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VENTRICULAR STANDSTILL IN YOUNG MALE A RARE PRESENTATION OF GRAVES' DISEASE A CHALLENGING DIAGNOSIS AND TREATMENT

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Abstract
Graves' disease is an autoimmune disorder accounts for 80% hyperthyroidism, predominantly in females. Its association with cardiac arrhythmias such as atrial fibrillation, sinus tachycardia and supraventricular tachycardia DCM is well established. We report the case of 16 year old male with GD and rare cardiac complication Ventricular standstill or higher degree AVB that reports only less than 35 cases in entire literature make it unique, interesting and challenging case for diagnosis and management.

Introduction:
Graves´ disease (GD) is an autoimmune disorder which accounts for up to 80% of hyperthyroidism cases. It was described by Robert Graves in 1835 and occurs predominantly in females. Common manifestations include weight loss, sweating, palpitations, diarrhoea, anxiety and heat intolerance.[1] Cardiac complications are common in patients with Graves' disease and include atrial fibrillation, sinus tachycardia and supraventricular tachycardia. Atrioventricular block (AVB) is a rare life threatening cardiac manifestation of hyperthyroidism.[2] AVB has been reported in some case reports, most commonly in association with infections, acute inflammatory states, electrolyte abnormalities or medications such as digoxin.[3] Further review of the literature revealed less than 35 cases of complete heart block associated with hyperthyroidism.[4] The evidence linking CHB with hyperthyroidism was first described in 1933 by the Mayo clinic.[5] This report highlights a rare case of Graves' disease with complete heart block in a 16 year old male chronic marijuana user.

Case presentation
A 16-year-old male, with no significant past medical history presented to A &E with complaints of fever, heat intolerance, generalized weakness, fatigue and weight loss of 20lbs over 3 months. He also experienced palpitations, tremors and feelings of anxiety without triggers. There was no history of any recent immunizations, travel, infections or sick contacts. He had an umbilical hernia repair done 8 years ago and he was not on any medications; herbal or over the counter medications. There was no family history of thyroid disease; father had ischemic heart disease. He smoked marijuana daily for the past 3 years and was sexually active.

On examination vital signs were stable; Blood pressure was 129/74mm/hg, pulse 98bpm and regular and Spo2 was 99% on room air. He was afebrile with a GCS of 15. He was ambulant and tremulous with a thyroid goitre. He had mild exophthalmos with normal extra ocular movements and a thyroid bruit.
Blood investigations revealed the following: Wbc 8x 10^3uL, Hemoglobin 12g/dl and a Platelet count of 338 x 10^3uL. Renal and liver function test were normal and the Covid Antigen test and Rapid HIV test were both negative. Thyroid function test confirmed hyperthyroidism: TSH 0.01IU/ml (0.27 – 4.2), T3 6.5 ng/dl (0.8 – 1.3), T4 24.9 ng/dl (5.1 – 14.1), TRAB was and the Burch Wartofsky score was 25. Blood and Urine cultures were negative.

A Chest Xray revealed no consolidation, effusions or masses with a normal cardiothoracic ratio and ECG showed normal axis with a pulse of 100 and nil signs of ischemia. Thyroid USS revealed that the thyroid gland demonstrated a heterogeneous, hypervascular and enlarged appearance throughout. No focal nodules or cystic collections were noted. The isthmus measured .97cm. The right lobe measured 8.2cmx 4.0cmx 4.2cm and the left lobe measured 9.9x3.9cm. There was no evidence of cervical lymphadenopathy or retrosternal extension.

He was admitted in the ward and on day 1 post admission he had two episodes of cardiac syncope and he was found in the bathroom with Ventricular Standstill Rhythm, and higher degree AVB .. On examination vital signs were as follow; Blood pressure 63/47mm/hg, pulse 120 (not palpable), Spo2 98% on room air, RBS 153mg/dl with a GCS 3/15. Cardiac monitor revealed Complete Heart block with Asystole. CPR was commenced and IV Atropine and Dopamine and isoprenalin infusion were started. Post resuscitation vital signs were; BP 111/94 mmHg, pulse 94bpm with a GCS of 15/15. He was transferred to cath lab for placement of pacing wires then to ICU for stabilization and monitoring. Patient remained stable in ICU post pacing, and he was stepped down to CCU (Coronary Care Unit) on the second day post ICU admission.

