Digitalis induced paroxysmal atrial tachycardia with AV block

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Twenty-four instances of digitalis induced paroxysmal atrial tachycardia with block in 20 inpatients are described. Cases of cor pulmonale with hypoxia were more prone to develop this arrhythmia. Electrocardiographic features consisted of an atrial rate ranging from 115 to 230 a minute and an altered configuration of the P wave which was diminutive in nearly half the cases. The block at the AV node was commonly varying or 2:1.

Four patients (20%) died within 12 hours of the recognition of this abnormality. PAT with block is ranked second to ventricular tachycardia in its malignancy.

Unlike paroxysmal atrial tachycardia of 'normal' hearts, paroxysmal atrial tachycardia with AV block (PAT with block) is commonly precipitated by digitalis in excess, with or without potassium depleting diuretics. It was originally reported by Lewis (1909) from a polygraphic recording of jugular and radial pulses. The causative relation to digitalis was first suggested by Mackenzie (1911) and was further clarified by Heyl in 1932. After a lapse of 22 years attention was redrawn to this arrhythmia by Lown and Levine (1954) by their extensive clinical and experimental work. Recent studies indicate that PAT with block is a common arrhythmia and is being increasingly recognized (Lown and Levine, 1958; Hejtmancik, Herrmann, and Wright, 1958; Goldberg *et al.*, 1960; Harris, Julian, and Oliver, 1960; Oram, Resnekov, and Davies, 1960; Burton, 1962; Wahi *et al.*, 1966). The largest series (112 episodes in 88 patients) is that of Lown and Levine (1958).

In this study examples of PAT with block were encountered in patients on digitalis. Some of the clinical and electrocardiographic features of this arrhythmia are presented.

Material and methods

A total of 292 patients was put on digitalis in a period of 18 months from January 1968 to June 1969. Only one proprietary brand of digitalis glycoside (Lanoxin) was used both orally and parenterally throughout this period. A 12-lead reference electrocardiogram was taken immediately on admission which was often before the

patient had received any digitalis. During the period of observation, tracings consisting of long rhythm strips of leads II, aVF, and V₁ were frequently recorded. If P waves were not easily identifiable in routine leads a special bipolar chest lead (S₅) with the right arm electrode over the manubrium and the left arm electrode over the right fifth interspace was used. The response to carotid sinus massage was continuously monitored.

The genuineness of an arrhythmia as a toxic manifestation in a patient on digitalis is always suspect as it may also be the result of underlying heart disease. Fairly rigid criteria were, therefore, applied before PAT with block was attributed to overdosage of the glycoside.

- (1) Intake of adequate digitalizing or maintenance dose of the drug with or without potassium depleting diuretics in the immediate past.
- (2) Abolition of the ectopic rhythm after withdrawal of digitalis and institution of corrective therapy.
- (3) Presence of concurrent or preceding manifestations of digitalis intoxication, namely gastrointestinal symptoms, ventricular bigeminy, various grades of AV block, etc.

Digitalis effect in the electrocardiogram was only considered a corroborative evidence of digitalis intake.

Results

Cardiac arrhythmias and conduction defects directly attributable to digitalis poisoning were recorded in 105 (36%) out of 292 patients receiving this drug (Agarwal and Agrawal, 1970). There were 24 instances of PAT with block in 20 patients, comprising 19 per cent of the toxic cases.

