SLE psychosis.

Due to her severe heart failure and psychotic episodes, both attributed to SLE, a decision was made to start treatment with high dose IVlg. The patient was treated with 0.4 g/kg IVlg per day for 5 consecutive days with dramatic results. One week later, she was able to start physical therapy. The edema completely disappeared and her psychotic episodes subsided. Follow-up echocardiography showed improvement in pulmonary hypertension, although evidence of heart failure remained.

2.5. Patient 5

This 35-year-old woman had been diagnosed a month previously with SLE by presenting with 4 of 11 ACR criteria\[^{[29]}\], including: anemia, nephropathy, oral ulcers, and arthritis. She was being treated with prednisone and was admitted with a chief complaint of shortness of breath that started several hours prior to her admission. She also noted fever at home but denied chest pain. Her vital signs on admission were: temperature 38°C, blood pressure 156/111, heart rate 120/min, respiratory rate 18/min, 0₂ saturation 93% on room air, 97% with 2 L nasal cannula. Hemoglobin was 8.0 g/dL, WBC count was 5.17 × 10³/L, and platelet count was 88 × 10³/L. A chest X-ray in the ED demonstrated centrally located bilateral alveolar infiltrates and bilateral pleural effusions. With a working diagnosis of pulmonary edema, secondary to a lupus flare, treatment was begun with IV corticosteroids, as well as broad spectrum IV antibiotics and furosemide. A non-contrast CT scan performed 2 days after admission showed a moderate pericardial effusion, moderate bilateral pleural effusions with surrounding atelectasis, multiple parametional nodules and bilateral parietal infiltrates described as ground glass. Echocardiography revealed LV dysfunction with an EF of 35%, right ventricular hypokinesis, biatrial enlargement, moderate mitral regurgitation, mild to moderate tricuspid regurgitation, moderate pulmonary hypertension and a small pericardial effusion. It should be noted that a previous echocardiogram, performed approximately 1 month earlier, demonstrated normal LV function. The patient continued to require large doses of furosemide, carvedilol, and IV nitroglycerin without significant abatement of symptoms. Her oxygen saturation on room air remained in the high 80s-low 90s. On the fifth day of admission, a decision was made to start treatment with high dose IVlg and she received 0.5 g/kg IVlg per day for 4 days. Thereafter, her condition improved dramatically and she no longer required oxygen by nasal cannula. Repeat echocardiography demonstrated marked improvement in LV function.

3. Discussion

IVlg is effective for treating several autoimmune conditions including some manifestations of SLE. However, it is usually reserved for cases when conventional therapies have failed or are contraindicated.

Evidence is accumulating that autoimmune processes are involved in the pathogenesis of cardiovascular diseases, specifically congestive heart failure (CHF) and cardiomyopathy.\[^{[30,31]}\] Several studies have shown that IVlg downregulates inflammatory responses in CHF patients and has potential beneficial effects on LVEF.\[^{[32–33]}\]

In a placebo controlled, double blind study, Gullestad et al\[^{[33]}\] demonstrated that the antiinflammatory effect of IVlg in chronic CHF was significantly correlated with improvement in LVEF, suggesting a potential for an immune-modulating therapy in addition to optimal, conventional cardiovascular treatment regimens in CHF patients. This effect was found independent of the cause of heart failure. Beneficial effects of IVlg have also been suggested in the acute setting—in acute myocarditis and cardiomyopathy.\[^{[34–38]}\] McNamara et al\[^{[34]}\] reported a series of patients with new-onset dilated cardiomyopathy treated with high-dose IVlg, resulting in marked improvement of ventricular function. Nevertheless, in another placebo-controlled study by
the same group, IVlg had no effect on 62 patients with recent-onset cardiomyopathy. We believe that a certain percentage of spontaneous improvement in recent-onset cardiomyopathy, accompanied by differences in the dosage schedule between studies (for example, maintenance therapy was given only to patients with chronic CHF) are accountable for the discrepant results between these studies. A recent meta-analysis conducted by Huang et al. concluded that IVlg therapy resulted in lower in-hospital mortality and superior recovery of left ventricular function in patients with acute myocarditis. Others have described the successful use of IVlg in peripartum cardiomyopathy and in viral cardiomyopathy. The use of IVlg for CHF and cardiomyopathy remains controversial.

LM is a severe cardiac manifestation of SLE, treated with high-dose corticosteroids, with or without other immunosuppressive therapy, in addition to standard cardiac management. Because SLE-related myocarditis is rare, there are few prospective studies, and management is based on isolated cases or small-series reports. Our belief that IVlg could have a central role in the management of LM/cardiomyopathy was based on the positive effects of IVlg on the ventricular function in cardiomyopathy and heart failure, along with its benefits for SLE, in general.

