Case Report

Peripartum Cardiomyopathy with Ischemic Hepatitis, Thyroid Storm and Right-sided Pneumonia in a Patient of Type 2 Diabetes Mellitus: A Case Report

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Abstract:

Peripartum Cardiomyopathy in association with Diabetes mellitus and Thyroid storm is an extremely rare. Here we describe a young aged Bangladeshi lady, who admitted with progressive breathlessness, high grade intermittent fever, productive cough and altered level of consciousness in Coronary Care Unit. She was a diagnosed case of Diabetes Mellitus and Graves ' disease but during her last pregnancy the patient voluntarily stopped taking anti-thyroid medication and delivered a healthy male baby through LUCS (two months before admission). After thorough clinical evaluation and laboratory investigations she was diagnosed as having Peripartum Cardiomyopathy, Thyroid Storm, Pneumonia and Metabolic Acidosis. Her condition improved by closely monitored therapy guided by team consisting of Cardiologists, Endocrinologists, Pulmonologists and Gynecologists. There are very few reports in the world which have depicted this unusual association.

Key words: Peripartum Cardiomyopathy, Heart failure, Diabetes mellitus, Thyroid storm.

(Bangladesh Heart Journal 2015; 30(2) : 87-91)

Introduction:

Thyroid storm is a rare, life-threatening condition characterized by severe clinical manifestations of thyrotoxicosis. In a national survey from Japan, the incidence of thyroid storm in hospitalized patients was 0.20 per 100,000 per year.[1] The reported incidence of PPCM varies. Much of the reported discrepancy is due to wide geographical variation, with reported incidences of 1:2289 to 1:4000 live births in the United States, 1:1000 in South Africa, 1:300 in Haiti, and 1:100 in Zaria, Nigeria.[2,3-9] It is defined as a condition meeting four criteria:[10,11]

I. Development of heart failure (HF) in the last month of pregnancy or within five months of delivery.

II. Absence of another identifiable cause for the HF.

III. Absence of recognizable heart disease prior to the last month of pregnancy.

IV. LV systolic dysfunction (e.g. left ventricular ejection fraction [LVEF] below 45 percent or a reduced fractional shortening).

Associations of such diseases are very rare. In Bangladesh perspective there is no research data yet available, and hence such a case is reported bellow.

Case Note:

A 35 year-old Diabetic, Normotensive lady was admitted in CCU with the complaints of high grade intermittent fever with productive sputum for 7 days and progressive breathlessness along with altered level of consciousness for 1 day. She was a known case of Grave's Disease but during her last pregnancy (eight months prior to this admission) the patient voluntarily stopped taking anti-thyroid medication and delivered a healthy male baby through LUCS (two months before

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admission). Her previous pregnancy was uneventful and there was no history of still birth or abortion.

On general examination, she was dyspnoic, restless, confused, agitated, non-cooperative, below-average body-built, having Temp- 102^0F, Respiratory rate-30/min, Blood Pressure - 80/60 mmHg, rapid feeble pulse of 120 beats/min and raised JVP of 5 cm from Sternal Angle. The Thyroid gland was diffusely enlarged measuring about 5cm x 4cm, firm in consistency, non-tender, mobile, smooth surface with normal overlying skin without any bruit or any retrosternal extension. On bed side urine examination there was 1+ Sugar with no Albuminuria or Ketonuria.

On Precordium Examination, there was no visible Apical Impulse; Apex Beat was shifted in left 5^{th} ICS 10 cm from the midline which was diffuse in character with no parasternal heave or palpable P_2. On auscultation the S_1 was normal with loud P_2 and there was no added sound.

On Examination of Respiratory System there was tachypnea with restricted chest movement in the right lower chest along with features of consolidation.

On Neurological Examination the Patient was restless, confused, agitated with 12/15 GCS, generalized reduced muscle bulk, brisk exaggerated all deep tendon reflexes with bilateral flexor plantar response. She had bilateral exophthalmos and lid retraction with bilateral normal fundi. Her muscle power was 5/5 in all four limbs with no sign of meningeal irritation or cranial nerve palsy. Gait and Sensory function could not be assessed.