TABLE Clinical and therapeutic details of patients with digitoxic PAT with block

Case No.	Age (yr)	Heart disease	Associated complications	Lanoxin in the immediate preceding period	Diuretics	Toxic manifestations preceding PAT with block	Treatment (besides withdrawal of digitalis)	Return to sinus rhythm
1	25	Rheumatic heart disease	Acute bronchitis	3.50 mg in 3 dy	Nil	Headache, nausea, and vomiting; atrial fibrillation	Nil	5 dy
2	40	Rheumatic heart disease	Acute bronchitis	0.37 mg daily for 8 dy	Frusemide 40 mg daily	Atrial fibrillation	Nil	2 dy
3	10	Rheumatic heart disease	Acute rheumatic carditis	1.75 mg in 3 dy	Hydrochlorothiazide 25 mg daily	Anorexia, nausea, and vomiting	Potassium chloride	3 dy
4	50	Severe anaemia with CCF	Nil	3 mg in 3 dy	Frusemide 40 mg daily	Anorexia, nausea, and vomiting	Nil	3 dy
5	50	Cor pulmonale	Carbon dioxide narcosis	0.25-0.50 mg for one mth (maintenance dose)	Mersalyl 2 ml biweekly	Nil	Potassium chloride	7 dy
6	20	Rheumatic heart disease	Nil	3.50 mg in 4 dy	Hydroflumethiazide 50 mg daily	Vomiting	Potassium chloride	3 dy
7	40	Cor pulmonale	Nil	3.75 mg in 5 dy	Mersalyl 2 ml biweekly	Nausea and vomiting	Potassium chloride	4 dy
8	55	Constrictive pericarditis (postoperative)	Nil	0.37 mg daily for 15 dy (maintenance dose) + 0.5 mg intravenously postoperatively	Hydrochlorothiazide 50 mg on alternate dy	Nil	—	Died after one hr
9	30	Rheumatic heart disease	Nil	2.5 mg in 3 dy	Hydrochlorothiazide 25 mg on alternate dy	Nil	Nil	2 dy
10	15	Rheumatic heart disease	Nil	0.37 mg daily for 10 dy (maintenance dose) + 0.25 mg intravenously after valvotomy	Hydrochlorothiazide 25 mg on alternate dy	Nil	Nil	6 hr
11	65	Cor pulmonale	Nil	3.50 mg in 6 dy	Hydrochlorothiazide 50 mg once daily	Nil	Potassium chloride	3 dy
12	66	Hypertension with left ventricular failure	Pre-existing left bundle-branch block	2.75 mg in 2 dy	Frusemide 40 mg once daily	Nil	Potassium chloride	4 dy
13	50	Cor pulmonale	Nil	2.75 mg in 3 dy	Mersalyl 2 ml biweekly	Nil	Potassium chloride	3 dy
14	65	Cor pulmonale	Central cyanosis ++	0.50 mg for 20 dy (maintenance dose)	Hydrochlorothiazide 25 mg on alternate dy	Vomiting	Nil	3 dy
15	8	Rheumatic heart disease	Nil	2 mg in 3 dy	Hydrochlorothiazide 50 mg on alternate dy	Nil	Nil	10 hr
16	22	Rheumatic heart disease	Nil	0.5 mg for a mth (maintenance dose)	Hydrochlorothiazide 50 mg on alternate dy	Nil	Potassium chloride	3 dy
17	12	Cardiomyopathy	Pulmonary tuberculosis	1.75 mg in 3 dy	Hydrochlorothiazide 50 mg daily	Nil	Potassium chloride	Died after 6 hr
18	40	Cor pulmonale with CCF	Carbon dioxide narcosis	2.25 mg in 4 dy	Hydrochlorothiazide 50 mg once daily	Anorexia, nausea, and vomiting	Potassium chloride	Died after 12 hr
19	35	Cor pulmonale with CCF	Central cyanosis	3.25 mg in 5 dy	Hydrochlorothiazide 50 mg once daily	Nil	Potassium chloride	2 dy
20	61	Myocardial infarction with left ventricular failure	Nil	2.75 mg in 2 dy	Frusemide 80 mg daily for 2 dy	Nil	Potassium chloride	Died after 4 hr

CCF = Congestive cardiac failure.

Details of these patients as to age, type of heart disease, digitalis dosage, diuretics, and therapy are given in the Table. The nature of the cardiac disorders of these patients was roughly representative of the distribution of various types of heart disease seen in patients in hospital except for cor pulmonale which was proportionately more. Four out of 7 suffering from pulmonary heart disease had central cyanosis or fully fledged manifestations of carbon dioxide narcosis. All patients were in congestive heart failure except one with constrictive pericarditis to whom the drug was given erroneously. The initial digitalizing or maintenance dosages of the glycoside were well within the recommended limits. Four patients developed this arrhythmia during low maintenance therapy.

