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Case Report Open Access

"Hibernating" Lupus

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Abstract

We report a case of a 64-year-old Chinese lady, who was admitted for two weeks' history of fever, cough and breathlessness. She was diagnosed with community acquired pneumonia and treated with antibiotics. Her co-morbidity includes plaque psoriasis treated with topical steroids and oral methotrexate for 4 years by private physicians. Her symptoms persisted for weeks post-discharge. After workup, a diagnosis of basal interstitial lung disease with restrictive defect likely drug-induced was established. Her methotrexate therapy was switched to phototherapy. However, her psoriatic rashes worsened after phototherapy, thus, treatment was changed to subcutaneous injection of adalimumab. She then developed inflammatory arthritis, dry mouth and worsening dyspnoea and psoriasiform rashes. Repeat spirometry showed worsening of transfer factor (from 76% to 51%). In light of this peculiar development, her previous laboratory investigations performed in the other private hospitals were retrieved. They were remarkable for positive Anti-nuclear antibodies which were of homogenous pattern and high in titre with Anti-Ro/SS-A positivity. Skin biopsy of the lesion displayed typical histology of psoriasis. This clinical scenario describes a case of psoriasis coexisting with "hibernating" lupus which was "awakened" by use of anti-TNF. With an assemblage of cutaneous signs, interstitial lung disease, arthritis without severe systemic involvement together with strong association with anti-Ro/SS-A antibody, subacute cutaneous lupus erythematosus (SCLE) is suspected to be the most likely underlying lupus that remained dormant and smouldering until it was triggered and worsened by the use of adalimumab and phototherapy. These are the pitfalls associated with the diagnosis of connective tissue diseases which have protean manifestation. This is clinically significant as the diagnosis will affect the choice of immunosuppressants and biologics. The learning point is, in clinical practice, incongruity of enigmatic clinical and histo-pathological findings mandate critical scrutiny and second look as starting biologics without a clear clinical picture is potentially harmful.

Keywords: Lupus; Anti-TNF; Psoriasis; Interstitial lung disease; Anti-nuclear antibodies

Case Report

We report a case of a 64-year-old Chinese lady, presenting with two weeks' history of cough and breathlessness. At presentation, she was febrile and tachypnoeic. On chest auscultation, there were bilateral lung crepitations. Chest radiograph revealed bilateral pulmonary infiltrates. Her co-morbidity included plaque psoriasis that was treated with topical steroids and oral methotrexate for 4 years by a few private physicians prior to the current admission. Methotrexate was withheld and broad spectrum antibiotics were given for community acquired pneumonia. Her symptoms improved and she was discharged.

A few weeks later, upon clinic review, she complained of worsening psoriatic rashes, persistent breathlessness and intermittent dry cough. A high resolution computed tomography of the chest showed bibasal subpleural ground glass opacities with reticulonodular changes. Her spirometric findings were notable for restrictive defect. Our impression of her pulmonary findings was that of methotrexate-induced interstitial lung disease (ILD). Methotrexate was discontinued. Treatment was switched to phototherapy and topical steroids. The rashes worsened after phototherapy, and subcutaneous injections of adalimumab therapy were added. After adalimumab injections, she developed inflammatory arthritis, dry mouth and worsening dyspnoea, along with persistence of psoriasiform rashes. With this peculiar clinical development, previous physicians who used to treat her for psoriasis were contacted. The clinical manifestations described by those physicians were consistent with plaque psoriasis. Blood investigations done in the private practice a few years ago were retrieved. It was remarkable for positive anti-nuclear antibodies (ANA) of homogenous pattern, at high titre, and positive Anti-Ro/SS-A antibody. A repeat ANA and Anti-Ro/SS-A done after commencing adalimumab remained positive. Other autoantibodies like anti-double stranded DNA antibodies, anti-histone antibody, anti-riboneucleopeptide antibody, rheumatoid factor and anti-cyclic citrullinated peptide were negative. Complement levels, haematological and renal panel were within normal limits. A repeat spirometry done to evaluate her worsening respiratory symptoms showed worsening of the underlying restrictive lung defect with deterioration of transfer factor (from 76% to 51%). Skin biopsy of the lesion showed typical histology of psoriasis with psoriasiform epidermal acanthosis, parakeratosis and perivascular dermatosis, with absence of interface changes and immune deposits.

Retrospectively, this patient could have coexisting psoriasis and an evolving connective tissue disease, most likely lupus erythematosus that was unveiled by the use of anti-tumor necrosis factor (anti-TNF). Her psoriasiform rashes, arthritis and ILD improved after

immunosuppressants were switched to oral corticosteroids and cyclosporine.

Discussion

This clinical scenario describes a case of psoriasis coexisting with "hibernating" lupus which was "awakened" by use of anti-TNF. Given the strong association with anti-Ro/SS-A antibody [1,2], subacute cutaneous lupus erythematosus (SCLE) is suspected to be the most likely underlying lupus that remained dormant and smouldering until it was triggered by the use of adalimumab and phototherapy [3]. A large proportion of SCLE (up to 50%) do not fulfill the American College of Rheumatology criteria [2,4,5]. These are the pitfalls associated with the diagnosis of connective tissue diseases which have protean manifestation [6]. This patient presented with an assemblage of cutaneous signs and arthritis without severe systemic involvement. These clinical manifestations were typically described in patients with SCLE [5].

The psoriasiform lesions of SCLE were not evident clinically and histologically in this patient as it might have occurred interlacedly with psoriatic plaques, hence upon healing, left non scarring pigmented changes seen at the time of the biopsy [1]. Psoriasis and cutaneous lupus are easily differentiated if they occur in their typical forms. However, due to their wide morphological spectrum, sometimes, it is difficult to differentiate [4,7]. Evidence for immunological screening with ANA levels prior to initiation of anti-TNF remains anecdotal. According to literature, the administration of anti-TNF in patients who already have positive ANA to begin with, leads to elevation of ANA titre in a homogenous pattern [8]. To date, there are no official guidelines on ANA screening prior to anti-TNF treatment. It is known that ANA positivity is observed in a proportion of healthy individuals, hence, a positive ANA level should not, by itself, be a contraindication for anti-TNF treatment [8]. However, we suggest clinicians to exercise caution in the use of anti-TNF when ANA titre is high prior to initiation of anti-TNF.

ILD is a potentially fatal adverse event of various anti-rheumatics and biologics. Up to two thirds of the patients with ILDs associated with anti-TNF had previous or concomitant methotrexate therapy and a majority of these patients had no resolution of pulmonary involvement even after cessation of anti-TNF and initiation of immunosuppresants [8].

Conclusion

In practice, incongruity of enigmatic clinical and histo-pathological findings mandate critical scrutiny and second look as starting immunosuppressant or biologics without a clear clinical picture can be potentially harmful. While the pathogenesis of anti-TNF induced ILD and its association with potentiated pulmonary toxicity when there is prior exposure to methotrexate remained unknown, it is advised that clinicians should respect all pulmonary complaints from patient receiving anti-TNF and adopt a high index of suspicion and low threshold for ILD screening.

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