An Echocardiogram was performed which revealed an ejection fraction of greater than 60% with nil evidence of structural abnormalities. A non-contrast CT brain was performed which was normal. His CTCA and cardiac MRI was normal as well.
Endocrine team reviewed and commenced carbimazole 15mg po tds and propranolol once after the PPM Repeated ECGs performed on CCU revealed intermittent atrial tachycardia with dissociated ventricular response and patient was still pacing depending at day 10 post admission MDT meeting involving Cardiologist, electrophysiologist, Endocrinologist decided to offer PPM in light patient was pacing dependent and Antithyroid treatment was started with an aim to achieve Euthyroid status. A decision was made for permanent pacemaker (PPM) placement and to continue with the medical management of hyperthyroidism. However, if atrial tachycardia persists, despite treating hyperthyroidism and cessation of marijuana use ablation may be considered. He was discharged in stable condition after a 1 week stay in hospital. He was given MOPC, COPC, and Endocrine follow up.
Six week follow up patient was clinically euthyroid and PPM interrogation shows less than 1% pacing need. Decision to explant the PPM were made. Patient was seen two further close follow ups and did not report in any symptoms and TFT showed Euthyroids status.
GD in young male is less frequent presentation and associated with Ventricular Standstill rhythm is very rare that emphasis we need very low threshold for GD screening on careful and through history, examination and relevant investigation. Early diagnosis, appropriate specific treatment, timely escalation is paramount to reduce life threatening cardiac and non-cardiac complications.

DISCUSSION

Cardiac complications which frequently occurs in Graves' disease include Atrial fibrillation, Sinus tachycardia and Supraventricular tachycardia. Cardiac failure, dilated cardiomyopathy and pulmonary hypertension can also occur.[4] On review of the literature, AVB has been reported to be rare in patients

diagnosed with hyperthyroidism. Despite few case reports documenting the occurrence of AVB with hyperthyroidism previously, more research is needed to further elucidate the clinical course, mechanism and management of AVB in patients diagnosed with Graves disease. The link between Graves' disease and CHB (Complete Heart Block) appears to be multifactorial involving the use of drugs, preexisting heart conditions or infections.[5]
A study concluded that AVB was due to infection in most cases, with hyperthyroidism indirectly causing CHB due to excess circulating thyroid hormones.[6] Possible mechanisms for the development of AVB in hyperthyroidism are direct throtoxic effects on cardiac contractility and indirectly via known triggers such as medications, electrolyte disturbances in particular hyperkalemia and infection.[7]

On review of the literature treatment of the underlying hyperthyroidism led to resolution of the AVB however few required pacing. Kuo et al.,[7] and Khan et al.,[8] described cases in the literature who benefitted from PPM. However much more research is needed regarding permanent pacemaker implantation. According to the European society of Cardiology and the European heart Association Guidelines, PPM is indicated in patients with CHB for both symptom control and prognosis. However, this applies for only irreversible cases of AVB. The duration of PPM also requires further research.[9] Sampana and Jasul reported a case of CHB in a patient with Graves disease which occured on stopping antithyroid medications. This patient required temporary pacing which once patient became euthyroid was withdrawn. The authors stressed that treatment involves management of the underlying Graves disease with temporary external pacing instead of PPM insertion.[10] Atri et al also stated the importance of management of the underlying hyperthyroidism in preventing CHB.[11]