Important laboratory investigations revealed: Hb%-12.8 gm/dl, WBC- 14,420/mm^3, ESR- 40 mm in 1^{st} hour, RBS-21.2 mmol/L, $S.FT_3$- 9.59 nmol/L, $S.FT_4$- 56.4 pmol/L, S.TSH- 0.10 ìIU/ml, Urine Pus Cell- 2-3/HPF, X Ray Chest (P/A view)- Cardiomegaly with Rt. sided consolidation and pleural effusion (Fig. 1). ECG-Sinus Tachycardia, ST-T changes in Anterior and Inferior leads. Her ABG was; P^H: 7.2, PO_2- 80 mmHg, PCO_2- 17.8 mmHg, HCO_3- 7.1 mmol/L, SpO2- 90%. Blood Urea- 30 mg/dl, S. Creat- 1.0 mg/dl, AST- 670 IU/L, ALT-540 IU/L, S. Bilirubin- 1.8 mg/dl, Blood C/S – No Growth, Na^+- 142 mmol/l, K^+- 4.5 mmol/l, Cl^--105 mmol/l, TCO_2- 09 mmol/l, S. BNP- 2770 pg/ml. Echocardiography- Global Hypokinesia, All Chambers are dilated, LVEF-32%, Mild Pericardial Effusion, Moderate MR with restrictive filling defect Moderate TR, Moderate Pulmonary HTN (PASP= 65 mmHg) (Fig. 2).

The patient was initially treated the patient with; I/V Normal Saline, Inj. Dopamine, Inj. Nor-adrenaline, Inj. Sodium Bicarbonate, Inj. Hydrocortisone, Regular insulin via syringe pump, Oxygen inhalation, Inj. Ceftriaxone, Inj. Levofloxacin, Inj. Frusemide, Inj. Thiamine,Tab. Carbimazole ,Tab. Phenobarbitone , Tab. Propranolol and Tab. Clopidogrel. A team consisting of Cardiologists, Endocrinologists and Obstetricians regularly monitored the patient and advocated treatment strategies and other

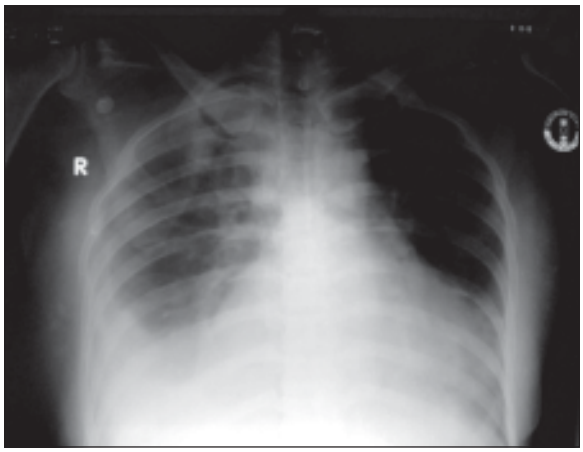

Fig.-1: *Chest X-ray postero-anterior view.*

necessities from time to time. After initial treatment patients condition was improved and hemodynamically stable. The patient was transferred to general ward after a 7 day stay in CCU. The inotrope support was withdrawn along with adding of Tab. Digoxin, Combination of oral Frusemide and Spironolactone, oral Iron and Calcium supplements. The patient was discharged with proper counseling regarding outcome of future pregnancy and chances of recurrence of peripartum cardiomyopathy with essence of effective contraception and advice to follow up in Endocrine and Cardiology OPD after 6 weeks with review Thyroid Function Tests, Echocardiography and Serum BNP.

