GRAVES' DISEASE WITH WPW SYNDROME

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Introduction

Cardiac arrhythmias are common in thyrotoxicosis and almost invariably supraventricular. About 10%-25% manifest AF [1-3]. The mechanism of arrhythmias in thyrotoxicosis is explained by direct action of thyroid hormones on the heart. Atrial flutter and AF can occur in thyrotoxicosis irrespective of the accessory pathway. Patients with WPW Syndrome have a muscular connection between atria and ventricles (Bundle of Kent), outside the special conducting tissue. These patients have symptoms due to tachyarrhythmias with sudden onset and offset. They are usually because of re-entrant tachycardia which may be antidromic or orthodromic. AF occurs in 4% cases and Paroxysmal Supraventricular Tachycardia (PSVT) is reported in 3% cases of WPW syndrome [1]. In patients of Graves disease who have associated WPW syndrome onset of supraventricular tachycardia/tachyarrhythmia can lead to accelerated antidromic conduction through the accessory pathway permitting a rapid ventricular response including life threatening ventricular fibrillation.

Case Report

A 40-year old serving soldier was hospitalised at a service hospital in August 96 when he complained of sudden onset palpitations on several occasions over preceding one month. Each episode had lasted for a few minutes with sudden offset. One such episode which occurred while he was journeying by train had been associated with severe giddiness and had alarmed him. The patient had lost 15 Kg of body weight over preceding 5 months and felt weak. He admitted to lack of sleep and irritability. He was not known to have had any medical ailments in the past. Examination revealed a thin built patient with body mass index of 18, resting heart rate of 118 per minute, regular, a blood pressure of 140/60 mm Hg. He had fine digital tremors with moist palms. Exophthalmos was stage III with lid lag and lid retraction. There was Grade II thyromegaly without bruit. Other systems examination was unremarkable. Investigations done revealed :- Hb 16 gram/., blood glucose (F)-108 mg/dl and (post prandial)-117 mg/dl; Serum T₃-3.1 ng/ml; T₄-13.1 microgram/dl; TSH 0.1 µIU/ml. EKG rate 110/min, Normal sinus rhythm, QRS-minus 30 degree, PR-0.06 sec, delta waves seen in V₁ which were upright, LBBB pattern indicating Type B WPW syndrome (Fig 1). Fine Needle Aspiration Cytology-of thyroid was consistent with the

picture of Graves' disease. I¹³¹ thyroid scan revealed diffuse thyromegaly. Radioactive iodine uptake (RAIU) at 2h was 31% and at 24h was 74%. Holter monitoring done for 24h did not reveal any AF/PSVT episode. Echocardiography showed ejection fraction 65% and there was no evidence of structural heart disease. The EKG abnormality, however, persisted. Electro-physiologic studies done were suggestive of right posterolateral accessory pathway. Patient was administered Carbimazole 45 mg per day and euthyroid state was achieved. Radio Frequency Ablation (RFA) of accessory pathway was done. Subsequently his thyroid was ablated with 5 mCi of I¹²⁵. Presently he is euthyroid and EKG does not show any evidence of preexcitation.

Discussion

There are rare case reports [4-6] of coexistence of WPW syndrome with Graves disease. Transient electrocardiographic features of pre-excitation syndrome may become manifest in Graves's disease, disappearing after the thyrotoxic phase is controlled [5,6]. The occurrence and incidence of such transient WPW syndrome in Graves's disease is uncertain. The exact cause of such abnormality is not known. These two diseases are generally viewed as separate entities, occurring together by chance, in a given patient thyrotoxicosis is not known to produce structural lesions that may lead to pre-excitation. Both conditions can lead to cardiac arrhythmias independently.

The arrhythmias in thyrotoxic patients are mediated by the direct effects of elevated levels of circulating thyroid hormones. The receptor protein activation results in increased transcription of T₃ responsive cardiac genes. T₃ increases myocardial transcription of the myosin heavy chain(MHC) alpha gene and decreases the transcription of the MHC betagene. This leads to increased myosin adenosinetriphosphatase (ATPase) activity. T₃ responsive messenger ribonucleic acids (mRNAs) have been identified, including those, which increase the sarcolemmal sodium pump sites as well as calcium channels. T₃ also causes a higher calcium influx across the sarcolemma and stimulates plasma membrane Ca-ATPase activity [5,7].

The mechanism by which AF is initiated in the

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Fig. 1: EKG showing delta waves

presence of the accessory pathway is not fully understood. It has been shown that preceding reciprocating tachycardia plays an important role in the genesis of AF. More recently it has been shown that the accessory pathway itself may initiate the AF by virtue of its architecture. Intrinsic atrial factors such as longer intraatrial conduction time, shorter atrial functioning refractory period may also be important. Several factors

determine the ventricular rate during atrial fibrillation in patients with WPW syndrome. The electrophysiological properties of both pathways (A V Nodal pathway and accessory pathway) are important factors (Table 1). Available data does indicate that the length of the refractory period of the accessory pathway has definite predictive value for ventricular rate during AF. Short refractory period of accessory pathway is

TABLE 1

Factors determining ventricular rate during atrial fibrillation in WPW syndrome

Accessory pathway

- 1) Refractory period (effective refractory period of 250 ms)
- 2) Input, transmission and output characteristics. Width, length type of accessory pathway.
- 3) Concealed Conduction - In atrioventricular direction; In ventriculoatrial direction.
- 4) Re entry

Atrioventricular nodal pathway

- 1) Refractory pathway
- 2) Input transmission and output characteristics
- 3) Concealed Conduction
- 4) Re entry

Ventricles

- 1) Refractory period.

far from uncommon [7]. Ventricular fibrillation may develop from AF or occur when a very early supra-ventricular beat falls in the ventricular phase of the preceding ventricular complex [8,9]. Coexistence of Graves' disease with WPW syndrome is interesting for several reasons.

