

Autoimmune thyroiditis and delayed onset psoriasis in association with combination therapy for chronic hepatitis C infection

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ABSTRACT

A combination of pegylated interferon and ribavirin is currently the gold standard for the treatment of chronic hepatitis C infection. Interferon therapy can lead to the development of an autoimmune phenomenon that can be sub-clinical or clinical, and the presence of autoantibodies increases the risk. Thyroiditis is the most common autoimmune manifestation of interferon therapy and can present during treatment or after the completion of treatment. On the other hand, psoriasis is rare, and has been reported to occur within weeks of starting the treatment. We report a case of a 46-year-old indigen woman who was positive for multiple autoantibodies, and developed autoimmune thyroiditis that manifested as hypothyroidism during pegylated interferon and ribavirin therapy for chronic hepatitis C infection. She also developed plaque psoriasis after the completion of therapy. In our case, the association with thyroiditis was definite, whereas that with psoriasis was less definite. However, it is still important for clinicians to be aware of such rare associations.

Keywords: adverse effects, chronic hepatitis C, hypothyroidism, interferons, psoriasis

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INTRODUCTION

Chronic hepatitis C infection (CHC) is an important cause of liver disease and the leading indication for liver transplantations in the West. Currently, a combination therapy of pegylated interferon with ribavirin is the standard treatment.^(1,2) The common side effects of this therapy include flu-like symptoms, haemolytic anaemia, mood disorders and mild discomfort at the site of injections.⁽²⁾ Autoimmune manifestations in association with interferon therapy are well recognised,

and thyroiditis is the most commonly encountered manifestation.⁽³⁾ On the other hand, exacerbations or new-onset psoriasis are extremely rare associations.^(4,8) We report a case of a 46-year-old woman who developed autoimmune thyroiditis that manifested as hypothyroidism during treatment and as plaque psoriasis 16 months after completion of pegylated interferon and ribavirin therapy for CHC.

CASE REPORT

A 46-year-old indigen woman was referred for the evaluation of abnormal liver profile and mild macrocytic anaemia. Physical examination did not show any stigmata of chronic liver diseases or evidence of any dermatological disorders. Ultrasonography of the abdomen did not show any evidence of chronic liver diseases. Serum hepatitis C virus (HCV) IgG, antinuclear antibodies and anti-smooth muscles were positive, while the other markers of liver diseases were negative or normal (HBsAg, serum ceruloplasmin and transferrin). Anti-parietal cell antibody was also positive. Thyroid function test, serum vitamin B₁₂ and folate level were all normal. Serum ribonucleic acid (RNA) was positive (viral load 128,000 copies/mL) and the viral genotype was type 1b. A liver biopsy showed significant fibrosis (Metavir score Grade III and Stage III). The patient's past medical history was only significant for hypertension, previous tubal ligations and caesarean section. She did not receive any blood transfusion or develop any clinical hepatitis after her surgery.

The patient was started on a combination of 80 µg pegylated interferon (subcutaneous weekly) Peg Intro-α2a and ribavirin (800 mg daily). She experienced the expected side effects that consisted of flu-like symptoms, fever and myalgia, which usually last for two days. After two months into treatment, she experienced mild hair loss. Scalp examination at that time only showed slight thinning of the hair but no bald patches. Apart from the skin changes at the injection sites, there were no other skin or nail changes. There was no further worsening

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of hair loss. After six months into the treatment, the patient developed clinical hypothyroidism and was started on thyroxine (50 µg daily). Thyroid antibodies (serum antimicrosomal and thyroglobulin antibodies) were positive. At this point, the serum HCV RNA was negative and the treatment was discontinued. After termination of treatment, the patient's symptoms settled and thyroid replacement therapy was eventually stopped.

One year after treatment, the patient remained well and serum HCV RNA remained negative, indicating successful viral clearance. However, she began to develop scattered dusky dark pigmentations on her body and later developed itchy scalp and scaling rash. 16 months after treatment, the patient developed salmon-coloured plaques on her body, which were consistent with plaque psoriasis (Fig. 1). She was referred to the dermatology department for further management and was started on topical tar treatment. Apart from the medications provided, she had not used any other medications. 24 months after developing psoriasis, she remained well; her psoriasis was under control and regressing with topical treatment.

