

# Thalidomide induced Thyrotoxicosis - a Rare Case Report

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Thyrotoxicosis is a condition characterized by distorted metabolism in most of the tissues of the body due to presence of excess thyroid hormones, triiodothyronine (T<sub>3</sub>) and thyroxine (T<sub>4</sub>). Commonly over functioning of thyroid gland, Graves' disease and autonomously functioning nodules are the causes. Thyrotoxicosis may also occur due to some other causes like thyroiditis, after radiation exposure to the thyroid, presence of ectopic thyroid tissue etc. Alpha (α) sub unit of hCG is same of TSH and can activate thyroid receptor in choriocarcinoma or seminoma. It also may arise by exogenous use of thyroxin.

In thyrotoxicosis due to presence of excess thyroid hormone, body metabolism is increased causing a number of signs and symptoms. Thyroid hormone level of blood is regulated by pituitary gland in brain by formation of TSH. Increased formation of hormone causes increased formation of antibody, which decrease by therapy but therapy can not completely prevent formation of antibody. Some drugs also influence these process and may cause thyrotoxicosis.

Here a case is reported who developed thyrotoxicosis after use of rare immunomodulatory drug thalidomide for long standing low back pain.

## CASE REPORT

A 38 years old male was suffering from low back pain for seven years. MRI revealed ankylosing spondylitis at lumbar vertebrae. He was given sulfasalazine group of drug by his rheumatologist. But his low back pain and discomfort continued

even after medication. Then the patient was given thaltrol, a thalidomide group of drug. Initial dose was 100 mg/day and then gradually raised to 200 mg per day. After about four months, patient started to complain weakness and palpitation. On examination, he had tremor and increased pulse rate. He was advised for thyroid hormone test, which revealed high T<sub>3</sub>, T<sub>4</sub>, FT<sub>3</sub>, FT<sub>4</sub> and low TSH. His T<sub>3</sub> level was 4.43 nmol/L (normal 1.3 to 3.5 nmol/L), T<sub>4</sub> was 221 nmol/L (normal 54 to 173 nmol/L), FT<sub>3</sub> - 9.97 Pmol/L (normal 2.8 to 9.5 Pmol/L), FT<sub>4</sub> - 55.56 Pmol/L (normal 9.5 to 25.5 Pmol/L) and TSH was 0.17 mIU/L (normal 0.3 to 5 mIU/L)]. Anti TPO antibody was 17.75 % (normal ≤ 20%) and anti Tg antibody 49.65 % (normal ≤ 30%).

Unfortunately, local general practitioner started anti thyroid drug (ATD) carbimazole without waiting for the thyroid hormone level report after stopping thalidomide. This masked the induction effect of thalidomide on thyroid gland and probably made a false negative clinical condition. Finally thalidomide as well as carbimazole were stopped and again sulfasalazine group of drug was started. Patient was euthyroid on follow up.

## DISCUSSION

Thalidomide is an immunomodulatory (a cytokines) drug which shares the antiangiogenic and anti-tumor properties. Initially it was prescribed as a sedative or hypnotic and was claimed to cure anxiety, insomnia and tension (1). Afterwards thalidomide was started to prescribe for nausea and morning sickness in pregnant

women. But the end result was very sad. About 5000 to 7000 baby were born with malformation (phocomelia). After that marketing of thalidomide was stopped.

In February 2013 FDA of USA approved thalidomide as a treatment for relapsed and refractory multiple myeloma (2, 3). Commonly hypothyroidism is most common side effect, although hyperthyroid or effect on thyroid stimulating hormone secretion, thyroid hormone metabolism also been described (4). Not only thalidomide, but other similar drugs like tyrosine kinase inhibitors, bexarotene, denileukin diftitox, alemtuzumab, interferon  $\alpha$ , interleukin-2, lenaledomide has the same property like thalidomide on thyroid.

Stein EM and Rivera C reported a case of transient hyperthyroid while receiving thalidomide group of drug during a clinical trial for metastatic renal cell carcinoma (5).

More recently, the World Health Organization (WHO) has stated: "The WHO does not recommend the use of thalidomide in leprosy as experience has shown that it is virtually impossible to develop and implement a full-proof surveillance mechanism to combat misuse of the drug. The drug clofazimine is now a component of the multidrug therapy (MDT), introduced by WHO in 1981 as the standard treatment for leprosy and now supplied free of charge to all patients worldwide"(6).

It is also advocated that patients receiving thalidomide should not donate semen and donate blood. To be very careful, not to make female partner pregnant or female partner reviving thalidomide, not to be get pregnant.

## CONCLUSION

Emphasis to be given to the patients who are receiving immunomodulatory drugs like thalidomide, interferon  $\alpha$ , interleukin-2 or others and should undergo estimation of thyroid hormone levels periodically. Patients may develop both hypo and hyperthyroid state. Hypothyroid state may be over masked by the effect of immunomodulatory drug on body cell. It is better to stop immunomodulatory drugs in both states; follow up hormone estimation to be done before starting definitive treatment regarding thyroid dysfunction.

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