Sinus rhythm was restored in 16 survivors in 6 hours to 7 days after withdrawal of the drug, with or without administration of potassium chloride. Four patients died soon after this abnormal rhythm was recorded (Cases 8, 17, 18, and 20).

Discussion

A digitoxic cardiac arrhythmia can be suspected at the bedside if it is preceded or accompanied by familiar symptoms of overdosage of the drug or tell-tale pulsus bigeminus. PAT with block may, however, develop without any premonitory symptoms (Lown and Levine, 1954). In 60 per cent of cases in this series (Table) there were no warning symptoms or signs. Strong presumptive evidence of its occurrence is often manifested in a paradoxical tachycardia or aggravation of heart failure in spite of adequate digitalis dosage. Even then a physician has to lean heavily on frequent electrocardiographic monitoring for early recognition.

In the published series of digitalis induced cardiac arrhythmias the relative incidence of PAT with block is variable (Herrmann, Decherd, and McKinlay, 1944; Flaxman, 1948; Crouch, Herrmann, and Hejtmancik, 1956; Shrager, 1957; von Capeller, Copeland, and Stern, 1959; Rodensky and Wasserman, 1961; Dreifus *et al.*, 1963; Dubnow and Burchell, 1965; Chung, 1970). On pooling the results of the above reports the mean percentage of this arrhythmia is 14 per cent. Our observation of 19 per cent is a little higher than the pooled result.

It was not surprising to find a high incidence of toxic arrhythmia in cor pulmonale as compared to other forms of cardiac lesions in this series. Significant depletion of body potassium has been reported in hypoxia associated with chronic pulmonary insuffi-

ciency by Baum *et al.* (1959). They have presented electrocardiographic evidence of sensitivity to a test dose of acetylthiothiophen. Frequent association of PAT with block in chronic pulmonary heart disease has also been the subject of other reports (Goldberg *et al.*, 1960; Burton, 1962).

Electrocardiographic features Diagnosis of PAT with block rests essentially on the

FIG. 1 (Case 16) PAT with latent AV block. The strip in the first row shows sinus conducted beats before administration of digitalis. PAT 1:1 with latent block is seen in the second strip. The block has increased after carotid massage in the third strip (increased PR interval). After further carotid sinus pressure Wenckebach block developed (last strip). P waves are marked with a dot.

electrocardiogram. The distinctive features have been clearly laid down by Lown and Levine (1958) and are a usual atrial rate of 140–220 a minute, a baseline which is isoelectric between atrial complexes, an atrio-ventricular block latent or overt, and an altered but commonly upright P wave in standard leads II, III, and aVF.

Atrial complex

The contour of the P wave is nearly always altered in at least one of the leads, II, III, aVF, or right praecordial leads. We did not confine ourselves to examination in lead II alone. In at least one patient (Case 9) the P waves were unchanged in lead II, III, and aVF and there was an unequivocal change in its morphology in VI betraying the ectopic nature of the pacemaker. Upright sinus P waves of lead II became diminutive in II, peaked in 4, bifid in 3, inverted in 4, and remained unaffected in the other 2. The pathognomonic diminutive P waves (including 3 examples of bifid P) were thus seen in a little over half the cases (58%) as compared to 75 per cent cases of Lown and Levine (1958) and El-Sherif (1970).

A variation in the PP cycle length, if present, is considered to be diagnostic of digitalis induced PAT with block and had been noted by most workers in one-third to one-half of their cases (Lown, Wyatt, and Levine, 1960; Phillips *et al.*, 1966; El-Sherif, 1970). It has been attributed to a negative chronotropic effect of ventricular systole and is termed ventriculophasic arrhythmia by Rosenbaum and Lipeschkin (1955). It ranged from 0.02 sec to 0.06 sec in 9 out of 19 instances where the block was 2:1 or more.

The atrial rate varied from 115 to 230 a minute in this series, the average being 170. Rates as low as 72 (El-Sherif, 1970) and as

FIG. 2 (Case 14) PAT with varying AV block (1:1 response with prolonged PR interval, 2:1 and 3:1). The morphology of P waves is different from that of the sinus pacemaker (first strip).

high as 400 (Simonson and Berman, 1951) have been recorded.