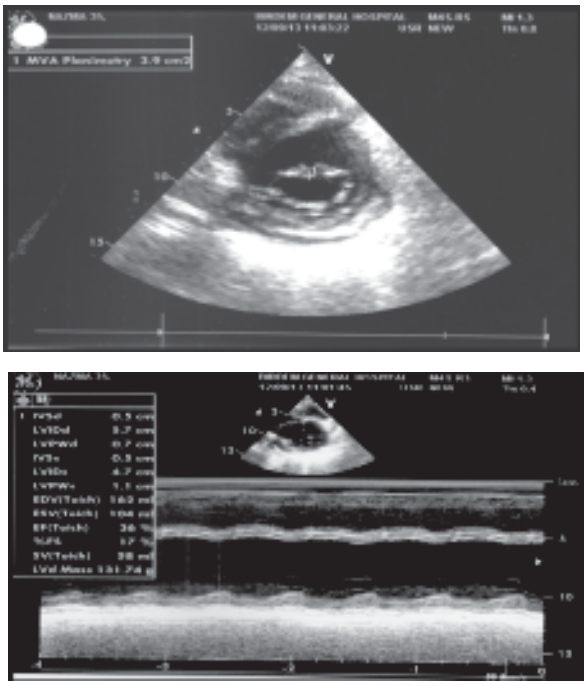

Fig.-2: *2D and M-mode echocardiography showing dilated chambers.*

Fig

Discussion:

Although thyroid storm can develop in patients with long-standing untreated hyperthyroidism (Graves' disease, toxic multinodular goiter, solitary toxic adenoma), it is often precipitated by an acute event such as surgery, trauma, infection, an acute iodine load, or parturition. Patients with severe and life-threatening thyrotoxicosis typically have an exaggeration of the usual symptoms of hyperthyroidism. Cardiovascular symptoms in many patients include tachycardia to rates that can exceed 140 beats/minute and congestive heart failure. Hypotension, cardiac arrhythmia, and death from cardiovascular collapse may occur.[12] Hyperpyrexia to 104^0 to 106^0 F is common. Agitation, anxiety, delirium, psychosis, stupor, or coma are also common and are considered by many to be essential to the diagnosis. Severe nausea, vomiting, diarrhea, abdominal pain, or hepatic failure with jaundice can also occur. There are no universally accepted criteria or validated clinical tools for diagnosing thyroid storm. In 1993, Burch and Wartofsky introduced a scoring system using precise clinical criteria for the identification of thyroid storm[13]. This scoring system is likely sensitive, it is not very specific. The degree of hyperthyroidism is not a criterion for diagnosing thyroid storm. Other nonspecific laboratory findings may include mild Hyperglycemia, mild Hypercalcaemia, abnormal liver function tests, leukocytosis, or leukopenia. Full support of the patient in an intensive care unit is essential, since the mortality rate of thyroid storm is substantial (10 to 30%).[1] Many patients require substantial amounts of fluid, while others may require diuresis because of congestive heart failure. Digoxin and beta-blocker requirements may be quite high because of increased drug metabolism. Infection needs to be identified and treated, and hyperpyrexia should be aggressively corrected. The therapeutic regimen typically consists of multiple medications, each of which has a different mechanism of action:[14]

a) A beta-blocker to control the symptoms and signs induced by increased adrenergic tone

b) A thionamide to block new hormone synthesis

c) An iodine solution to block the release of thyroid hormone

d) An iodinated radiocontrast agent (if available) to inhibit the peripheral conversion of T_4 to T_3

e) Glucocorticoids to reduce T_4-to-T_3 conversion, promote vasomotor stability, and possibly treat an associated relative adrenal insufficiency.

Long-term management — after there is evidence of clinical improvement (afebrile, resolution of CNS and cardiovascular manifestations), iodine therapy can be discontinued and Glucocorticoids tapered and discontinued. Beta blockers can be withdrawn, but only after thyroid function tests have returned to normal. The dose of thionamides should be titrated to maintain euthyroidism.

Thyroid hormone has important effects on cardiac muscle, the peripheral circulation, and the sympathetic nervous system that alter cardiovascular hemodynamics in a predictable way in patients with hyperthyroidism. The main changes are:[15]

- Increases in heart rate, cardiac contractility, systolic and mean pulmonary artery pressure, cardiac output, diastolic relaxation, and myocardial oxygen consumption.
- Reductions in systemic vascular resistance and diastolic pressure.

