

CASE REPORT

Carbimazole Induced Pleural Effusion: A Case ReportAgrawal Prabhat¹, Yadav Subash Chandra², Dubey Prashant³, Bansal Manish⁴, Upadhyay Shalini⁵**ABSTRACT**

Introduction: Carbimazole is a drug used for treating thyrotoxicosis, can lead to pleural effusion. Here is the case study of a patient who developed pleural effusion after short duration of carbimazole treatment.

Case Report: A Middle aged women presented in emergency of S.N Medical college, Agra with symptoms of hyperthyroidism and she was put on carbimazole therapy, however after completion of one week, patient developed breathlessness. On further evaluation, it was found that patient had developed pleural effusion .no other etiology of pleural effusion was found, assuming it as a side effect of therapy carbimazole was stopped and improvement in symptoms was found.

Conclusion: On stopping the medications there were resolution of symptoms which proves our diagnosis. In conclusion, this case illustrates the importance of being aware of the relatively rare and not so well-known adverse effect of carbimazole

Keywords: Carbimazole, Pleural Effusion, Agranulocytosis

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INTRODUCTION

A myriad of complications are associated with antithyroid medications, but pleuropulmonary complications are not commonly encountered. ANCA-positive vasculitis in association with antithyroid drugs has been described since 1992,¹ and

27% of patients may present with respiratory tract involvement.² Most of the cases are predominantly linked to propylthiouracil, but sporadic cases of lung involvement due to methimazole have also been reported.³ Interestingly, there is no much published data regarding patients who are ANCA negative and develop systemic vasculitis or serositis leading to third space collections in relation to carbimazole or methimazole. We hereby present the case of a middle aged woman who developed an exudative pleural effusion after a short duration of carbimazole treatment and had a negative immunology. We suspect that this is due to a local inflammation or vasculitic reaction in the pleural space although a conclusive explanation is elusive.

CASE REPORT

A 45-year-old female was admitted in emergency of S.N Medical College, Agra with symptoms of weight loss, palpitation and increased frequency of stools for last 3-4 months. She had no history suggestive of hypertension, diabetes mellitus or ATT intake. She gave no history of any other drug intake. On examination there was no pallor, icterus, oedema, cyanosis or clubbing. On systemic examination there was tachycardia (pulse rate 134/min), B.P 144/70 mm of Hg. Central nervous system, Gastrointestinal tract, Respiratory system were normal. On local examination of neck there was a goiter. Examination of eye and skin were normal, no changes suggestive of exophthalmos or graves dermopathy. On laboratory examination routine blood investigations Complete blood count (Hb-11.2, TLC-6200, DLC- neutrophils 82%, lymphocyte 18%, platelets 2,20,000, ESR -44), Liver Function Test (SGOT-22, SGPT-44), Kidney Function Test (serum creatinine-0.9, blood urea-34mg/dl) were unremarkable. Chest X ray PA view was within normal limits. HIV, HbsAg, HCV were negative. A thyrotoxic picture with an FT4 of 100 pmol/ml (12-22pmol/l), FT3 of 54pmol/l(3.7-6.5pmol/l) and a suppressed TSH of 0.005µU/mL (0.27-5.5 µU/mL) was found. Anti TPO antibodies was high 100iu/ml (normal range <9iu/ml) and a thyroid ultrasound showed a multinodular goiter. On the basis of clinical and laboratory parameter patient was diagnosed as case of hyperthyroidism. She was

started on carbimazole 10 mg tds, propranolol 40mg tds. Her palpitation and frequency of stool improved gradually. She was discharged satisfactorily with follow up advice.

After one week of discharge she presented to us with complains of sore throat, fever and breathlessness at rest. On suspicion of carbimazole induced agranulocytosis, she was advised Complete blood counts (Hb-5.5, TLC-570, DLC-neutrophil 30%, lymphocyte 70%, platelets-50000). Examination of chest confirmed dullness on the left side on percussion, absent breath sounds in the same region on auscultation, Xray chest PA view was done, showing left sided pleural effusion. Further investigation in form of diagnostic pleural tap and evaluation of pleural fluid did not reveal a tubercular or bacterial aetiology. Pleural fluid was however exudative in nature (Pleural Fluid Cytology: TLC-20, DLC-All lymphocyte, Biochemistry: Protein-4.5 gram, albumin 2.5, globulin 2.0 ADA-7.6). Gram stain, AFB stain, and culture was negative. Her fluid was therapeutically drained following which she had a thoracoscopy which only showed benign looking pleura, and biopsy confirmed inflammatory changes. She was stopped on carbimazole in view of agranulocytosis and pleural effusion.

