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Clinical and Serological Profile of Multiple Autoimmune Syndrome with Digeorge Syndrome Phenotype: Case Report and Literature Review

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Abstract Multiple autoimmune syndrome (MAS) is a form of polyautoimmunity that encompasses three or more autoimmune diseases with well-defined diagnostic criteria in the same individual, reflecting a shared genetic susceptibility and overlapping immunopathogenic mechanisms (autoimmune tautology) and alters the clinical and serological manifestations, as well as the prognosis of the diseases involved. Its association with chromosomal abnormalities such as DiGeorge syndrome (22q11.2 deletion syndrome) is uncommon. We present the case of a young woman with MAS which includes systemic lupus erythematosus, Sjögren's syndrome, and limited cutaneous systemic sclerosis with a DiGeorge syndrome phenotype (facial dysmorphism, mild cognitive impairment, dysthymia, and a history of cheiloplasty and palatoplasty for incomplete cleft palate). Her karyotype was normal, and her FISH test was negative, which did not rule out DiGeorge syndrome. It presents with severe lupus nephritis, pericarditis, pancytopenia and febrile neutropenia, with a poor clinical course. Its clinical and immunological characteristics and management are described, and a review of the medical literature is presented.

Keywords: *Multiple autoimmune syndrome (MAS), systemic lupus erythematosus (SLE), systemic sclerosis, Sjögren's syndrome, DiGeorge phenotype*

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1. Introduction

Multiple autoimmune syndrome (MAS) is a form of polyautoimmunity (PA) characterized by the co-occurrence of three or more autoimmune diseases with defined diagnostic criteria [1]. Genetic risk factors such as the alleles HLA-DRB1*03, *15, and *16 and shared clinical subphenotypes, known as autoimmune tautology, have been identified. The clinical manifestations of the involved diseases are altered, and the prognosis worsens [2]. Humbert and Dupond [1] proposed a classification of three types: 1. Type 1: myasthenia gravis (MG), thymoma, dermatomyositis and autoimmune myocarditis. 2. Type 2: Sjögren's syndrome (SS), rheumatoid arthritis (RA), primary biliary cholangitis (PBC), systemic sclerosis (SSc), and autoimmune thyroid disease. Type 3: alcohol-induced thrombocytopenic disease (AITD), myasthenia gravis (MG) and/or thymoma, Stevens-Johnson syndrome, pernicious anemia (PA), immune thrombocytopenic purpura (ITP), Addison's disease (AD), type 1 diabetes mellitus (T1DM), vitiligo (VIT), autoimmune hemolytic anemia (AH), and systemic lupus erythematosus.

There may be an association between MAS and specific chromosomal abnormalities such as DiGeorge syndrome (22q11.2 deletion syndrome), which has a prevalence of approximately 1 in 4,000 live births [3]. It is characterized by facial dysmorphism, multi-organ involvement, thymic hypoplasia, and lymphopenia, leading to immune dysfunction that predisposes mostly to autoimmune diseases such as juvenile arthritis, Graves' disease, immune thrombocytopenic purpura, autoimmune hemolytic anemia, autoimmune hypothyroidism, vitiligo, and autoimmune neutropenia [4].

We present a case of MAS comprising systemic lupus erythematosus, Sjögren's syndrome, and limited cutaneous systemic sclerosis with a clinical phenotype characteristic of DiGeorge syndrome. Its clinical and immunological characteristics and management are described.