Our patient was a young male with a history of using marijuana. Graves disease was newly diagnosed. He was not on any medications and there was no evidence of infection or electrolyte abnormalities based on blood investigations. Echocardiogram also revealed no evidence of structural heart disease. The decision for temporary pacing and hence PPM was made since patient was deemed hemodynamically unstable and to assist with prognosis since the patient was a young male. Beta blockers are essential in the management of Graves disease and review of the P-R interval as well as identification of any conduction abnormalities on a baseline ECG can identify patients at risk of AVB[4]. B blockers are administered to manage adrenergic symptoms such as palpitations, tachycardia and heat intolerance. On review of the literature B blocker therapy was found to be associated with drug induced AVB in 54 percent of cases.[12] Although most patients had AVB due to hyperthyroidism, it was noted that AVB occurred before or immediately after starting treatment with B blockers. Thus further providing evidence that it is unlikely that all cases of AVB are drug induced. However much more data is required to confirm hyperthyroidism induced AVB to B-blocker therapy.[13] Careful case by case evaluation will be important in the management of such patients. Our patient was not on any medications and the baseline ECG showed no evidence of conduction abnormalities. Hence he was started on propranolol which was subsequently held by the Cardiology team when CHB was diagnosed following the syncopal episode.

Miller et al has reported that CHB in thyrotoxicosis if unrecognised can be a significant cause of mortality and morbidity.[3,14] On review of the literature if hyperthyroidism is poorly controlled or the patient is not compliant with use of medications then thyroid iodine ablation or subtotal thyroidectomy are suitable.[15]

We presented a rare case of CHB in a young male patient with newly diagnosed Graves. As mentioned previously CHB may be reversible with management of the underlying thyrotoxicosis. Examination of the PR interval in a baseline ECG is critical in identifying patients at risk of heart block on commencing and during treatment with B blocker therapy. If a patient is deemed hemodynamically unstable then temporary pacing or PPM may be suitable. Much more research and guidelines for the

optimal management of Graves' disease or hyperthyroidism with AVB including PPM implantation and duration is required.

Conclusion:

Graves' disease in young males is an infrequent presentation, and its association with ventricular standstill rhythm is exceedingly rare. Comprehensive screening for GD through detailed history, examination, and relevant investigations is crucial. Early diagnosis, appropriate specific treatment, and timely escalation are paramount to reducing life-threatening cardiac and non-cardiac complications.

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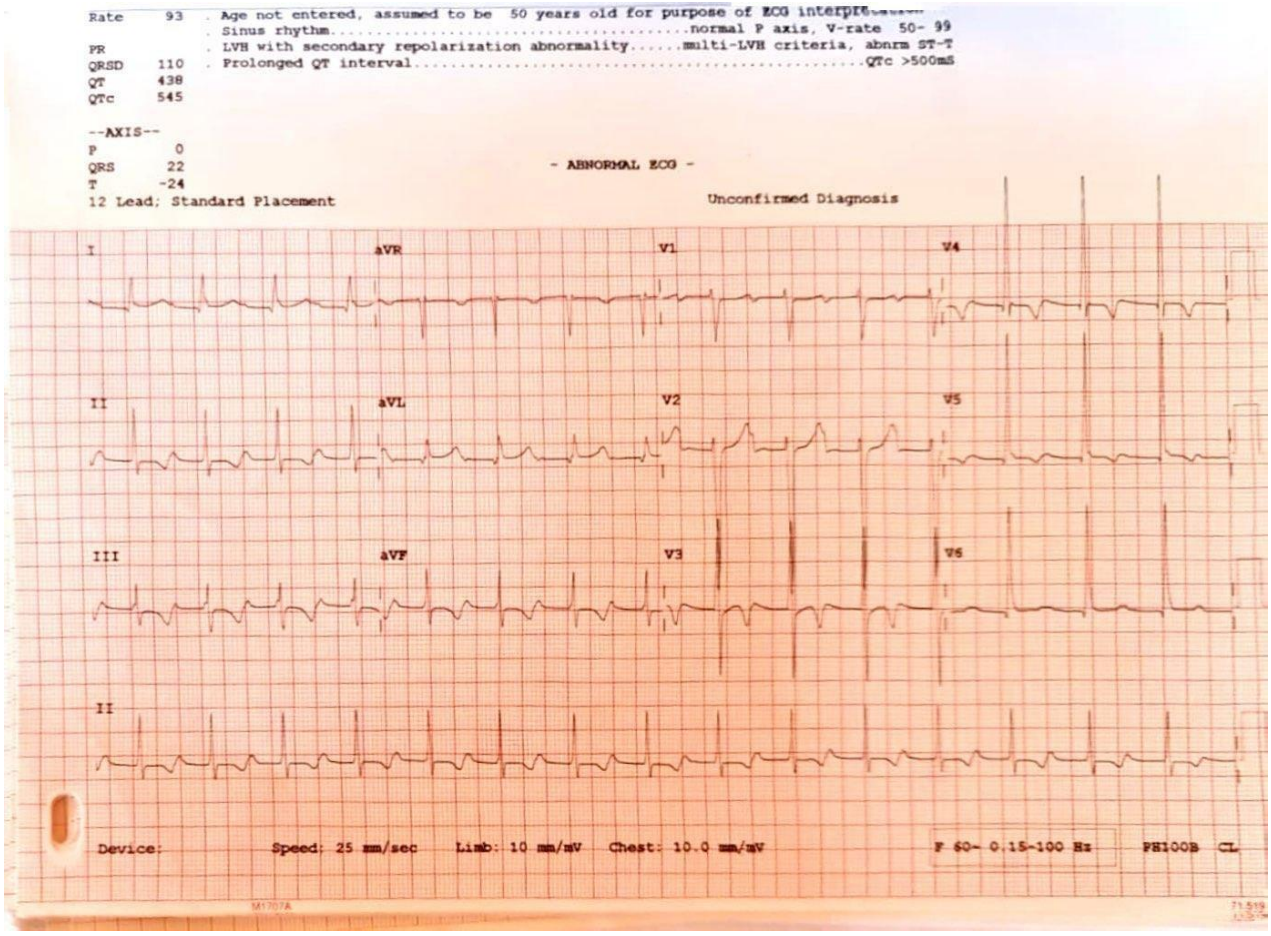

