Thyroiditis induced by interferon in dialysis

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ABSTRACT

We describe a dialysis patient who acquired acute Hepatitis C infection. Her primary renal disease was systemic lupus erythromatosis. She was having goitre but clinically euthyroid and her thyroid function test was normal. To avoid long term complications of Hepatitis C we elected to treat her with Interferon 3 million units subcutaneously 3 times a week. During treatment she developed some transient side effects initially which subsided but later she felt pressure symptoms around her neck. When we checked her TSH and thyroid antibodies these were elevated. Though this could be related to HCV, rarely, but we think the thyroid change is mostly related to Interferon. Some possible explanation of the effect of Interferon on thyroid have been reviewed and we think patients getting such drugs should be under close monitoring to avoid permanent thyroid dysfunction.

Keywords: Renal failure, Hepatitis C, interferon, thyroiditis.

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A 24 year old lady who started on hemodialysis in May 1995. The cause of her renal failure was lupus nephritis. Shortly after initiating hemodialysis her disease was inactive clinically, and her serological markers were within normal. She was not complaining of any other problems except a goitre, and she was clinically euthyroid. After a holiday, where she was treated in another dialysis centre, she came to us with raised liver enzymes and HCV antibodies were positive. She was enrolled in a study to treat acute hepatitis C infection with interferon for 3 months. She was given 3 million units subcutaneously 3 times per week. At the first two weeks she suffered from interferon toxicity in the form of fever, joint pains and loss of hair. Her SLE serology markers remained normal. Thyroid function tests as a baseline were normal, but thyroid antibodies were not checked. During the 3rd week of treatment, she started to complain of pressure symptoms and pain around the neck anteriorly. She remained euthyroid clinically, but biochemically thyroid stimulating hormone (TSH) was very high and thyroid antibodies, including thyroglobulin antibodies (ThgAbS) and antiperoxidase antibodies (TPOAbs), had risen to very high levels. (Figure 1). Her liver enzymes normalized by the 3rd week and her primary renal disease remained silent.

We continued to observe her closely and continued with the interferon treatment. By the end of the 3rd month of treatment, her thyroid function (TSH) normalized, while her thyroid antibodies continued to be high 4 months after stopping interferon. She had a liver biopsy preparing for renal transplant which shows minimal hepatitis. Two years later she had a cadaveric renal transplant and she remained euthyroid clinically and TSH within normal.

Discussion. Our patient was HCV negative just before she went for a holiday, and she came back within 6 weeks with raised liver enzymes and HCV was positive. To prevent chronic hepatitis C changes in the liver, she was given interferon. Interferon has been reported to exacerbate autoimmune reactions, particularly autoimmune thyroid diseases and SLE, but in her case her primary renal disease remained silent.[1] Her thyroid antibodies were not checked before the treatment, but thyroid function was

