**INTRODUCTION**

Hepatitis C is an infectious disease affecting primarily the liver, caused by the Hepatitis C Virus (HCV). It is estimated that 150 - 200 million people, or ~3% of the world's population, are living with chronic hepatitis C. \(^1\) Pegylated Interferon-\(\alpha\) (IFN-\(\alpha\)), along with ribavirin, is used for the treatment of hepatitis C infection. Development and/or the exacerbation of pre-existing autoimmune phenomena, such as systemic lupus erythematosus (SLE), autoimmune hepatitis, rheumatoid arthritis, thyroid disease, idiopathic thrombocytopenic purpura and others, has been reported in patients receiving IFN-\(\alpha\) for a number of indications, such as myeloid leukemia and HCV infection. \(^2\) In these patients, an unexpectedly high incidence (20%) of autoantibodies was observed, including antinuclear antibodies (ANA), parietal cell antibodies, thyroid microsomal antigens and thyroglobulin\(^2\) and before the onset of SLE, duration of IFN-\(\alpha\) therapy ranged from 2 weeks to 7 years. \(^3\)

We present a case of development of full-blown SLE after treatment with IFN-\(\alpha\).

**CASE REPORT**

A 48-year female was admitted to our hospital with complaints of low grade fever, joint aches and pains, painful mouth ulcers and fatigue for the past one month. She also developed shortness of breath, dry cough and pleuritic chest pain since last six days. She was diagnosed with chronic hepatitis C infection one year ago. At that time, the platelet count and coagulation profile were normal. There was no family history of autoimmune diseases. The HCV genotype was 3. She began therapy with pegylated IFN-\(\alpha\) at a dose of 180 microgram per week subcutaneously, and ribavirin at a dose of 1200 mg orally daily in three divided doses for 6 month resulting in normalization of the serum transaminases and undetectable levels of HCV RNA, achieving end of the treatment response.

Chest examination revealed reduced air at right lower lobe with some crackles, pleural rub and a dull percussion note. There were also muffled heart sounds on auscultation of precordium. Rheumatologic examination demonstrated tenderness on palpation of both ankles and wrists. There was no malar or discoid rash.

Complete blood count revealed anemia (hemoglobin 10.1 g/dl) and thrombocytosis (platelets 542000/ microliter). Reticulocyte count was 2%. Blood biochemistry analysis and urine analysis were normal. Anti-Nuclear Antibody (ANA) was strongly positive (3+) with homogeneous pattern. Other laboratory findings showed an ESR 140mm/hour (6 - 20), CRP 15 (0 - 10), complement factor C3 1.20 g/l (0.83-1.93), complement factor C4 0.18 g/l (0.15 - 0.57) and anti-dsDNA antibody 949.77 IU/ml (strong positive > = 801 IU/ml). Anti-Sm/RNP antibody, anti-RO antibody, anti-LA antibody, anti-smooth muscle antibody, anti-mitochondrial antibody, anti-Scl-70 antibody and rheumatoid factor were negative. Chest X-ray showed mild right sided pleural effusion and echocardiography demonstrated mild to moderate pericardial effusion. Abdominal ultrasonography was normal. There was no systemic involvement associated with ocular, neurologic and renal diseases. Blood and sputum cultures were negative and HCV RNA remained undetectable, indicating sustained virological response.

A diagnosis of SLE was made. Steroids therapy was recommended. She was seen in outpatient department two months later and was taking prednisolone and...
hydroxychloroquine. Her fever, joint pains, mouth ulcers and dyspnea had much improved. During further follow-up, her symptoms remained under control and repeat HCV RNA by PCR was negative.

DISCUSSION

Produced by multiple cell types in response to viral infection, IFN-α plays an important role in immune regulation. Plasmacytoid Dendritic Cells (PDC) have a key importance in the production of IFN-α and are the main source of serum interferon. Main mechanism by which IFN-α is produced is via Toll-Like Receptor (TLR) signalling. TLR7 recognizes single-stranded RNA, leading to Interferon Regulatory Factor (IRF) 5 and IRF 7 activation and production of IFN-α. Antibody production against RNA-containing protein complexes such as nRNP, Ro, La and Sm is an important characteristic of most of the cases of lupus; and production of IFN-α through the stimulation of TLR7 is secondary to the presence of RNA in these complexes.

Two important characteristics of lupus are excess serum IFN-α and IFN-α response gene expression, which is most likely the result of excessive activation of PDC. By promoting immune activation rather than tolerance, such high levels of interferon can play a part in lupus. Dendritic cells, primary activators of T-cells, affect both T-cell tolerance and activation, depending on the state of the dendritic cell and these cells mature and become more prone to activate T-cells upon treatment with IFN-α.

Myeloid dendritic cells from lupus patients can phagocytize and present self-antigens to T-cells in a stimulatory rather than regulatory fashion which is an interferon-dependent process. This leads to loss of T-cell tolerance to self-antigens and results in autoimmunity. A number of patients treated with IFN-α have developed lupus or lupus-like syndrome.

In some case reports, many characteristic manifestations of idiopathic lupus such as malar or discoid rash, renal involvement, photosensitivity, oral ulcers and anti-Sm and anti-dsDNA antibodies, were represented; supporting the idea that these cases were not "drug-induced" SLE but instead resembled idiopathic SLE. The idea that IFN-α is a primary causal factor in human SLE is further strengthened by the clustering of high serum IFN-α in lupus families. Patients with lupus and their healthy relatives have higher serum IFN-α activity as compared to healthy unrelated individuals.

Therapy for IFN-α induced SLE has involved discontinuation of the IFN-α. Steroids were given in majority of these cases and the use of hydroxychloroquine has also been reported. Initial improvement was typically seen rapidly, within a few weeks to months in most of the case reports.

Since, there is an increasing use of IFN-α for a variety of indications, so physicians must be well aware of the risk of delayed autoimmune side-effects of IFN-α therapy. Therefore, treated patients should be monitored diligently for autoimmune manifestations, especially since these may be mistaken as benign effects of IFN-α.

REFERENCES