Figure-1: Sinus Rhythm with First Degree AVB (1st ECG)

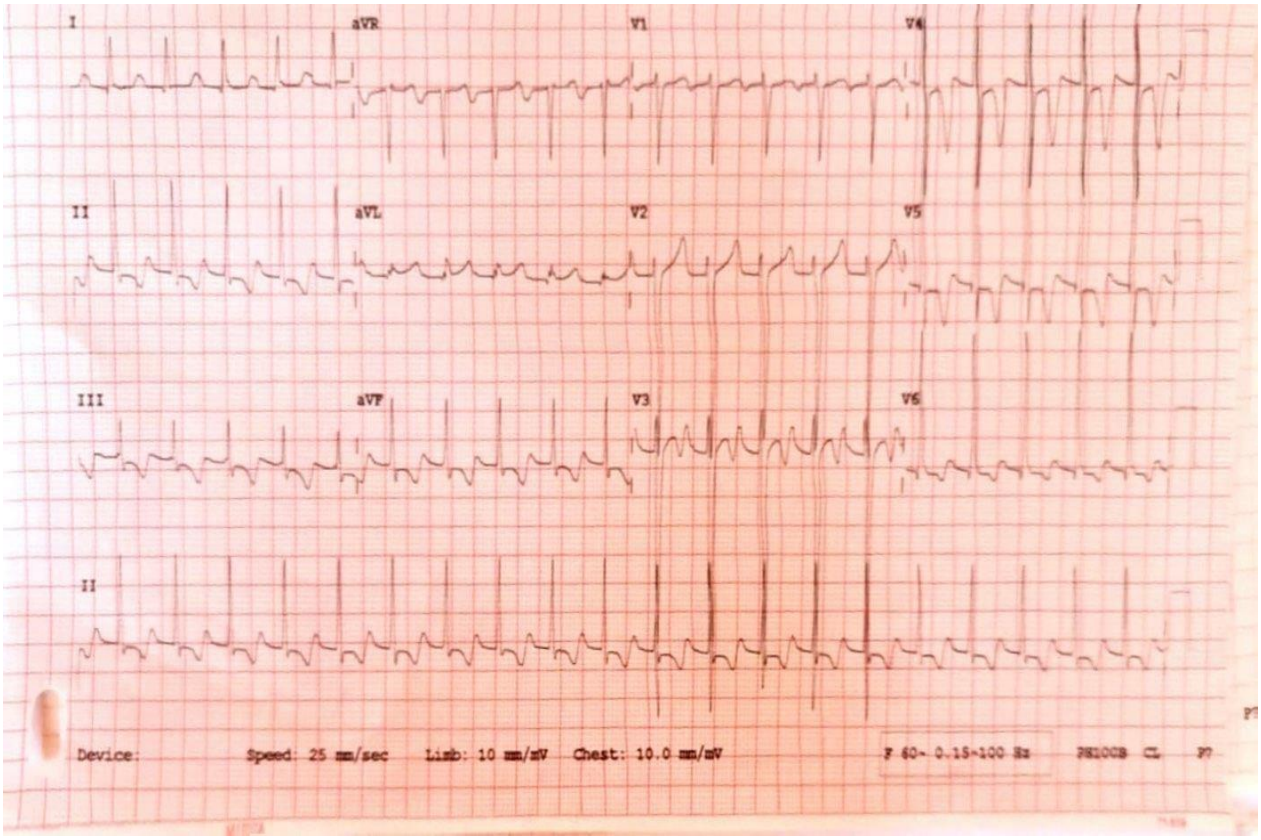

Figure-2: Sinus Rhythm with First Degree AVB (2nd ECG)

