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Pulmonary Cryptococcus's in rarely associated systemic lupus erythematosus and primary biliary cirrhosis

Smita Sharma[1] ✉, Gyanendra Agrawal[1]

[1]Dept. of Pulmocritical Care, Jaypee Hospital, Noida, Uttar Pradesh, India.

Email: smita.sm.gs@gmail.com

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Abstract

We hereby present a case report of rare associated diseases with systemic lupus erythematosus (SLE) like primary biliary cirrhosis, autoimmune haemolytic anemia complicating the course of SLE patient with pulmonary Cryptococcus's. ICU physicians in depth knowledge about SLE association and complications can change the overall prognosis of the disease.

Introduction

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by the presence of autoantibodies such as anti-double stranded DNA or anti-histones. Liver dysfunction is not the main organ pathology in SLE as liver function abnormalities are not included in the classification and diagnostic criteria of SLE. Primary biliary cirrhosis and autoimmune haemolytic anemia are rare complications in SLE which we can came across in our patient. SLE and COVID also make patient prone for opportunistic infection like aspergillosis, mucormycosis, Cryptococcus's and CMV infections.

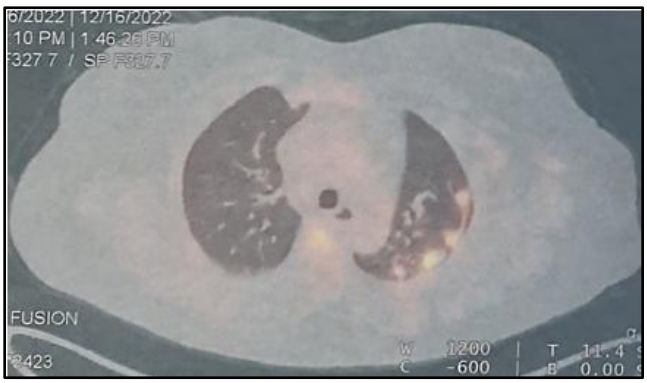
Case presentation

A 53-year-old female with previous history of systemic lupus erythematosus (SLE), primary hypothyroidism and recent COVID infection were admitted to our medical facility with chief complains of fever, intractable dry cough, worsening dyspnoea, and chest pain for three months. The patient completely recovered from severe COVID-19 illness 3 months back when he required oxygen therapy and hospitalization. All routine blood investigations, ECG and CXR were done. The hemogram reports were Hb-7.7.4gm/dl; TLC-14000/cumm; Platelet count-230000/cumm, Procalcitonin (PCT-0.01ng/ml), cardiac markers (troponin I &NTPROBNP), coagulation profile, kidney (KFT) and liver function (LFT) test were within normal limits (WNL). She was initially treated with broad spectrum antibiotics, NIV, oxygen, blood products and other supportive treatment PET CT whole body done for evaluation showed multiple FDG avid nodule (largest 12x20mm) in of left upper lobe (

Figure *1*). CT guided transthoracic trucut biopsy of the lung lesion was done for definitive diagnosis by Interventional Radiologist. Histopathology of the biopsy revealed granulomas with encapsulated rounded

yeast forms, morphologically suggestive of Cryptococci infection (**Figure 2**). In view evidence of invasive mycosis and presence of hypoxemia, patient was started on broad spectrum antifungal regimen of liposomal amphotericin (5 mg /kg/day) for 14 days in induction phase. MRI brain, orbit, and paranasal sinuses were done to look for invasive fungal infection at other sites. Detailed investigations of CSF were also done which ruled out CNS cryptococcosis. Blood and urine culture grew no bacteria or fungus. The patient was further managed with liposomal amphotericin, oxygen therapy and other supportive treatment. PET scan showed lobulated outline suggested of chronic liver disease (CLD).Patient was further evaluated for CLD by fibro scan and autoimmune markers. Fibroscan (Ekpa-73.9) suggestive of CLD.

Figure 1: *FDG avid pulmonary nodules in left upper lobe*



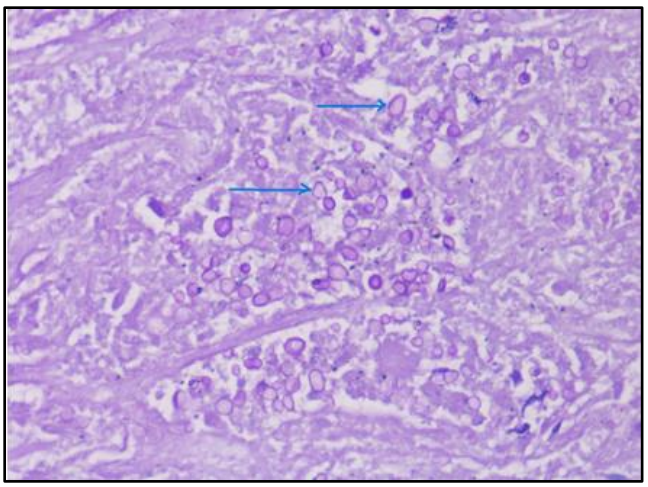


Figure 2: H&E-stained histological section shows a few pale refractive ovoid fungal spores of Cryptococcus species engulfed by giant cells within the granuloma.