2. Case Presentation

A 22-year-old female patient, born and residing in Lima, Peru, presented with a three-month history of exertional dyspnea, orthopnea, and edema, along with hair loss, worsening edema, and Raynaud's phenomenon. Four days prior to admission, she developed diarrhea, hypersomnia, dyspnea at rest, oliguria, hematuria, fever, and dysthymia, for what it wasadmitted to a general hospital. An echocardiogram revealed severe pericardial effusion, and pericardiocentesis was performed. Medical history: Menarche: 13 years. Last menstrual period: 15 days prior to admission. Blood type: “0” Rh positive. Denies sexual activity. Cheiloplasty and palatoplasty in 2015 at a general hospital. Paternal aunt diagnosed with systemic lupus erythematosus (SLE). Physical examination: BP: 140/90 mmHg. HR: 132 bpm. RR: 24 breaths/min, T°: 39.9°C, SatO2 93%, FiO2: 21%. Weight: 42 Kg, height: 1.50 m, BMI: 18.6. Poor general condition. Awake and oriented to time, place and person. Moderate pallor, skin hyperpigmentation, mild jaundice, anasarca, sclerodactyly (Figure 1), no lymphadenopathy.

Figure 1. Sclerodactyly (induration of the skin of the fingers with obliteration of the folds) and edema of the hands

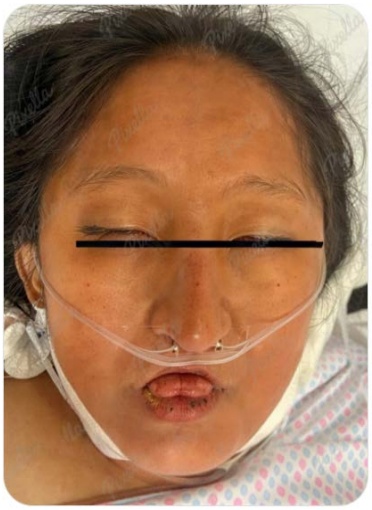

Figure 2. DiGeorge syndrome phenotype: hypoplasia of the outer third of the eyebrows; high and prominent nasal bridge; tip of nose bulbous; low-set ears, macroglossia and micrognathia

No synovitis. Hypoplasia in the outer third of the eyebrows, xerophthalmia, 3mm photoreactive pupils; high and prominent nasal bridge; tip of nose bulbous; small nostrils, short and poorly defined nasolabial fold. Decreased oral opening, xerostomia, macroglossia and micrognathia (Figure 2).

Neck: Jugular vein distension at 30° (+). Carotid pulse: 3+ bilaterally. Thyroid not palpable. Respiratory system: decreased vocal fremitus and breath sounds, dullness and crackles in the lower third bilaterally. Examination of the cardiovascular system: percutaneous pericardial catheter observed. No friction rubs. Heart sounds rhythmic and of moderate intensity. No added sounds. No murmurs. Peripheral arterial pulses: radial: +2, femoral: +3, dorsalis pedis: +2. Abdomen: Globular. Bowel sounds 6/min, soft, non-tender. Positive tidal wave. No organomegaly. Urinary system: Normal. Nervous system examination: Glasgow Coma Scale: 15/15. Folstein Scale: 26/30. Cranial nerves normal. Muscle strength 5+, decreased muscle mass throughout and normal muscle tone. Reflejos osteotendinosos: 2+. Normal superficial-proprioceptive sensitivity normal coordination tests. No meningeal signs.

Ancillary tests:

Hematology: complete blood count with leukocytes 2215/mm3, neutrophils: 554/mm3, lymphocytes: 1041/mm3; hemoglobin: 7.22 g/dL; MCV: 94.7 g/dL; platelets: 15500/mm3; reticulocytes: 4%. PT: 14 seconds; aPTT: 35 seconds. Biochemistry: Blood glucose: 85 mg/dL; creatinine: 2.2 mg/dL; urea: 108 mg/dL; albumin: 2.7 g/dL; total bilirubin: 2.8 mg/dL; indirect bilirubin: 2 mg/dL; AST: 150 U/L; ALT: 112 U/L; GGT: 320 U/L; LDH: 750 U/L (120-246 U/L). Serum electrolytes: potassium: 4.8 mEq/L, sodium: 129 mEq/L, ABG: pH: 7.15, HCO3: 14 mMol/L,PCO2: 43,BE:-12,AGAP:19, PaO2 / FiO2: 324, FiO2: 30. Lactate: 2.9 mmol/L