The 5 patients described in this report suffered from severe, acute cardiomyopathy, which can probably be attributed to SLE. Diagnosis was based on clinical manifestations and on electrocardiographic, echocardiographic and biochemical characteristics. Two patients underwent coronary angiography demonstrating no evidence of obstructive coronary disease; thus, ruling out thrombotic events, or vasculitis as the etiology of cardiomyopathy. Recent studies suggested that cardiac magnetic resonance (CMR) can assist in detection of myocardial ischemia in SLE patients, potentially caused by microvascular coronary dysfunction, in the absence of obstructive coronary artery disease. Due to limited access to CMR, these 5 patients did not undergo this test. The gold standard for confirming the diagnosis remains endomyocardial biopsy. However, this procedure is not routinely used because of its low sensitivity and potential complications. Thus, it was not performed in our patients. In our case series, the response to high dose IVlg therapy was fast. A single course of 2g/kg delivered over 2 to 5 days (as recommended for autoimmune diseases) led to prolonged improvement in cardiac status.

Previous reports have demonstrated the beneficial effects of IVlg on LM, but the number of patients was small and none focused on IVlg as the main treatment strategy. The largest recent report on LM was a multicenter, retrospective study conducted by Thomas et al. in which 29 patients were diagnosed with LM. Similarly, to our cases, most had elevated troponin, abnormal electrocardiogram, and echocardiography revealed low (<45%) LVEF. Eight of the 29 patients with LM were treated with IVlg in addition to high-dose corticosteroids. Seven received a single perfusion (2g/kg delivered over 3–5 days). One patient underwent repeated perfusions (monthly for 6 months). Overall, LVEF recovery rates were high: 81% exhibited an LVEF ≥55% at the end of a median follow-up of 37 months. Nevertheless, the authors compared outcomes in patients who received cyclophosphamide vs those who did not. Therefore, conclusions as to the effectiveness of IVlg treatment could not be drawn.

In a retrospective case series, Zawadowski et al. described the treatment and outcome of 24 patients with LM. Only 1 received IVlg for 5 days. The choice of immunosuppressive regimen, including dosage and length of treatment was based on the treating physician’s preference. Similarly, in a retrospective case-control study, Zhang et al. reported that 12 of the 25 patients diagnosed with LM were treated with IVlg, with results similar to those of other immunosuppressive therapies. In contrast, Du Toit et al. in a retrospective study in South Africa found that IVlg given to 3 of 28 patients with LM was not effective.

IVlg has also been suggested as an effective therapy for myocarditis secondary to other autoimmune diseases such as dermato-polymyositis, adult-onset Still disease and Kawasaki disease.

IVlg exhibits diverse mechanisms of action in autoimmune diseases, which include enhanced suppressor activity, Fc receptor blockade, complement regulation, B and T cell regulation and other mechanisms – all contributing to immunomodulation. The specific mechanism of immunomodulation in SLE is not completely understood but it involves the effect of IVlg on T and B cell intracellular signaling, the interferon signaling pathway and the disrupted elimination of immune complexes and other cellular debris.

In recent years, there has been a surge in the development of novel molecules that target Fc receptors and may offer an alternative to IVlg. The use of these agents for autoimmune diseases including SLE is being investigated in clinical trials.

Another future potential therapy is based on the fact that glycosylation patterns of IgG in IVlg preparations interfere with its antiinflammatory response. In vivo sialylation is a potent, novel approach to attenuate harmful autoantibody-mediated inflammation through glycoengineering endogenous antibodies and converting them to antiinflammatory mediators.

The current study has inherent limitations and interpretation of the findings is limited by aspects of the study design and the generalizability of the results. As mentioned above, neither myocardial biopsy nor CMR were undertaken to support our patients’ diagnoses, therefore, other causes for myocardial dysfunction could not be completely ruled out. Furthermore, treatment protocols differed and were dependent on the treating physician’s decision. The sample size was small, as well. Nevertheless, we believe this series is of great interest because it emphasizes the important role of IVlg in acute lupus cardiomyopathy. Randomized control trials are needed to elucidate the actual effect of IVlg vs other immunosuppressive therapies.

In conclusion, our 5 cases emphasize the complicated diagnosis and management of cardiac involvement in SLE, as well as the beneficial role of IVlg treatment. IVlg is increasingly being used for the treatment of various autoimmune diseases and it appears to be relatively well-tolerated and safe. Our belief is that its high cost justifies its use, especially in severe cases, such as the 5 discussed in this report. Even though spontaneous recovery was a possibility for our patients, we believe that IVlg was a major contributing factor to the fast recovery of cardiac function.