The markers of autoimmune hepatitis (anti-smooth muscle antibodies, anti-liver/kidney microsome type 1 antibody and/or anti-liver cytosol type 1 antibodies) were negative. Antimitochondrial antibody (AMA) was suggestive of primary biliary cirrhosis (PBC). Patient was discharged normoxemic on the maintenance therapy with oral fluconazole 400 mg per day and ursodeoxycholic acid 450 mg twice daily. After a month patient presented to emergency with chief complains of fatigue shortness of breath, yellowish discolouration of body and on and off nasal bleed. Provisional diagnosis was acute on chronic liver failure. All routine blood investigations, ECG and CXR were done. The hemogram reports were Hb-5gm/dl; TLC-3000/cumm; Platelet count-15000/cumm, LFT were serum bilirubin total6.5 mg/dl mainly indirect, SGOT-80IU/L, SGPT-65IU/L, alkaline phosphatase-1200 U/l, LDH 800U/L.KFT, ECG and Echocardiography was within normal limit. Direct antiglobulin test was positive for IgG antibodies raised LDH, low haptoglobin, presence of spherocytes on peripheral smear and indirect hyperbilirubinemia suggestive of autoimmune

haemolytic anemia (AIHA). SLE flare up in this admission was indicated by elevated level of ds DNA antibody titre by ELISA (871 IU/L). Hence diagnosis of SLE, PBC, AIHA and pulmonary cryptococcosis was made. She was treated with broad spectrum antibiotics, antifungal, NIV, oxygen, blood products, anti-hepatic coma regime, steroids, and other supportive treatment. Rheumatology and gastroenterology consultations were taken and incorporated. Patient required mechanical ventilation and inotropic support for multiorgan failure. Unfortunately, patient scummed to her illness.

Discussion

The main predisposing factors for pulmonary cryptococcosis in above case were SLE and recent COVID infection. SLE patients are prone for opportunistic infections due to various genetic and intrinsic immunologic defects like complement deficiencies, decreased expression of cellular complement receptors, mannose-binding lectin (MBL) deficiency associated with homozygous MBL variant alleles, low levels of soluble Fc gamma receptor III levels, impaired chemotaxis and phagocytosis of macrophages and polymorphonuclear cells, abnormal T-cell-mediated cytotoxicity, functional asplenia. The use of glucocorticoid and immunosuppressive therapy for SLE are also predisposing factors for opportunistic infections.[1] COVID-19 infection makes patient susceptible to multiple opportunistic infections like infections like aspergillosis, mucormycosis and reactivation of cytomegalovirus infection as evident from multiple case report and case series.[2] Liver involvement in SLE is infrequent. The frequency of liver dysfunction during the course of SLE ranged from 19% to 60%. Lupus hepatitis (SLE-related hepatitis) is characterised by transaminitis. Lupus hepatitis is associated with SLE exacerbation which improves with glucocorticosteroid therapy. In lupus hepatitis, the fluctuations in alanine transaminase occur parallel to SLE activity. Lupus hepatitis is subclinical and rarely progresses to end-stage liver disease.[3] The identification of the aetiology of liver dysfunction in SLE (other than lupus hepatitis) is often difficult .The other causes of liver dysfunction in SLE are autoimmune hepatitis(AIH), primary biliary cirrhosis (PBC),primary sclerosing cholangitis(PSC), hepatic steatosis, non-alcoholic fatty liver disease, viral hepatitis, and drug-induced liver diseases(like by glucocorticosteroids, nonsteroidal anti-inflammatory drugs, and immunosuppressant). AIH is diagnosed based on elevated liver enzymes, and presence of anti-nuclear antibodies (ANA) or anti-smooth muscle antibodies, or anti liver/kidney microsome type 1 antibody or anti-liver cytosol type 1 antibodies and characteristic histological changes.[4] In above case SLE associated with PBC, diagnosed by presence of raised alkaline phosphatase and antimitochondrial antibody, which as per medical literature is rare. SLE often coexists with other autoimmune disorders like rheumatoid arthritis Sjogren's but association with primary biliary cirrhosis (PBC) is rare. The incidence of coexisting PBC in patients with SLE is ≤2%, with results ranging from 0% to 2.7%.[5] The diagnosis of PBC is established if two of the three objective criteria are present:[1] elevated serum alkaline phosphatase;[2] presence of AMA which is present in 90%–95% of patients[3] liver histology findings (presence of chronic, nonsuppurative, and destructive cholangitis) PBC is characterized by the selective destruction of intrahepatic cholangiocytes.[6] Autoimmune haemolysis

occurs in less than 10% of patients with SLE. Haemolytic anemia can occur years before or after a diagnosis of SLE. Warm autoimmune haemolytic anemia is more common than cold agglutinin type. Above case has warm autoimmune haemolytic anemia with IgG antibodies causing haemolysis by Fc-mediated extravascular phagocytosis of the IgG-coated red blood cells (RBC) in the spleen, resulting in spherocytes due to loss of RBC membrane. [7-8]

Conclusion

This case report and review of literature highlights SLE has multiorgan disease with various frequent and rare complications. Awareness among ICU physicians about varied SLE presentation and complications can lead to early diagnosis and can change the overall prognosis of the disease.

Source of Funding

None.

Conflict of Interest

None.

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