Table 1. Serological profile of rheumatic diseases and their relationship with clinical manifestations and severity in patients with multiple autoimmune syndrome (MAS)

Autoantibodies		Clinical manifestations	Autoimmune disease
Anti-dsDNA	988.5	Lupus nephritis, polyserositis, cytopenias	severe SLE
AntiSMD AntiSMB	988.5 988.5	Lupus nephritis, neuroSLE, autoimmune hemolytic anemia, thrombocytopenia	severe SLE
AntiRNP C AntiRNP 68	760.8 760.7	Lupus nephritis, cutaneous and hematological manifestations	severe SLE
AntiRNP A	979.6	Lupus nephritis	severe SLE
AntiPO	889.1	NeuroSLES, cutaneous SLE	severe SLE
Antinucleo-soma	988.5	Severe lupus nephritis	severe SLE
Antihistona	225.3	Lupus nephritis, cytopenias	severe SLE
AntiKu	340.9	Lupus nephritis, myopathies, interstitial lung disease	MAS
AntiSCL70	988.5		It is diffuse
AntiCENP A	445.3		Limited cutaneous ES
Anti-Ro52	769.4	ES, SS, LES, neonatal LES and Raynaud's phenomenon	
Anti-Ro60	834.3	SS, LES and neonatal LES	
Anti-La	754.1	SS and SLE	
AntiDFS70	241.8	SS	

ENA profile (normal range: 185-210). SLE: Systemic lupus erythematosus, SSc: Systemic sclerosis, and SS: Sjögren's syndrome. 1. Anti-RNP A, C, and 68: SLE, MCTD*, and Raynaud's phenomenon. 2. Anti-Ku: SLE, MCTD, and PM/SS. 3.Anti-Ro-52: SS, SLE, neonatal SLE, and Raynaud's phenomenon. 4. Anti-Ro-60 and Anti-La: SS and SLE. 5. Anti-DFS70: SS
*MCTD: mixed connective tissue disease

PaO2/FiO2: 324, FiO2: 30. Lactate: 2.9. Calcium: 7 mg/dL, phosphorus: 5.2 mg/dL (2.5-4.5), CRP: 112 mg/dL.Total cholesterol: 197 mg/dL.HDL: 45mg/dl. LDL: 119mg/d. Triglycerides: 164. 24h proteinuria: 2.1 g. Urinalysis: red blood cells: 70 x/h. Red blood cell casts: 2+. Pericardial fluid analysis: protein 3.2 g/dL, leukocytes: 840/mm³, erythrocytes: 300/mm³. ADA: 14 U/L. Vitamin B12: normal. Immunology: Direct Coombs test positive. PTH: 265 mg/dL (7.5-53). ANA: positive with a speckled pattern 1/160.

ENA profile: 1. Positive markers for systemic lupus erythematosus (SLE): AntiDNA (S: 57%; E: 97-99%), AntiSm (Anti-Smith) (S: 20-26 and E: 98-98), AntiRNP (against protein and RNA complexes in the cell nucleus) (S: 25-47 and E: 82-89), AntiPO (antiperoxidasa tiroidea) (S: 35.7% and E: 93.5%), antinucleosome (S: 50-61% and E: 90-99%), Anti-Ku (against DNA repair proteins) (S: 30.5 and E: 97.3%) and antihistone (S: 99% and E: 50-90%). 2. Positive markers autoimmune for systemic sclerosis AntiSCL70 (S: 33-40 and E: 96) and AntiCENP A (S: 30-40% and E: 98-99%). 3. Positive markers for Sjogren's syndrome: Anti-Ro52 (anti-SSA subtype with sensitivity: 39.3% and specificity: 83%), Anti-Ro60 (anti-SSA with sensitivity: 40-68% and specificity: 96-98%), anti-La or anti-SSB (sensitivity: 39-44% and specificity: 97-100%), and anti-DFS70 (sensitivity: 19% and specificity: 93%). Antineutrophil cytoplasmic antibodies: negative. Anticardiolipin and beta-2-glycoprotein antibodies: negative. C3: 70 (90-180) mg/dL, C4: 6 (10-40) mg/dL. TSH, free T3, and free T4: normal. IgM: 0.2 g/L. ELISA for HTLV-1, HBsAg, and total anti-HBc: negative. Microbiology: Blood culture: Candida parapsilosis. Radiological imaging: renal ultrasound: early signs of chronic kidney disease. Echocardiogram: LVEF: 55%, pericardial effusion. Chest X-ray: pleural effusion and alveolar-interstitial infiltrate. Genetic study: Normal karyotype. FISH: negative.