AV response

The block by definition is an essential criteria of this dysrhythmia. All types of delay in conduction from a latent block to 12:1 were noted. The former was unmasked after carotid sinus pressure (Fig. 1, Case 16). The common 2:1 response was seen in 8 cases but even more often (9 cases) the block was changing in the same strip (Fig. 2, Case 14).

Concurrent electrocardiographic abnormalities

Accompaniment of other digitoxic stigmata in the tracing establishes the toxic nature of the arrhythmia, as stated earlier. Four patients had ventricular bigeminy, one of whom had in addition a salvo of 3 ventricular ectopic beats (Fig. 3, Case 18). One of the patients (Case 17) had nodal rhythm with AV dissociation (Fig. 4) and another frequent nodal extrasystole.

FIG. 3 (Case 18) PAT with 2:1 response, ventricular bigeminy, and a salvo of 3 ventricular extrasystole. Ectopic beats are multiform and multifocal.

FIG. 4 (Case 17) The first 3 ventricular complexes of the second strip are equidistant and aberrant (nodal rhythm with AV dissociation). The latter part of the strip shows PAT with 2:1 block and ventriculophasic arrhythmia of 0.02 sec.

Diagnosis Even with rigid diagnostic criteria, difficulty may arise in distinguishing it from a number of conditions. In a case with 1:1 response it may be mistaken for sinus tachycardia if an earlier tracing of a sinus rhythm is not available to compare the altered morphology of P waves. A classical PAT with 2:1 block may be dismissed as sinus rhythm if the first P is superimposed on QRS or T of the preceding complex. For the same reasons, nodal rhythm or tachycardia can be simulated in 1:1 conduction. Carotid massage by increasing the AV block and unmasking the P will expose the real nature of the arrhythmia. Oesophageal leads or percutaneous right atrial lead (S₅) can also bring to light the culprit P but that is hardly ever done simultaneously with the standard leads. If the P waves are not identifiable and the block variable it can mimic atrial fibrillation (Fig. 5, Case 4). Conventional paroxysmal atrial tachycardia can be easily distinguished from the toxic one by the history, response to

vagal stimulation by carotid sinus compression, and constant cycle lengths. It is important not to mistake PAT with block for atrial flutter as digitalis is 'poison' for the former and 'food' for the latter. The distinction is easy in an average case with P inscribed at a rate faster than 250 and a saw-tooth baseline in even one lead. In borderline cases where the rate varies between 200 and 250, real difficulty in diagnosis may arise. History of digitalis intake in excess, its stigmata in the form of ventricular premature beats if present, and finally response to potassium chloride will help to unravel the mystery.

Prognosis According to Lown and Levine (1958), PAT with block carries a grave prognosis as 60 per cent of the lethal dose is likely to have been received by the time it is recorded. Fifty-eight per cent of their patients, most of whom had severe forms of heart disease, died shortly after this arrhythmia. The reported mortality figures are fairly

FIG. 5 (Case 4) PAT with varying AV block in lead II simulates atrial fibrillation as diminutive P waves are barely discernible. The block is 2:1 in aVF.

high and range from 28 per cent (Freiermuth and Jick, 1958) to 58 per cent (Nadas, Rudolph, and Reinhold, 1953). The case fatality of a series depends on the seriousness of heart disease of its constituents, period of observation, and time taken in detection of this arrhythmia. Of our 20 cases, only 4 died (20%). The number of younger patients with a relatively milder form of heart disease (8 rheumatic hearts) was probably responsible for the lower death rate in our series. Lown and Levine (1958) had themselves stated that if PAT was recognized early and appropriate measures taken, the mortality was 35 per cent, but if digitalis was continued or increased it was doubled. Observations of El-Sherif (1970) are revealing in this respect: there was an overall mortality of 22 per cent in his series of digitalis induced supraventricular tachycardia but in those in whom it was detected early and specific treatment given it was reduced to 9 per cent. Even more illustrative is the report of Dreifus *et al.* (1963) who noted a mortality of 100 per cent in 7 cases of PAT with block where its sinister nature was not recognized and digitalis continued, while in the other 16 where digitalis was stopped, with or without corrective therapy, only one died. In our opinion PAT with block should be considered second to ventricular tachycardia in its malignancy.

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