Electrocardiogram and vectorcardiogram in Turner phenotype with normal chromosomes and pulmonary stenosis

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Electrocardiograms and vectorcardiograms from 7 boys with the 'Ullrich-Turner phenotype', pulmonary stenosis, and normal chromosomes were systematically compared with recordings from 37 unselected patients with uncomplicated pulmonary stenosis. The 7 patients had a highly characteristic QRS pattern which differed greatly from that of the control group. The frontal plane QRS loop was almost completely localized to the upper right quadrant with a mean frontal QRS axis between 180 and 240 degrees. Initial leftward and inferior forces were minimal. Quantitative criteria were found which gave complete separation of the two groups.

The relation between the electrocardiogram and right ventricular systolic pressure was clearly atypical in the Ullrich-Turner phenotype patients. At each pressure level the posterior and rightward forces exceeded by far the corresponding forces of the control group.

The pattern may be caused either by abnormalities of the specialized conduction system or by an atypical kind of ventricular hypertrophy in these subjects.

It has been known for some time that subjects with features resembling those described by Turner (1938) in adult women, but without sex anomaly and with normal sex chromosomes, have an increased incidence of various congenital cardiac lesions. This clinical syndrome is seen in both sexes and the autosomal complement is generally normal. In males the condition has been usually described as 'male Turner's syndrome' (see e.g. Levy *et al.*, 1970), but at times the eponym of 'Ullrich's syndrome' has been used (Siggers and Polani, 1972). Most of these male subjects with 'Ullrich-Turner's phenotype' have short stature, skeletal anomalies, cryptorchidism, mild intellectual retardation, hydro-nephrosis, a peculiar facies; and webbing of the neck is an essential trait. Recently, a subgroup of the 'Ullrich-Turner phenotype' characterized by pulmonary valve stenosis, and a normal chromosome complement, has been more clearly defined (Noonan and Ehmke, 1963), but webbing of the neck does not seem to be an obligatory clinical association.

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In 1968, Noonan reported that the electrocardiogram in these patients might differ from that usually found in 'pure' pulmonary stenosis, especially with regard to an extreme right axis deviation and an unusually small R in lead V₁. Similar observations have been made by others (Celermajer, Bowdler, and Cohen, 1968; Dupuis *et al.*, 1971). The aim of this report is to document these and other characteristics of the electrocardiogram and vectorcardiogram in further detail.

Subjects and methods

During the past 2 years 7 patients have been seen with the Ullrich-Turner's phenotype and pulmonary stenosis (Table 1). We shall use this double eponym here but wish to stress that not all our patients had neck webbing. All were boys and all had a normal chromosome complement. Six of the patients had valvular pulmonary stenosis, while one (Case 2) had a discrete infundibular stenosis. Three patients had additional small atrial septal defects. Two patients had been unsuccessfully operated on three years previously.

In order to clarify the characteristics of the electrocardiographic pattern in this syndrome, the group was

TABLE 1 Clinical and haemodynamic data in patients with XY Ullrich-Turner's phenotype, ranged according to right ventricular pressure

	Case No.						
	1	2	3	4	5	6	7
Age (yr)	6	9	5	2.5	8	8	9
Right ventricular peak systolic pressure (mmHg)	41	74	80	132	140	140	154
Pulmonary to systemic flow ratio	1, 3	1	1	1	1	1, 3	1, 5
Growth retardation	++	+	+	+	-	++	+
Mental retardation	+	+	(+)	+	-	+	-
Hypertelorism	+	++	(+)	+	+	(+)	+
Ptosis	(+)	+	-	-	(+)	-	+
Chest deformity	++	+	+	+	+	(+)	+
Undescended testis	-	+	+	+	+	+	++
Hydronephrosis	-	-	+	+	+	-	+
Webbed neck	-	+	+	+	(+)	-	+

compared with 37 consecutive nonselected patients with isolated unoperated pulmonary stenosis and otherwise normal somatic features. The mean age of the control group was 16 years compared with 7 years in the Ullrich-Turner phenotype group. Neither this difference nor the presence of small atrial septal defects in the 3 subjects was thought to invalidate the comparison between the groups. Mean right ventricular systolic pressure in the Turner phenotype group was 109 mmHg, and in the control group 85 mmHg.