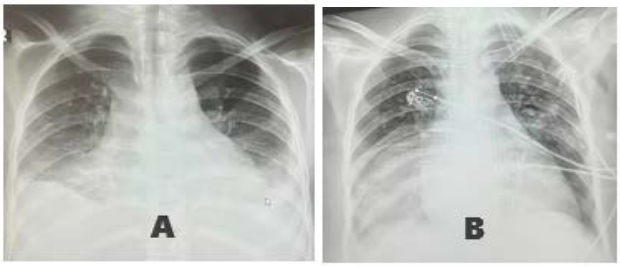

Figura 3. Chest X-ray AP: A. Pleural and pericardial effusion and bibasilar reticular interstitial parenchymal infiltrate. B. One week later, right pleural effusion in the middle of the right lung field and predominantly left-sided alveolar-interstitial infiltrate

Treatment

Methylprednisolone 1g IV pulses every 24 hours for 5 days, followed by prednisone 50 mg PO every 24 hours, hydroxychloroquine 200mg PO every 24 hours, mycophenolate mofetil, antibiotic coverage with meropenem 500mg IV every 24 hours, as well as calcium carbonate and folic acid.

Current Events

On day 7, the patient presented with drowsiness, hypertension, and an elevated serum creatinine level (7.82 mg/dL), requiring the initiation of renal replacement therapy (hemodialysis) due to superimposed acute kidney injury.

By day 10, the patient's condition deteriorated, with severe respiratory failure and lethargy. Candida parapsilosis was isolated from blood culture. The patient was transferred to the ICU and placed on mechanical ventilation.

3. Discussion

We present the case of a young woman with a family history of autoimmune diseases who presented with multisystemic involvement, raising the possibility of a diagnosis of multiple autoimmune syndrome (MAS) with the coexistence of three rheumatic diseases: systemic lupus erythematosus (SLE), Sjögren's syndrome (SS), and limited cutaneous systemic sclerosis (SSc). Anaya et al. reported that in the MAS the most frequent first autoimmune diseases were SLE, AITD (autoimmune thyroid disease) and SS, occurring in 32.7, 21.43 and 10%, respectively. [5].

On the other hand, we were struck by the patient's clinical phenotype, which was consistent with DiGeorge syndrome (22q11.2 deletion syndrome), the most common chromosomal deletion in humans [6]. He presented with facial dysmorphism. (hypoplasia of the outer third of the eyebrows; high, and prominent nasal bridge; tip of nose bulbous (enlarged); low-set ears, macroglossia, and micrognathia), mild cognitive impairment, dysthymia, and a history of cheiloplasty and palatoplasty for incomplete cleft palate. The association between DiGeorge syndrome (DGS) and autoimmune rheumatic diseases is uncommon. Giardino et al [7] found in 467 patients with SDG: 7 cases (1.4%) with autoimmune thyroid disease, 6 cases (1.34%) with juvenile arthritis, three cases (0.7%) with Raynaud's phenomenon and only 1 case (0.2%) with SLE/juvenile dermatomyositis.