Author contributions

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References

[1] Bayry J, Negi VS, Kaveri SV. Intravenous immunoglobulin therapy in rheumatic diseases. Nat Rev Rheumatol 2011;7:349–59.
[2] Galeotti C, Kaveri SV, Bayry J. IVIG-mediated effector functions in autoimmune and inflammatory diseases. Int Immunol 2017;29:491–8.
[3] Gelfand EW. Intravenous immunoglobulin in autoimmune and inflammatory diseases. N Engl J Med 2012;367:2015–25.
[4] Schroeder JO, Zeuner RA, Euler HH, et al. High dose intravenous immunoglobulins in systemic lupus erythematosus: clinical and serological results of a pilot study. J Rheumatol 1996;23:71–5. http://www.ncbi.nlm.nih.gov/pubmed/8838511. Accessed November 7, 2019.
[5] Fieschi C, Galantucci M, Fioravanti A, et al. Long-term i.v. Ig treatment in systemic lupus erythematosus. Clin Exp Rheumatol 1994; 1994;12:163–8. http://www.ncbi.nlm.nih.gov/pubmed/8039283. Accessed November 7, 2019.
[6] Puddu P, De Pittà O, Ruffelli M, et al. Intravenous immunoglobulin therapy: modification of the immunofluorescence pattern in the skin of six patients with systemic lupus erythematous. Arthritis Rheum 1996;39:704–5.
[7] Levy Y, Sherrer Y, Ahmed A, et al. A study of 20 SLE patients with intravenous immunoglobulin-clinical and serologic response. Lupus 1999;8:705–12.
[8] Sherrer Y, Kuechler S, Scali JJ, et al. Low dose intravenous immunoglobulin in systemic lupus erythematosus: analysis of 62 cases. Int Med Assoc J 2008;10:55–5.
[9] Nieto-Aristizábal I, Martínez T, Urbano M-A, et al. Treatment with intravenous immunoglobulins in systemic lupus erythematosus: a single-center experience with 63 patients. Lupus 2019;28:1566–70.
[10] Camara I, Scascia S, Simeos J, et al. Treatment with intravenous immunoglobulins in systemic lupus erythematosus: a series of 52 patients from a single centre. Clin Exp Rheumatol 2014;32:41–7.
[11] Zandman-Goldgur D, Levy Y, Shoennfeld Y. Intravenous immunoglobulin therapy and systemic lupus erythematosus. Clin Rev Allergy Immunol 2005;29:219–28.
[12] Mulhern B, Bruce IN. Indications for IVIG in autoimmune and inflammatory diseases. Rheumatol (United Kingdom) 2015;54:383–91.
[13] Zandman-Goddard G, Krauthammer A, Levy Y, et al. Long-term therapy with intravenous immunoglobulin is beneficial in patients with autoimmune diseases. Clin Rev Allergy Immunol 2012;42:247–55.
[14] Hundt M, Manger K, Dörner T, et al. Treatment of acute exacerbation of systemic lupus erythematosus with high-dose intravenous immunoglobulin [10]. Rheumatolog 2000;39:1301–2.
[15] Aharon A, Levy Y, Bar-Dayan Y, et al. Successful treatment of early secondary myelofibrosis in SLE with IVIG. Lupus 1997;6:408–11.
[16] Levy Y, Sherrer Y, George J, et al. Intravenous immunoglobulin treatment of lupus nephritis. Semin Arthritis Rheum 2000;29:321–7.
[17] Bolets JN, Ioannides JPA, Boki KA, et al. Intravenous immunoglobulin in systemic lupus erythematosus: a series of 52 patients from a single centre. Clin Exp Rheumatol 2014;32:41–7.
[18] Zandman-Goddard G, Levy Y, Shoennfeld Y. Intravenous immunoglobulin therapy and systemic lupus erythematosus. Clin Rev Allergy Immunol 2005;29:219–28.
[19] Mulhern B, Bruce IN. Indications for IVIG in autoimmune and inflammatory diseases. Rheumatol (United Kingdom) 2015;54:383–91.
[20] Zandman-Goddard G, Krauthammer A, Levy Y, et al. Long-term therapy with intravenous immunoglobulin is beneficial in patients with autoimmune diseases. Clin Rev Allergy Immunol 2012;42:247–55.
[21] Hundt M, Manger K, Dörner T, et al. Treatment of acute exacerbation of systemic lupus erythematosus with high-dose intravenous immunoglobulin [10]. Rheumatolog 2000;39:1301–2.
[22] Aharon A, Levy Y, Bar-Dayan Y, et al. Successful treatment of early secondary myelofibrosis in SLE with IVIG. Lupus 1997;6:408–11.
[23] Levy Y, Sherrer Y, George J, et al. Intravenous immunoglobulin treatment of lupus nephritis. Semin Arthritis Rheum 2000;29:321–7.