Her myeloma screen, vasculitic screen, immunoglobulins and serum tumor markers were all within normal limits. Patient was being planned for radioactive ablation as propylthiouracil was also contraindicated in such patients. She was discharged on propranolol 40mg tds. She came to us after 14 days with a chest Xray PA view which was normal CBC (Hb -10.1 TLC-4100, DLC-neutrophils-68, lymphocyte-32, Platelets-221000) within normal limits. As agranulocytosis, hepatitis, an SLE like reaction, are a life threatening complication of anti thyroid drugs they were not started again in this patient. Patient was later lost in follow up.

DISCUSSION

Several adverse effects are related to antithyroid medications like gastro intestinal intolerance, skin rashes, joint pain, loss or greying of hair, loss of taste. Pleural and pulmonary complications are usually rare in relation to these agents. Pulmonary involvement associated with vasculitis and a positive ANCA secondary to antithyroid medication are known⁽²⁾ but the majority of them has been with propylthiouracil, and carbimazole induced vasculitis is exceedingly rare.⁴⁻⁵ Patients usually present with pulmonary capillaritis, intra-alveolar hemorrhage, and respiratory failure⁶ but reports suggest that eosinophilic pleural effusion may be encountered due to propylthiouracil



Figure-1: Chest X-Ray PA View at the time of admission



Figure-2: Chest XRay PA View-after 1 week of carbimazole therapy

alone.^{7,8} Several drugs (betablocker, hydralazine, cabergoline, isoniazid, phenytoin, sulphonamide, imatinib, bleomycin, pioglitazone) have been known to cause exudative pleural effusion⁹⁻¹⁰ but there is no such reports in the literature implicating carbimazole as the offender. A possible mechanism could be due to local pleuritis or leukocytoclastic vasculitis, but it remains to be proved. There are no data to suggest whether carbimazole can alter the configuration of myeloperoxidase² leading to significant ANCA negativity in most cases, hence it could be assumed that patients may have vasculitic features with serosal involvement without a positive immunology when treated with carbimazole. It is a matter of debate whether the unilateral exudative effusion in our patient could be explained by a similar mechanism, but our argument is based on the fact that her symptoms of unilateral effusion started only after carbimazole was commenced, and all potential causes for an exudative effusion were excluded by thorough investigations, and there was a complete resolution of the effusion after cessation of carbimazole therapy.

CONCLUSION

In conclusion, this case illustrates the importance of being aware of the relatively rare and not so well-known adverse effect of carbimazole in relation to pulmonary disease. Stopping the medicine with resolution of symptoms proves the diagnosis, but the mechanism remains unclear in patients who are ANCA negative. Development of such complications limits the use of alternative such as propylthiouracil; hence, patients should be considered for definitive treatment like radioiodine or surgery in such circumstances.

REFERENCES

1. S. J. Stankus and N. T. Johnson, Propylthiouracil-induced hypersensitivity vasculitis presenting as respiratory failure *Chest* 1992;102:1595–1596,.
2. J. E. Gunton, J. Stiel, P. Clifton-Bligh, E. Wilmshurst, and A. Mc Elduff. Prevalence of positive anti-neutrophil cytoplasmic antibody (ANCA) in patients receiving anti-thyroid medication. *European Journal of Endocrinology* 2000;142:587–590.
3. H. K. Tsai, J. K. Chen, H. J. Cheng et al., Graves disease with ANCA positive vasculitis and pulmonary hemorrhage- A case report. *Formosan Journal of Endocrinology and Metabolism* 2003;5: 23–27.
4. C. Day, J. Bridger, P. Rylance, M. Jackson, J. Nicholas, and J. Odum, Leukocyto clasticvasculitis and interstitial nephritis with carbimazole treatment *Nephrology Dialysis Transplantation* 2003;18:429–431,.
5. P. S'ève, K. Stankovic, V. Michalet, T. Vial, J. Y. Scoazec, and C. Broussolle. Carbimazole induced eosinophilic granulomatous vasculitis localized to the stomach. *Journal of Internal Medicine* 2005;258:191–195,.
6. E. Y. F. Lau, S. Y. So, E. Chan, J. Kwok, J. Ma, and A. W.C. Kung. Methimazole-induced antineutrophil cytoplasmic antibody-associated diffuse alveolar haemorrhage in a Chinese woman with Graves' disease. *Hong Kong Medical Journal* 2009;15:209–212,.
7. K. L. Middleton, R. Santella, and J. I. Couser Jr., Eosinophilic pleuritis due to propylthiouracil, *Chest* 1993;103:955–956,.
8. N. Sen, H. Ermis, M. Karatasli, M. A. Habesoglu, and F. O. Eyuboglu, Propylthiouracil-associated eosinophilic pleural effusion: a case report, *Respiration* 2007;74:703–705,.
9. N. A. Maskell and R. J. A. Butland, BTS guidelines for the investigation of a unilateral pleural effusion in adults *Thorax* 2003;58:ii8–ii17.
10. S. Y. Morelock and S. A. Sahn, Drugs and the pleura, *Chest* 1999;116:212–221.