An ENA profile of 44 antigens was requested (Table 1), revealing positive antibodies for SLE, SSc, and SS. Anaya et al. found the following in 84 patients with MAS: Anti-Ro, Anti-dsDNA, Anti-RNP, Anti-La, and Anti-Sm in 67%, 58%, 35%, 29%, and 28% of cases, respectively [8]. The SLE markers detected in the patient were: 1. Anti-dsDNA with very high titers, which are highly specific for diagnosis and indicate severity; they also correlate with lupus nephritis due to glomerular damage from immune complexes. 2. Anti-Sm D (against Sm D1, D2, and D3 antigens) and anti-Sm B (against Sm B1, B2, and B3 antigens) with very high titers, which are associated with lupus nephritis, neuroSLE, hemolytic anemia of autoimmune origin and thrombocytopenia. 3. AntiRNP A with high titer, antiRNP C and 68 with intermediate titer, correlate with hematological and cutaneous manifestations (rash and photosensitivity); when the titer is greater than 1000/ml it is compatible with Mixed Connective Tissue Disease (MCTD). 4. Anti-PO (the PO antigen is a ribosomal protein) is associated with neuropsychiatric manifestations, skin lesions, and hematological abnormalities; it is also an indicator of disease activity. 5. Anti-nucleosome (the antigen is the nucleosome, the fundamental unit of chromatin) is associated with severe lupus nephritis and is also an indicator of disease activity. 6. Anti-Ku (directed against the Ku70/Ku80 complex) is

associated with lupus nephritis, hepatic and neurological involvement, or with myopathy and interstitial lung disease (ILD); it is also positive in polyautoimmunity (PA): polymyositis (PM) /systemic sclerosis and SLE. 7. Anti-histone antibodies (histone H1, H3, and H4) are associated with severe lupus nephritis. 8. Anti-Ro and Anti-La are associated with pericarditis and photosensitivity.

The serological markers for Sjögren's syndrome identified were: 1. Anti-Ro52 (against TRIM21) and anti-Ro60 (SSA2) with intermediate titers correlate with increased B-cell activity, glandular inflammation, and lymphoma risk. When both antibodies are positive, they are associated with pulmonary complications [9]. 2. Anti-La or Anti-SSB (against the La or SSB protein, a ribonucleoprotein) is T-cell dependent and is associated with certain HLA-DR and DQ haplotypes. 3. Anti-DFS70 (Dense Fine Speckled 70), which has greater specificity when other autoantibodies coexist. In patients with positive ANA, the presence of only Anti-DFS70 rules out or excludes an autoimmune rheumatic disease.The systemic sclerosis autoantibodies detected were: 1. Anti-SCL70, which is associated with a higher risk of interstitial lung disease (ILD), rapid progression of skin involvement, and scleroderma renal crisis. 2. Anti-CENP A (against centromeric protein A) is a variant of histone H3 essential for centromere identity and function.

The diagnosis of SLE was confirmed using the EULAR/ACR1 classification criteria, with a score of 50 (including positive anti-dsDNA and anti-Sm antibodies), in addition to the positivity of other serological markers: anti-RNP A, C, and 68, anti-PO, anti-Ku, anti-histone, anti-Ro, and anti-La. ANA was positive with a speckled pattern, which is associated with anti-Sm and anti-RNP. From a genetic standpoint, it has been established that HLA-DRB1*16 predominates in SLE with multiple autoimmune syndrome (MAS) (OR=2.67, p = 0.031) [2]. The activity of this disease was also determined using the SLEDAI-2K index [10], indicating severe SLE. Associated diseases were Sjögren's syndrome (SS) and systemic sclerosis (SSc). The high anti-RNP titers correspond to SLE and not mixed connective tissue disease (MCTD), since the patient only met 2 of the 5 symptoms of this entity: Raynaud's phenomenon, hand edema, synovitis, myositis, and acrosclerosis, and the titer did not exceed 1000/ml. Chambers et al. found a prevalence of SLE with polyautoimmunity (PA) of 25% and of SLE with MAS in 1% to 7% of cases. The most frequent coexisting diseases identified in this study group were: autoimmune thyroid disease (AITD), antiphospholipid syndrome (APS), and Sjögren's syndrome (SS) in 18%, 14%, and 14% of cases, respectively [11].