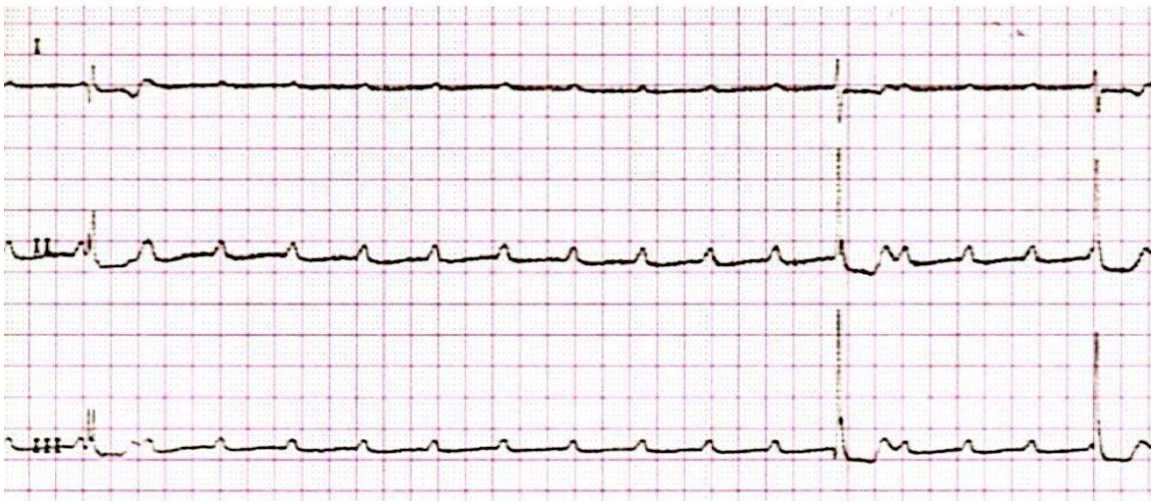

Figure-3: ECG shows ventricular stands still/ Asystole during collapse episode

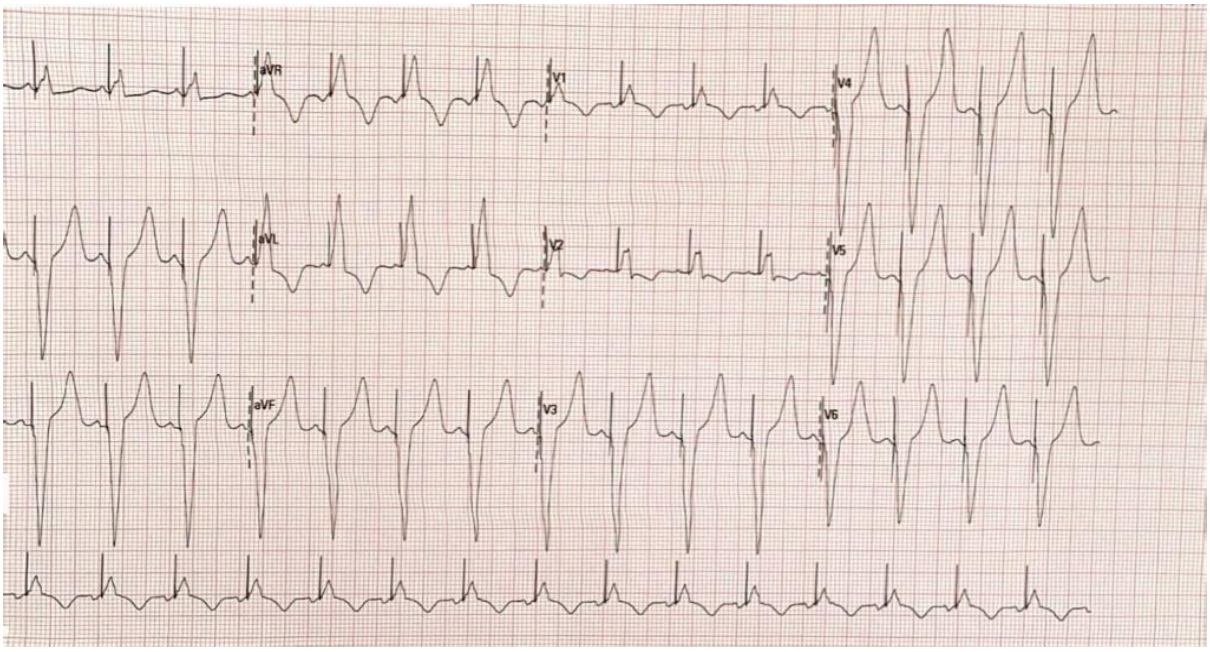