Some actions of T_3 on the heart produce clinical findings similar to those of beta-adrenergic stimulation.[16] Cardiovascular symptoms and signs are common in patients with hyperthyroidism;

- Systolic hypertension with widened pulse pressure[17]
- Exertional dyspnea, which is due more to respiratory and skeletal muscle weakness than cardiac dysfunction
- Angina-like chest pain, with EKG changes suggesting myocardial ischemia, which can occur especially in women; this appears to be the result of coronary vasospasm and responds to treatment with orally administered calcium channel blockers
- Increase in left ventricular mass index and left ventricular hypertrophy[18,19]
- Increased ventricular irritability, especially in Amiodarone treated patients with a prior history of ventricular ectopy (often in the setting of implanted cardiac defibrillators)[20]

Hyperthyroidism is also associated with an increased risk of atrial fibrillation (5 to 15 percent of patients), heart failure, pulmonary hypertension, and angina. Heart failure is most commonly seen as a result of coexistent atrial fibrillation. The signs and symptoms of heart failure resolve when the ventricular rate is slowed, normal sinus rhythm is restored, and the patients are rendered euthyroid.[16,21] Heart failure in the absence of underlying cardiac disease or arrhythmia is thought to reflect a rate-related cardiomyopathy, which disappears when the

hyperthyroidism is treated. There is no clear histopathologic correlate of this cardiomyopathy, and treatment is primarily directed at rate control with beta-adrenergic blockade. Pulmonary hypertension can also produce signs of isolated right heart failure with a rise in central venous pressure, neck vein distension, and hepatic congestion. Hyperthyroidism is associated with an increase in N-terminal pro-B natriuretic peptide (NT-proBNP) in hyperthyroid patients without cardiac insufficiency. Despite many attempts to uncover a distinct etiology of PPCM, the cause still remains unknown and may be multifactorial. No distinct hormonal disorder has been identified in patients with PPCM, even though estrogen, progesterone, and prolactin have significant effects on the cardiovascular system.[22-25] Although the etiology of PPCM remains unclear, a number of factors have been associated with increased risk, including the following: Age greater than 30 years, multiparity, African descent[23], Pregnancy with multiple fetuses[24], A history of preeclampsia, eclampsia, or postpartum hypertension, maternal cocaine abuse[25], Long-term (>4 weeks) oral tocolytic therapy with beta adrenergic agonists such as terbutaline[26].

Treatment of PPCM is largely similar to that for other types of heart failure (HF). Additional therapeutic issues include anticoagulation and arrhythmia management. Immunosuppression and immune globulin therapy have also been evaluated, although the role of these treatments in PPCM is not established. The prognosis of PPCM must take into account maternal, obstetric, and neonatal outcomes, and the effect of subsequent pregnancy. The largest series of 123 cases of PPCM cited above (23 with onset more than one month before delivery) described a cardiac transplantation rate of 4% and a mortality rate of approximately 10% at a mean follow-up of about two years.[27] Death due to PPCM is usually caused by progressive pump failure, sudden death, or thromboembolic events.

Our patient was suffering from DMT_2 and Graves' Disease but was not adherent to the treatment advice for and with that status of her metabolic derangement she became pregnant and delivered a healthy live baby through LUCS and thereby admitted in CCU BIRDEM for high grade intermittent fever with productive sputum for 7 days and progressive breathlessness along with altered level of consciousness for 1 day. Parturition along with development of pneumonia in a previously noncompliance patient of Diabetic and Grave's Disease lids to the development of Thyroid storm and metabolic acidosis and she also had Peripartum Cardiomyopathy at the same setting which was responsible for these kind of critical scenario of heart failure.