The clinical manifestations of SLE with MAS in the patient were: nephritis, hematological alterations, cardiovascular complications, polyserositis and pleuroparenchymal involvement (Table 1). Matusiewicz et al. have reported that SLE with MAS presents with synovitis and neuropsychiatric involvement, that we have not found in the present case [12]. Fidalgo et al. also found the predominance of hematological alteration (OR:3.1) and Raynaud's phenomenon (OR:2.94) but also subacute skin lesions (OR: 2.30), myopathy (OR:2) and neuroSLE (OR:2.99) [2].

The prevalence of lupus nephritis in SLE with monoautoimmune involvement is 20-60%, and in 38% of cases it is an initial manifestation. It occurs due to loss of immunological tolerance to nuclear antigens and activation of T and B lymphocytes [13]. In our case, it manifested as nephritic syndrome (edema, hematuria, and 24-hour proteinuria of 2.1 g/dL) and led to stage 4 chronic kidney disease (CKD), clinically expressed as a uremic syndrome: dermatopathy, encephalopathy, hypervolemic hyponatremia, anemia, hypocalcemia with increased PTH and hyperphosphatemia (due to secondary hyperparathyroidism). Regarding the serological profile, 9 of the 13 SLE serological markers found in the patient were related to lupus nephritis; of these, the anti-dsDNA, anti-Sm, and anti-RNP autoantibodies had the highest titers, associated with the severity of this complication. An increased risk of proteinuria has been found when anti-Ro/SS-A and anti-dsDNA antibodies are positive, as in this case. In the evolution, the chronic kidney disease (CKD) worsened due to a superimposed acute kidney injury, requiring renal replacement therapy (RRT).

Pericarditis with effusion is the most frequent cardiac complication of SLE, with a prevalence of 20–50%. It occurs in younger patients with high SLEDAI-2K levels and is associated with anti-La antibodies [14]. It can also occur in the context of multiple autoimmunity, as in this case. Risk factors such as proteinuria, increased serum lipids and hypertension have been identified. The patient had an intermediate anti-La level, 24-hour proteinuria of 2.1 g, a slight increase in LDL cholesterol and triglycerides, and secondary hypertension of renal etiology.

The prevalence of polyserositis due to systemic lupus erythematosus (SLE) ranges from 11% to 54%. It is associated with disease severity, lupus nephritis, cytopenias, and positive anti-dsDNA and anti-RNP antibodies. Pericardial (25%) and pleural (16.5%) effusions are more predominant. In polyautoimmune SLE or MAS the serositis is usually more frequent and severe [15]. The patient had a severe pericardial effusion that required drainage by pericardiocentesis.

Autoimmune hemolytic anemia occurs in 12% of patients, and neutropenia in 11%. Hematologic complications of SLE are more prevalent when the disease is severe, antiphospholipid antibodies (aPL) and anti-Ro / SSA antibodies are positive, and hypocomplementemia is present [16]. This patient had hemolytic anemia and pancytopenia due to peripheral autoimmune destruction, complicated by febrile neutropenia, with a high risk of severe infection.

The clinical manifestations of limited systemic cutaneous sclerosis (SCS) with MAS in our patient were sclerodactyly, decreased mouth opening, and Raynaud's phenomenon. The prevalence of polyautoimmunity in patients with SCS varies from 10.9% to 43.9% in different studies [17]. The most frequent concomitant autoimmune diseases are: autoimmune thyroid disease (AITD), SS, dermatomyositis/polymyositis (DM/PM), with a weighted prevalence of 10.4%, 7.7% and 5.6%, respectively [18].