Figure-4: Post PPM implant with paced Complexes

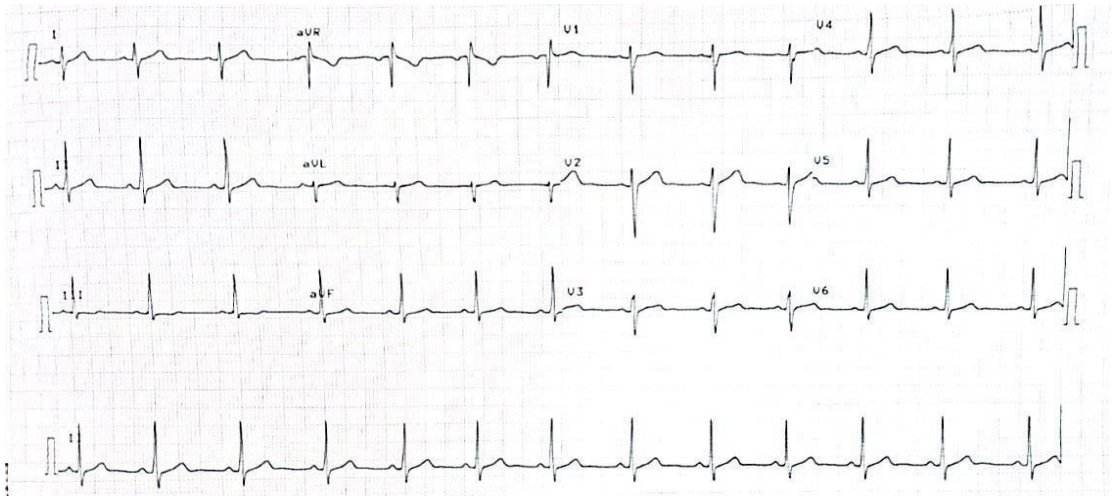

Figure-5: Post PPM Explant ECG showing normal intervals and complexes