References:

1. 1. Akamizu T, Satoh T, Isozaki O, et al. Diagnostic criteria, clinical features, and incidence of thyroid storm based on nationwide surveys. *Thyroid* 2012; 22:661.
2. Davidson NM, Parry EH. The etiology of peripartum cardiac failure. *Am Heart J* 1979; 97:535.
3. Pierce JA, Price BO, Joyce JW. Familial occurrence of postpartal heart failure. *Arch Intern Med* 1963; 111:651.
4. Sliwa K, Damasceno A, Mayosi BM. Epidemiology and etiology of cardiomyopathy in Africa. *Circulation* 2005; 112:3577.
5. Lampert MB, Lang RM. Peripartum cardiomyopathy. *Am Heart J* 1995; 130:860.
6. Fett JD, Christie LG, Carraway RD, Murphy JG. Five-year prospective study of the incidence and prognosis of peripartum cardiomyopathy at a single institution. *Mayo Clin Proc* 2005; 80:1602.
7. King TM, Whitehorn WV, Reeves B, Kubota R. Effects of estrogen on composition and function of cardiac muscle. *Am J Physiol* 1959; 196:1282.
8. Ueland K, Parer JT. Effects of estrogens on the cardiovascular system of the ewe. *Am J Obstet Gynecol* 1966; 96:400.
9. Schaible TF, Malhotra A, Ciambrone G, Scheuer J. The effects of gonadectomy on left ventricular function and cardiac contractile proteins in male and female rats. *Circ Res* 1984; 54:38.
10. Seftel H, Susser M. Maternity and myocardial failure in African women. *Br Heart J* 1961; 23:43.
11. Woolford RM. Postpartum myocardosis. *Ohio Med* 1952; 48:924.
12. Ngo SY, Chew HC. When the storm passes unnoticed—a case series of thyroid storm. *Resuscitation* 2007; 73:485.
13. Burch HB, Wartofsky L. Life-threatening thyrotoxicosis. Thyroid storm. *Endocrinol Metab Clin North Am* 1993; 22:263.
14. Bahn Chair RS, Burch HB, Cooper DS, et al. Hyperthyroidism and other causes of thyrotoxicosis: management guidelines of the American Thyroid

Association and American Association of Clinical Endocrinologists. *Thyroid* 2011; 21:593.

15. Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. *N Engl J Med* 2001; 344:501.
16. Klein I. Endocrine disorders and cardiovascular disease. In: *Braunwald's Heart Disease: A Textbook of Cardiovascular Medicine*, 9th, Bonow RO, Mann DL, Zipes DP, Libby P (Eds), Elsevier Saunders, Philadelphia 2012. p.1829.
17. Iglesias P, Acosta M, Sánchez R, et al. Ambulatory blood pressure monitoring in patients with hyperthyroidism before and after control of thyroid function. *Clin Endocrinol (Oxf)* 2005; 63:66.
18. Biondi B, Fazio S, Carella C, et al. Cardiac effects of long term thyrotropin-suppressive therapy with levothyroxine. *J Clin Endocrinol Metab* 1993; 77:334.
19. Dörr M, Wolff B, Robinson DM, et al. The association of thyroid function with cardiac mass and left ventricular hypertrophy. *J Clin Endocrinol Metab* 2005; 90:673.
20. Dahl P, Danzi S, Klein I. Thyrotoxic cardiac disease. *Curr Heart Fail Rep* 2008; 5:170.
21. Siu CW, Yeung CY, Lau CP, et al. Incidence, clinical characteristics and outcome of congestive heart failure as the initial presentation in patients with primary hyperthyroidism. *Heart* 2007; 93:483.
22. Bryant EE, Douglas BH, Ashburn AD. Circulatory changes following prolactin administration. *Am J Obstet Gynecol* 1973; 115:53.
23. Veille JC. Peripartum cardiomyopathies: a review. *Am J Obstet Gynecol* 1984; 148:805.
24. Homans DC. Peripartum cardiomyopathy. *N Engl J Med* 1985; 312:1432.
25. Mendelson MA, Chandler J. Postpartum cardiomyopathy associated with maternal cocaine abuse. *Am J Cardiol* 1992; 70:1092.
26. Lampert MB, Hibbard J, Weinert L, et al. Peripartum heart failure associated with prolonged tocolytic therapy. *Am J Obstet Gynecol* 1993; 168:493.
27. Elkayam U, Akhter MW, Singh H, et al. Pregnancy-associated cardiomyopathy: clinical characteristics and a comparison between early and late presentation. *Circulation* 2005; 111:2050.