The clinical manifestations of Sjögren's syndrome (SS) with MAS in this patient were sicca symptoms: dry mouth and dry eyes. This syndrome can also produce pulmonary fibrosis and polyneuropathy. The prevalence of

polyautoimmunity in patients with SS is 52%. It is frequently associated with atypical autoimmune disease (AIAD), rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis (SSc), autoimmune hepatitis (AIH), and primary biliary cholangitis (PBC) [19].

In this case, there was also bilateral interstitial lung involvement, with the three rheumatic diseases—SLE, SSc, and SS—being the potential culprits. Interstitial lung disease is the most frequent pulmonary involvement in the context of polyautoimmunity, with the prevalence increasing if systemic sclerosis is present [20].

On the other hand, the George Syndrome (GSD) phenotype was identified in the patient, but with a normal karyotype and negative FISH (fluorescence in situ hybridization) test; however, GSD is not ruled out. Rope et al. found in 64 patients with this chromosomal abnormality that 45% did not present a deletion of chromosome 22q11.2 [21] due to the heterogeneity of DiGeorge Syndrome. While DiGeorge syndrome is associated with autoimmune diseases, its co-occurrence with systemic lupus erythematosus (SLE) is infrequent. We found reports of three cases of DiGeorge syndrome coexisting with SLE. The first was described by Chen Sun et al. concerning a 12-year-old girl with alopecia, oral ulcers, fever, and thrombocytopenia, as well as short stature, dysmorphic features, and mild cognitive impairment; with positive anti-dsDNA, anti-PO, and anti-nucleosome antibodies [22]. The second case was reported by Lin et al. concerning a 22-year-old patient with a skin rash, antiphospholipid syndrome (APS), nephritis, and hemocytopenia [23]. The third case, involving a diagnosis of DiGeorge syndrome with SLE/juvenile dermatomyositis, was described by Giardino et al. (0.2%) [7].

The association between GBS and MAS increases the risk of severe immunosuppression and severe infections. Giardino et al. [7] have described that 283/447 patients (63.3%) with GBS presented with recurrent upper respiratory tract infections, while 5% had severe infections.

In the neuropsychiatric field, it is estimated that between 73% and 90% of patients with 22q11.2DS present some type of psychiatric disorder, with anxiety (40%–76%) and mood disorders (9%–35%) being the most frequent.. Our patient presented with dysthymia and mild cognitive impairment.

The treatment prescribed for the patient was methylprednisolone pulses followed by prednisone, as well as hydroxychloroquine and mycophenolate. it is recommended methylprednisolone pulses (250–1000 mg), followed by prednisone 0.35 to 1.0 mg/kg/day. Two immunosuppressants should be added: mycophenolate mofetil, in combination with belimumab (human monoclonal antibody that inhibits B-cell activating factor-BAFF). or a calcineurin inhibitor (CNI: tacrolimus, cyclosporine, voclosporin). One alternative is intravenous cyclophosphamide combined with belimumab [24].

4. Conclusion

The case presented illustrates a multiple autoimmune syndrome which includes SLE, Sjögren's syndrome, and systemic sclerosis in a young woman. The coexistence of all three rheumatic diseases in the same person is rare. Also tiene fenotipo de sindrome de DiGeorge but with a negative FISH test, which does not necessarily rule out this entity. We have not found any reports of the association of DiGeorge syndrome with MAS that includes the 3 autoimmune rheumatic diseases mentioned. The most serious complications were: lupus nephritis severa, pericarditis with severe effusion, and hematological abnormalities (hemolytic anemia and pancytopenia); which added to severe immunosuppression and opportunistic infections (Candida parapsilosis). Propose that the SDG phenotype worsens the prognosis of autoimmune rheumatic diseases coexisting, therefore a comprehensive evaluation and a multidisciplinary therapeutic approach are required.

Authorship CGA, CGL, JCZ, MSZ and RFV participated in the conception and design of the article; CGA, CGL, JCZ, and RFV in data collection and drafting; CGA, CGL, JCZ, MSZ, and RFV in the critical revision of the article. All authors participated in the approval of the final version.

Conflict of interest the authors declare no conflict of interest.

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