A 12-lead electrocardiogram was recorded with an Elema Schönander Mingograf. Vectorcardiogram was

recorded with the axial lead system (McFee and Parungao, 1961) using a Sanborn 185 B amplifier and a 569B Visoscope. Ordinary axis orientation was used. Planar vector loops were photographed with a beam interruption interval of 2.5 msec. Scalar X, Y, and Z leads were recorded with a Mingograf, using both 50 and 250 mm/sec paper speed. Spatial vector magnitudes and angular data were derived for each 10 msec QRS vector from the planar recordings, while maxima and minima were derived from the scalar recordings. All these data were systematically compared in the two groups of subjects.

TABLE 2 Comparison of selected scalar vectorcardiographic and electrocardiographic data in two groups

Parameter	Turner phenotype (N=7)		Control (N=37)		t	P	No. of control subjects overlapping Turner phenotype subjects
	Mean (mV)	Range	Mean (mV)	Range			
<i>Vectorcardiogram</i>							
X ₃₀	-0.59	-1.25-+0.20	+0.70	-1.25-+1.40	5.5	<0.001	6
X ₄₀	-1.84	-3.05-+0.10	+0.44	-2.30-+1.90	5.4	<0.001	11
X-max _F	-2.12	-3.80-+1.50	+0.22	-3.05-+2.20	4.1	<0.001	6
X-max	+0.16	+0.00-+0.35	+1.28	+0.40-+2.20	7.3	<0.001	0
X-min ₂	-2.36	-3.80-+1.45	-1.11	-3.70-+0.00	4.3	<0.001	8
Y ₃₀	-0.13	-0.52-+0.55	+0.64	-0.30-+2.10	4.2	<0.001	17
Y ₄₀	-0.60	-0.80-+0.40	+0.92	-1.00-+2.50	5.3	<0.001	2 (No. 26 and 28)
X-max _F	-1.44	-3.60-+0.25	+1.22	-1.20-+3.10	7.6	<0.001	1 (No. 26)
Y-max	+0.19	+0.05-+0.55	+1.47	+0.50-+3.10	5.4	<0.001	1 (No. 4)
Y-min	-1.67	-3.60-+1.00	-0.34	-1.30-+0.00	7.2	<0.001	1 (No. 26)
Y-max-Y-min	-1.48	-3.50-+0.70	+1.13	-0.50-+2.90	7.7	<0.001	0
Z-max	+1.92	+1.05-+3.90	+0.69	+0.00-+1.77	5.2	<0.001	10
<i>ECG:</i>							
R I	0.14	0.00-+0.25	0.56	0.10-+1.60	4.0	<0.001	5
R V ₆	0.11	0.00-+0.35	1.17	0.10-+2.10	6.1	<0.001	1 (No. 17)
S V ₆	1.52	0.75-+2.20	0.49	0.00-+1.50	6.0	<0.001	9
R aVF	0.18	0.05-+0.40	0.96	0.20-+2.00	4.5	<0.001	3 (No. 5, 6, and 28)
S aVF	1.09	0.60-+2.20	0.29	0.00-+1.00	6.2	<0.001	5
R/S aVF	0.19	0.05-+0.44	8.3	0.60-+30.00	2.1	<0.05	0
R aVR	1.36	0.85-+2.40	0.53	0.05-+1.40	5.8	<0.001	7
S or Q aVR	0.10	0.00-+0.15	0.66	0.20-+1.15	6.0	<0.001	0

Abbreviations used in the Table: X₂₀, etc. = X at 20 msec after QRS onset, etc. X-max_F = X at maximal QRS projection in frontal plane. R aVR = maximal R or R'.

Right heart catheterization had been performed in all the cases, and in most within a few days of the electrocardiogram and vectorcardiogram. Right ventricular angiograms had been made in all with a right ventricular systolic pressure above 50 mmHg.

Standard t-test and linear regression analysis were used in the statistical evaluations.

Results

Electrocardiograms from the 7 patients with Ullrich-Turner's phenotype are shown in Fig. 1 and 2. A uniform and characteristic pattern was found, with extreme right axis deviation to more than $+80$

degrees, small or absent R waves in leads I, V₆, and aVF, and large R waves in aVR. In two patients the R waves in V₁ were surprisingly small. P waves and PR segments were normal and the T waves were uniformly discordant to the QRS.