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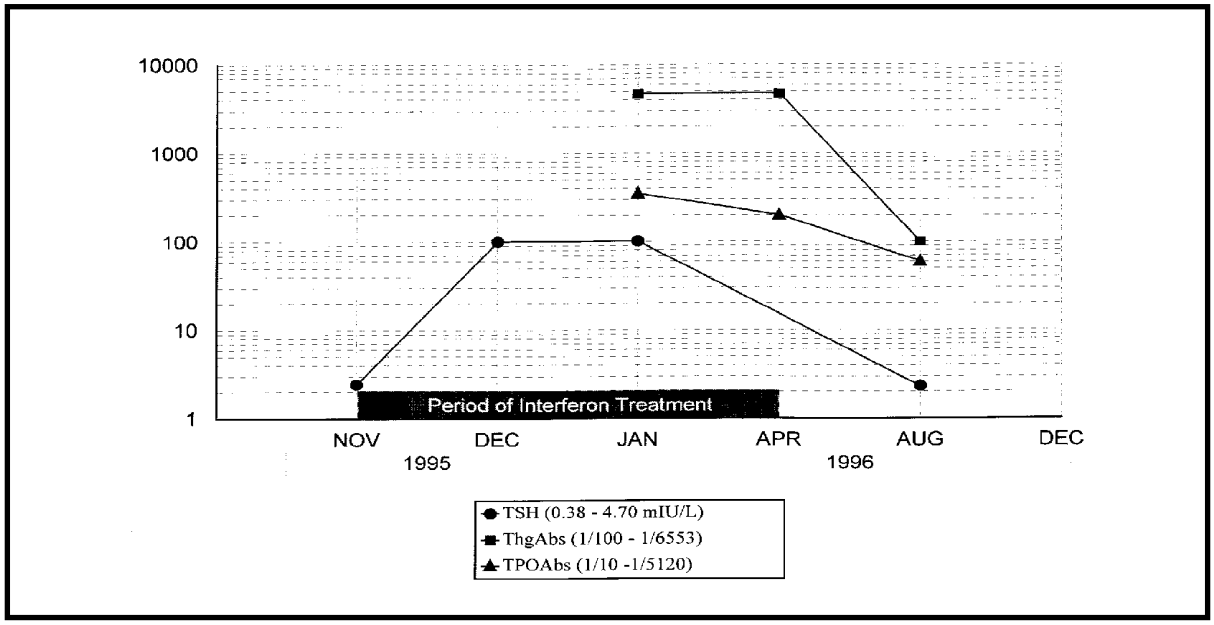

Figure 1 - Thyroid fuction test and thyroid antibodies during and after treatment.

normal. During the third week of treatment she developed signs and symptoms of thyroiditis, and that was confirmed by thyroid function tests and raised thyroid antibodies. Her course was completed and she was managed by simple analgesics alone. After she completed the course her thyroid stimulating hormone normalized. Interferon is the only link we could find as the cause of the thyroiditis.

Interferons are a group of related proteins produced by human cells in response to various stimuli. Some clinical studies have demonstrated its clinical efficacy in patients suffering from viral hepatitis.[1-3] The aim of treatment of acute hepatitis C infection directed towards prevention of chronic disease as chronic hepatitis or cirrhosis.[1]

Interferon has its own potential adverse effects reported in different studies.[1,4] Toxicity of interferon falls into 2 groups, acute complex as fever, malaise, arthralgia which is usually seen in almost every patient and is usually transient and reversible. Chronic constitutional toxicity remains for longer periods, such as weight loss, depression and anorexia. Permanent side effects are rare but hazardous, and we should be alert to them.[5]

Thyroid dysfunction is a recognized complication of interferon therapy,[4,6] the changes are multiple and the mechanism remained unclear.[5] It is usually transient and often associated with raised thyroid antibodies.[7] Permanent thyroid damage is rare, and most often a form of hypothyroidism requiring replacement therapy.[8] Possible explanations that interferon might induce Graves disease-like picture or Hashimoto's thyroiditis. It may develop while on treatment or shortly after.[8] Interferon is also known to increase MHC class I antigen expression on cell surface, in association with normal antigens, it might be sufficient to break tolerance and induce autoantibody formation.[8] Interferon has a direct effect on thyroid hormones, both synthetic and secretions[6] therefore during treatment interpretation must be taken cautiously.

Autoantibody formation has been seen with interferon and other cytokines Up to 87% of the patients that receive interferon, develop thyroid antibodies.[6,8] Pre-existing thyroid antibodies may be regarded as a risk factor for the appearance of thyroid disease during or after treatment.[9] This risk became more apparent in patient's having chronic liver disease HCV related.[10,11]

Our patient did not have thyroid autoantibodies checked pre-treatment, and she didn't have evidence of chronic liver disease. We think that our patient had transient thyroiditis while on interferon therapy, and the raised thyroid hormones were most likely secondary to the direct effect of interferon on thyroid hormones, which disappeared after completing the course. Up to 2 years she remained euthyroid in spite of very high titers that she developed while on treatment. The goitre size remained the same.

Patients subjected to interferon treatment are at risk of developing thyroid disease. The risk is high in patients having thyroid antibodies pre-treatment. Health care providers should be aware for such complications and a susceptible group of patients should be informed of the possibility of permanent thyroid dysfunction.

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