[24] Bolets JN, Ioannides JPA, Boki KA, et al. Intravenous immunoglobulin treatment of lupus nephritis. Semin Arthritis Rheum 2000;29:321–7.
[25] Tedeschi A, Airaghi L, Giannini S, et al. High-dose intravenous immunoglobulin in the treatment of acute myocarditis. A case report and review of the literature. J Intern Med 2002;251:169–73.
[26] Kishimoto C, Shioji K, Hashimoto T, et al. Therapy with immunoglobulin in patients with acute myocarditis and cardiomyopathy: Analysis of leukocyte balance. Heart Vessels 2014;29:336–42.
[27] Huang X, Sun Y, Su G, et al. Intravenous immunoglobulin therapy for acute myocarditis in children and adults a meta-analysis. Int Heart J 2019;60:359–65.
[28] McNamaar DM, Holubkov R, Starling RC, et al. Controlled trial of intravenous immune globulin in recent-onset dilated cardiomyopathy. Circulation 2001;103:2254–9.
[29] Bozkurt B, Villaneuva FS, Holubkov R, et al. Intravenous immune globulin in the therapy of peripartum cardiomyopathy. J Am Coll Cardiol 1999;34:177–80.
[30] Vanich B, Alter P. Treatment options in myocarditis and inflammatory cardiomyopathy: focus on IV. immunoglobulins. Herz 2018;43: 423–30.
[31] Ishimori ML, Martin R, Berman DS, et al. Myocardial ischemia in the absence of obstructive coronary artery disease in systemic lupus erythematosus. JACC Cardiovasc Imaging 2011;4:27–33.
[32] Caffaro ALP, Pankuweit S, Arbustini E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J 2013;34:2636–48. 2648a–2648d.
[33] Disla E, Rhim HR, Reddy A, et al. Reversible cardiogenic shock in a patient with lupus myocarditis. J Rheumatol 1993;20:2174.http://www.ncbi.nlm.nih.gov/pubmed/8104958. Accessed December 14 2019.
[34] Charton N, Bernard C, Richard JC, et al. Off-label use of intravenous immunoglobulin therapy in the treatment of lupus myocarditis: two case reports and literature review. Rev Med Interne 2017;38:204–9.
[35] Micheloud D, Calderon M, Caparros M, et al. Intravenous immunoglobulin therapy in severe lupus myocarditis: Good outcome in three patients. Ann Rheum Dis 2007;66:986–7.
[36] Barnado A, Kamen DL. Myocarditis successfully treated with intravenous immunoglobulin in a patient with systemic lupus erythematous and myositis. Am J Med Sci 2014;347:256–7.
[37] Suri V, Varma S, Joshi K, et al. Lupus myocarditis: marked improvement with intravenous immunoglobulin in a patient with systemic lupus erythematous and myositis. Isr Med Assoc J 2008;10:55–8.
[38] Zhang L, Zhu YL, Li MT, et al. Lupus myocarditis: a case-control study from China. Chin Med J (Engl) 2015;128:2588–94.
[51] Du Toit R, Herbst PG, van Rensburg A, et al. Clinical features and outcome of lupus myocarditis in the Western Cape, South Africa. Lupus 2017;26:38–47.
[52] Cuny C, Eicher JC, Collet E, et al. Dilated cardiomyopathy disclosing dermatomyositis. Management. Ann Cardiol Angeiol (Paris) 1993;42:155–8.
[53] Gerfaud-Valentin M, Sève P, Iwaz J, et al. Myocarditis in adult-onset Still disease. Med (United States) 2014;93:280–9.
[54] Neto NSR, Waldrich L, de Carvalho JF, et al. Adult-onset Still’s disease with pulmonary and cardiac involvement and response to intravenous immunoglobulin. Acta Reum Port 2009;34:628–32.
[55] Kuek A, Weerakoon A, Ahmed K, et al. Adult-onset Still’s disease and myocarditis: Successful treatment with intravenous immunoglobulin and maintenance of remission with etanercept. Rheumatology 2007;46:1043–4.
[56] Dionne A, Dahdah N. Myocarditis and Kawasaki disease. Int J Rheum Dis 2018;21:45–9.
[57] Martínez T, Garcia-Robledo JE, Plata I, et al. Mechanisms of action and historical facts on the use of intravenous immunoglobulins in systemic lupus erythematosus. Autoimmun Rev 2019;18:279–86.
[58] Zuercher AW, Spirig R, Baz Morelli A, et al. Next-generation Fc receptor–targeting biologics for autoimmune diseases. Autoimmun Rev 2019;18:102366.
[59] Pagan JD, Kitaoka M, Anthony RM. Engineered sialylation of pathogenic antibodies in vivo attenuates autoimmune disease. Cell 2018;172:564–77. e13.