Frontal and horizontal plane vector loops are presented in Fig. 3 and 4. In the frontal plane, almost the complete QRS loop was localized to the upper right quadrant. The rotation in this plane was clockwise in all cases except Case 2, in which a counterclockwise rotation and a more superiorly oriented loop was found. The T loops were completely discordant to the QRS loops. In the hori-

FIG. 1 Extremity electrocardiogram leads for the 7 patients with the Turner phenotype. Case numbering corresponding to Table 1. Paper speed: 50 mm/sec. Calibration: 1 mV = 10 mm. The complexes marked with a cross (Case 2) have an ectopic atrial P wave superposed on the T wave.

zontal plane the picture was more varied. The 4 patients with the highest right ventricular pressures had loop configurations about as expected, but the other 3 had posteriorly dislocated loops with unexpected counterclockwise rotation in 2 of them.

Some of the significant results from the statistical comparison of the two groups are presented in Table 2. A large number of measurements differed significantly in the two groups and four of the corresponding criteria separated them completely

FIG. 2 Praecordial electrocardiograph leads for the 7 patients with the Turner phenotype. Patient numbering corresponding to Table 1. Paper speed and calibration as in Fig. 1 except for tracings marked o where $1 \text{ mV} = 5 \text{ mm}$ and tracing marked oo where $1 \text{ mV} = 7 \text{ mm}$.

from each other. These criteria for the Turner phenotype were: (1) maximal positive deflection in lead X less than 0.4 mV; (2) maximal negative minus maximal positive deflection in lead Y exceeding 0.5 mV; (3) R/S ratio in lead aVF less than 0.6; and (4) maximal negative deflection in lead aVR (S or Q) less than 0.2 mV. Several other criteria gave almost complete discrimination.

Frontal plane angular data are shown in Fig. 5, also demonstrating the large differences between the groups. A criterion based on a 30 msec frontal

angle between 100 and 330 degrees gives complete separation of the groups.

Both scalar and angular data show that the initial QRS vectors were not significantly altered in the Turner phenotype group, but from 15 to 20 msec after the onset of ventricular depolarization the process takes entirely different directions.

For all types of electrocardiograph measurements a large scatter of values was found, reflecting the dominant influence of right ventricular pressure on the electrocardiogram in pulmonary stenosis. There-

FIG. 3 Frontal plane vectorcardiograph loops in the 7 patients with the Turner phenotype. Case numbering as in Table 1. Beam interruption interval, 2.5 msec. Calibration signal, 1 mV. Tracings marked with a cross have been calibrated to one-half of this. Arrows indicate the direction of loop rotation.

FIG. 4 Horizontal plane vectorcardiograph loops for the 7 patients. Recording conditions as in Fig. 3. Calibration as in Fig. 3. Arrows indicate the direction of loop rotation.

FIG. 5 Frontal plane angles for the initial 10 msec vectors, for the maximal vector in the frontal plane ($F_{\max}$), and for the frontal projection of the maximal spatial QRS vector ($SV_{\max}$) in control (filled circles) and Turner phenotype (triangles) group. One patient is missing in the control group at 10 msec and two are missing at 20 msec because the instantaneous vectors did not have any frontal projection.

fore, adjustment for this factor was made through a comparison of the correlations between scalar vectorcardiographic data and right ventricular systolic pressure in the two groups. Maximal superior, inferior, and leftward forces, which best separated the two groups (Table 2), were not significantly correlated with pressure. The criteria for discrimination based on these measurements may therefore be used without consideration of the degree of pulmonary stenosis. Posterior (Fig. 6) and rightward (Fig. 7)

forces were significantly related to pressure in the control group, and in both these directions the 7 patients showed considerably larger forces than expected. A regression line for the values in these patients about parallel with that of the control patients may be suggested. Anterior forces were also highly related to pressure, but the difference between the two groups in the pressure electrocardiogram relation was not so evident in this direction.

FIG. 6 Maximal posterior forces in scalar vectorcardiogram plotted against peak right ventricular systolic pressure. The regression line and its formula, in this and Fig. 7, have been calculated from the control data only.

FIG. 7 Maximal secondary rightward (after 20 msec of QRS) vectorcardiograph forces plotted against peak systolic right ventricular pressure.