DISCUSSION

Interferon- α is a naturally occurring glycoprotein that has important immune functions in response to viruses, parasites and tumour cells. Pegylation involves the attachment of a polyethylene glycol molecule to an interferon, creating a larger molecule that has a longer half-life. This allows weekly administration instead of the thrice-weekly administration for standard interferon. Overall, weekly administration is associated with fewer side effects. Currently, two pegylated interferons (12 kDal Peg Intro- α 2a[®] and 40 kDal Pegasy[®]) have been approved by the United States Food and Drug Administration for the treatment of CHC.

Both standard and pegylated interferons are associated with many side effects. The common side effects include flu-like symptoms, reactions and skin changes at the injection site, anorexia, weight loss, mood disorders and haematological abnormalities, namely neutropenia and thrombocytopenia.⁽²⁾ The last two adverse effects can be serious and need to be managed appropriately. Interferon therapies have also been reported to aggravate pre-existing autoimmunity, unmask silent autoimmune processes and even induce de novo autoimmune disorders.⁽³⁾ Induction of autoimmunity is usually evident with the appearance of various autoimmune markers that can be with or without clinical manifestations. Positivity for any autoimmune antibodies increases the predisposition to development



Fig. 1 Photograph shows plaque psoriasis with scaling over the back of the trunk

of autoimmune disorders when given interferon therapy. Reported autoimmune associations include diabetes mellitus, thyroiditis, vitiligo and autoimmune haemolytic anaemia.⁽³⁾ In fact, thyroiditis is one of the most common side effects of interferon-based therapy, with up to 40% of patients developing clinical or subclinical disease.^(3,9,10)

Interferon-associated thyroid dysfunctions can be categorised into autoimmune thyroiditis and non-autoimmune thyroiditis. Clinical thyroiditis can be clinical or subclinical, and can present with symptoms of classical Hashimoto thyroiditis or Grave's disease.⁽³⁾ Non-autoimmune thyroiditis can manifest as destructive thyroiditis, with early thyrotoxicosis and subsequent hypothyroidism, or as non-autoimmune hypothyroidism. Generally, hypothyroidism is the most common clinical manifestation and can develop during (early) and even more than six months after treatment (late). Our patient developed autoimmune thyroiditis during pegylated interferon therapy, and the presence of thyroid autoantibodies supported the autoimmune association. However, we cannot be certain whether the interferon therapy had aggravated a pre-existing silent autoimmune thyroid disease or induced a de novo manifestation, as we had not checked the antibody status before starting the treatment. It is also interesting to note that HCV itself is associated with thyroiditis. Increased anti-thyroid peroxidase antibodies (8.7% vs. 3.4%) have been found among patients with chronic hepatitis, significantly clustered among women, particularly those with CHC compared to hepatitis B and D. Treatment with interferon significantly increased the prevalence of antibodies (from 12.5% to 18.6%) and thyroid dysfunction (from 3.7% to 9.7%).^(3,11)

Common cutaneous reactions include dryness, itching, urticaria and hair loss.⁽⁷⁾ Our patient had local injection reactions and self-limiting thinning of hair.

Although the association in our case is less definite, it is worth mentioning so as to highlight the association of psoriasis and interferon.⁽⁴⁻⁸⁾ To date, there have been few reports of psoriasis in association with standard and pegylated interferon. However, there was one report of a 50-year-old woman who developed extensive psoriasis with pegylated interferon after two previous failed therapies with standard interferon- α 2b and lymphoblastoid interferon. Interestingly, there were no significant cutaneous side effects with the previous two treatments, and she was negative for all the autoimmune markers tested.⁽⁸⁾ Another case reported widespread plaque psoriasis with standard interferon for the treatment of CHC.⁽⁷⁾ The psoriasis in both cases remitted with discontinuation of treatment. Both cases did not report on autoimmune markers. Exacerbations of pre-existing psoriasis have also been reported.⁽⁶⁾ De novo psoriasis usually occurs within weeks of starting treatment. At the last follow-up, our patient's psoriasis remained controlled with only topical treatment and was showing signs of regression.

In conclusion, the adverse effects of pegylated interferon are common. However, clinicians should also be aware of the uncommon associations, as early detection allows appropriate measures to be taken. Adverse effects like thyroiditis can be managed without discontinuing interferon therapy. Although the association with psoriasis

in our case is weak, it is still important for clinicians to be aware of this rarely reported complication.

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