(a) whether such patients are at increased risk of cardiac arrhythmias is an unanswered question.

(b) there are therapeutic implications in managing patients having Graves disease and WPW syndrome for example beta blockers which are commonly used to control the symptoms of thyrotoxicosis also are known to prolong the AV nodal refractoriness but have no such effect on the accessory pathway. If AF develops in patients who have both thyrotoxicosis and WPW syndrome and are already receiving beta blockers, there is atleast a theoretical possibility of very rapid antidromic conduction of atrial impulses to ventricles via the accessory pathway. This is specially so, if the effective refractory period of the accessory pathway is shorter than 250 msec [10]. Also, when patients of Graves's disease with WPW syndrome have AF, drugs like verapamil, propranolol, digitalis need to be avoided. Class Ic antiarrhythmic drugs and Amiodarone have effect on the AV node and the accessory pathway and hence are preferred for controlling fast ventricular response [11,12]. Amiodarone itself is known to induce hypothyroidism when given for a long period of time due to its iodine content. Each 200 mg tablet of Amiodarone contains 75 mg of iodine which can result in hypothyroidism (more common) or hyperthyroidism (relatively less common). The total incidence of thyroid dysfunction induced by Amiodarone is about 4% [13]. In patients, who live in iodine deficient regions, iodine induced thyrotoxicosis due to Amiodarone therapy occurs in nearly 10%[14].

The best way to monitor Amiodarone induced hypothyroidism is by measurement of reverse T₃ in blood while hyperthyroidism is by TSH levels. For patients who are thyrotoxic and are being administered thionamides in doses sufficient to block iodine binding within the gland, the risk of iodine induced thyrotoxicosis is insignificant and perhaps even nonexistent. Moreover, iodine induced thyrotoxicosis needs to be treated with thionamides or with perchlorates.

However studies on natural history of WPW syndrome have shown that in several adult patients the typical EKG findings disappeared over the years, probably as a result of block in the accessory pathway or marked lengthening of the refractory period of the pathway [15]. This finding suggests that the danger of developing high ventricular rates after onset of AF diminishes with increasing age. It is not a routine practice to prescribe prophylactic medication against cardiac arrhythmias without electrophysiological studies (EPS) in asymptomatic individuals with WPW syndrome. In patients with documented episodes of AF, associated conditions favouring arrhythmias such as hyperthyroidism should be corrected. It is recommended that permanent ablation of the thyroid should be carried out to prevent occurrence of thyrotoxicosis in such patients. If accessory pathways with short refractory periods are found on EPS-Radio frequency catheter ablation of the tract should be done. Alternately class Ic drugs can be tried.

References

1. Zonszein J, Fein F, Sonnenblick E. The Heart and the endocrine disease. In : Schlant RC, RW Alexander Editors. Hursts The Heart. Vol 2. 8th Ed. McGraw-Hill 1908-10.
2. PR Larsen, TF Davies, ID Hay. The thyroid gland. In : Wilson JD, Foster DW, Kronenberg HM, Larsen PR, eds. Williams Text Book of Endocrinology. WB Saunders and Co. 9th ed. 1998; 427.
3. Mckenzie JM, Zakarija M. Hyperthyroidism. In : Leslie J Degroot ed. Endocrinology 3rd ed. WB Saunders and Co. 1995; 680.
4. JA Strong. Thyrotoxicosis with Ophthalmoplegia, Myopathy, WPW Syndrome and pericardial friction. Lancet 1949;1:959-61.
5. Jervell O. Thyrotoxicosis and WPW Syndrome. Nord Med 1941;10:1471.
6. Willis FA, Carrier HM. Electrocardiogram displaying short PR interval with prolonged QRS complexes. Proc Mayo Clinic 1946;21:438.
7. Wellens HJ, Durrer D. WPW Syndrome and Atrial Fibrillation. Relation between refractory period of accessory pathway and ventricular rate during atrial fibrillation. Am J Cardiol 1974;34:777-82.
8. Klein GJ, Bashore JM, Sellers JB. Ventricular fibrillation in WPW Syndrome. New Eng J Med 1979;301:1080-5

9. Dreifus LS, Halat R, Watanabe Y. Ventricular fibrillation : a possible mechanism of sudden death in patients with WPW syndrome. *Circulation* 1971; 43:520-7.
10. Naoki G, Karragai K, Matsuo K, Annouwa M, Morae K. Electro physiological properties in paroxysmal atrial fibrillation complicated with WPW syndrome. Comparison with paroxysmal AF alone. *Cardiology* 1994;84:292-7.
11. Garboys TB, Podrid PJ, Loun B. Efficacy of Amiodarone for refractory supraventricular tachyarrhythmias. *Am Heart J* 1983;106:870-6.
12. Horowitz LN, Spielman SR, Greenspan AM, Mintz GS, Morganroth J, Brown R et al. Use of Amiodarone in the treatment of persistent and paroxysmal atrial fibrillation resistant to Quinidine therapy. *J Am Coll Cardiol* 1985;6:1402-7.
13. Albert SG, Alver LE, Rose EP. Thyroid dysfunction during chronic Amiodarone therapy: *J Am Coll Cardiol* 1987;9:175-98.
14. Martino E, Safran M, Aghini-Lombardi F, Rajatanavin R, Lenziardi M, Fay M et al. Environmental iodine intake and thyroid dysfunction during chronic Amiodarone therapy. *Ann Intern Med* 1984;101:28-34.
15. Fujimura, Klein GJ, Yee R. Mode of onset of AF in WPW Syndrome : How important is the accessory pathway? *J Am Coll Cardiol* 1990;15:1802-6.