Discussion

The data presented establish that subjects with Ullrich–Turner's phenotype and pulmonary stenosis as a group have an electrocardiographic pattern distinctly different from that found in uncomplicated pulmonary stenosis. From this conclusion two important practical consequences emerge. First, this pattern may be of help in the identification of this syndrome and may thus contribute to the recognition of other anomalies linked with it. Clearly, the establishing of the exact specificity and sensitivity of the presented pattern must wait until a larger sample has been studied. When this has been done all the criteria proposed will probably become less sensitive and specific. This applies especially to the sensitivity, since the number of patients with the Ullrich–Turner phenotype was so small. Already, similar patients have been described without any atypical features in the electrocardiogram (Celemajer *et al.*, 1968; Dupuis *et al.*, 1971). One obstacle in the clarification of this problem will be the many syndrome definitions used in this field (Siggers and Polani, 1972).

Because the control group was fairly large, the high specificity found is more reliable. Previous reports indicate that patients with pulmonary stenosis occasionally may have a right axis deviation to more than 180 degrees (Scherlis, Koenker, and Lee, 1963; Tandon, Nadas, and Gross, 1965). Burch and DePasquale (1961) have described patients with pulmonary stenosis and atrial septal defects with a superior rightward axis. However, since these series may have included patients with the special phenotype under discussion, we elected to study a new series of control patients. Our conclusion is that the finding of the described electrocardiographic pattern in a subject with probable pulmonary stenosis warrants a close search for the other features of the Turner phenotype syndrome. During the same period as the 7 patients were observed, about 100 children with pulmonary stenosis were seen in our hospital, giving a proportion of about 7 per cent. This is in good agreement with the figures of Celermajer *et al.* (1968).

The high specificity will, however, also be reduced when all other kinds of heart disease are considered. Several types of congenital heart disease, including tetralogy of Fallot, transposition of the great arteries, and AV septal defects, may have a frontal QRS axis between 180 and 270 degrees (Martins de Oliveira *et al.*, 1959; Ayala y de Landero *et al.*, 1959). Transpositions do also frequently have small initial inferior and leftward forces, giving a pattern very similar to that described here. However, these patients can usually be differentiated clinically from

those with Ullrich–Turner phenotype and pulmonary stenosis. AV septal defects can be separated from the presently described subjects by means of the more superiorly oriented QRS axis (around 270 degrees), the larger initial leftward forces, and the constant counterclockwise rotation of the frontal QRS loop.

The second practical implication is that the commonly applied and usually highly reliable electrocardiographic and vectorcardiographic criteria for evaluating the degree of pulmonary stenosis cannot be used in this group (Strang *et al.*, 1963; Scherlis *et al.*, 1963; Witham, Rainey, and Edmonds, 1968; Gamboa, Hugenholtz, and Nadas, 1966). If criteria based on loss of leftward and increase in rightward forces (S in lead I and V6, R in lead I and V6, R in lead aVR and maximal rightward spatial vector) are used, right ventricular systolic pressure can be seriously overestimated. Correspondingly, the use of anterior-posterior force relation (R or R/S V1–2, maximal anterior or posterior vectors) may lead to serious underestimation of pressure. The latter situation is perhaps the most common (Noonan, 1968).

During the past years several successful efforts have been made to correlate electrocardiogram and vectorcardiogram with haemodynamic data in pulmonary stenosis (Witham *et al.*, 1968; Gamboa *et al.*, 1966). Patients with the presently described atypical pattern obviously represent one source of persisting variation in such studies. Improved correlations may be expected when these patients are treated as a separate entity.

The aetiology of the disturbance of ventricular depolarization is unknown and will remain so until anatomical and electrophysiological data from these patients have been presented. Recently, Ehlers *et al.* (1972) have reported eccentric ventricular hypertrophy with an abnormal left ventricle in patients with the Ullrich–Turner phenotype. Three of their 5 subjects with pulmonary stenosis had this hypertrophy and in all of them a superior QRS axis was found. In our case with a discrete infundibular stenosis the left ventricle was divided in two by a muscular ridge. In the other 6 no definite left ventricular abnormalities were found. It is also difficult to understand how left-sided eccentric hypertrophy alone may explain the genesis of this profound disturbance of depolarization. As also suggested by Ehlers *et al.* (1972), another possible cause is a specific disturbance of function or anatomy of the specialized conduction system, by analogy with the conduction system in AV defects. This may cause early depolarization of inferior-leftward parts of the heart with subsequent depolarization fronts moving up and rightwards.

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