

Dissection of the aorta in Turner's syndrome

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SUMMARY Three deaths from dissection of the aorta in a series of 157 adult women with Turner's syndrome are reported. These are greatly in excess of the numbers expected. None of the three patients had a coarctation of the aorta. One had aortic regurgitation but there was no reason to believe that the aorta in the other two patients had been subjected to unusual haemodynamic stresses. Cystic medial necrosis of the aorta was described in two patients on whom necropsies were carried out. It is concluded that there is probably a greatly increased risk of dissection of the aorta in Turner's syndrome even in the absence of any other abnormality of the aorta and aortic valve. Previously reported cases of aortic dissection in Turner's syndrome are discussed.

Dissection of the aorta is not a widely recognised complication of Turner's syndrome (TS), although it has been reported in at least seven patients.¹⁻⁷ In all but two of these⁴⁻⁷ there was an associated coarctation of the aorta. In this paper we describe three TS patients who died from dissection of the aorta but who had no evidence of coarctation.

Study population and case reports

The deaths occurred among 157 adult women with TS who have been observed for an average of 13 years. During that time 13 have died. The 157 patients had been reported to the Edinburgh MRC Cytogenetics Registry since 1959. They all had the clinical features of TS and the following chromosome abnormalities: 45,X (83); 46,XiXq (12); 45,X/46,XiXq (19); 45,X/46,XY (13); 46,XdelX(p) (5); 45,X/46,X+r (7); 45,X/46,XmarX (4); 45,X/46,XrX

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(5); other mosaics (9). A breakdown of years at risk by 10-year age periods and the number of deaths are shown in the table. In addition to the three patients described in this paper, a fourth who had a coarctation died from dissection of the aorta.

CASE 1 (2/62)

This patient was born in Scotland on 5.9.42. Redundant folds of skin were noted at birth and excised at the age of 11 years. She suffered from pneumonia at the age of 5 years and was investigated for primary amenorrhoea at the age of 20 years. Nuclear sex chromatin was negative and chromosome analysis of peripheral leucocytes showed 45,X. At laparotomy, no ovarian tissue was found. The patient was seen again shortly after she married aged 29 years. She was 132 cm in height and weighed 41 kg. Her sitting height was 72.5 cm and span was 138.5 cm. She still had webbing of the neck, the nipples were widely spaced, and the breasts under-

TABLE Years at risk and deaths from dissection of the aorta in 157 adult patients with Turner's syndrome, and mortality from aortic dissection per 100 000 of the Scottish female population.

	Age group						
	15-24	25-34	35-44	45-54	55-64	65-74	75+
Years at risk for 157 TS patients	676	768	318	112	19	10	0
Deaths from dissection of the aorta	1*	1	2	0	0	0	0
Approximate annual mortality rate per 100 000 of Scottish female population	0.5	0.3	1.3	3	13	27	48

*This patient also had coarctation of the aorta.

developed. The external genitalia were prepubertal and the growth of pubic hair sparse. Her IQ (WAIS full scale) was 85. Her blood pressure was 107/73 mmHg and no cardiovascular abnormality was detected. Chest x-ray and electrocardiogram were both normal. An intravenous urogram showed a horseshoe kidney with a duplex pelvis on one side. She was started on oestrogen replacement therapy with cyclical ethinyloestradiol. She remained well until 14.10.81 when she suddenly developed a severe retrosternal pain when walking up stairs. It was accompanied by light-headedness and paraesthesiae in the hands. The pain lasted for 20 minutes and was followed by a persistent dull ache. She was admitted to hospital with a suspected myocardial infarction but an ECG was normal. She died suddenly 2 days later. At necropsy there was a dissection of the aorta which had ruptured into the pericardial sac. The dissection between the adventitia and media extended over the arch to the lower thoracic aorta and along the left carotid artery as far as the bifurcation. There was a tear in the intima encircling the aorta 3 cm above and parallel to the aortic valve ring. There was puckering of the intima at the level of the ductus arteriosus but no coarctation of the aorta.

CASE 2 (40/62)

This patient was born in Scotland on 10.1.36. She presented at the age of 26 years with primary amenorrhoea and failure to develop secondary sexual characteristics. She was unmarried and worked as a cotton mill machine operator. The nuclear sex was chromatin negative and the karyotype of peripheral leucocytes was 45,X. A diagnosis of gonadal dysgenesis and TS was made and no further investigations were carried out. Replacement therapy was not instituted. At the age of 36 years she was 141 cm in height and weighed 60.5 kg. Her sitting height was 77 cm and span was 143 cm. There was webbing of the neck, the nipples were widely spaced, and the breasts underdeveloped. The external genitalia were prepubertal. The blood pressure was 160/91-73 mmHg. She had bilateral lymphoedema, the JVP was normal, the cardiac impulse was normal, and the apex beat was not displaced. The first and second heart sounds were normal but there was a loud early diastolic murmur at the left sternal edge. There was no radiofemoral delay and the peripheral pulses were normal. The chest x-ray and electrocardiogram were normal.

Two years later she complained of shortness of breath and she had clinical and ECG evidence of left ventricular hypertrophy. Left heart catheterisation and coronary angiography were carried out. These showed a marked degree of aortic regurgitation

and dilation of the ascending aorta. There was no coarctation. Aortic valve replacement was recommended but while awaiting surgery she was readmitted to hospital with a history of retrosternal chest pain. A diagnosis of myocardial infarction was suspected but the ECG was normal and there was no change in serial cardiac enzyme levels. Four days after admission to hospital she complained of left sided pleuritic chest pain and developed clinical and radiological evidence of a left sided pleural effusion. Twenty-four hours later she again complained of severe pain in her chest and in her legs and rapidly lost consciousness. A clinical diagnosis of dissection of the aorta was made and she died after unsuccessful attempts at resuscitation. Permission for necropsy was refused.

CASE 3 (98/65)

This patient was born in England on 22.9.45. At the age of 20 years she was referred to hospital with a history of primary amenorrhoea, failure of development of secondary sexual characteristics, and swelling of the left foot of 3 months' duration. She was 145 cm in height and weighed 69.5 kg. Her sitting height was 76 cm and span was 147.5 cm. She had a low nuchal hairline, no neck webbing, and only very slight breast development. Nipples were infantile and external genitalia prepubertal. Her IQ was 69. The blood pressure was 114/76 mmHg and no cardiovascular abnormality was detected. A chest x-ray and electrocardiogram were normal. Nuclear sex was chromatin negative and the karyotype of peripheral leucocytes and skin fibroblasts showed the presence of two cell lines. The majority of cells had a 45,X karyotype but between 10 and 20% of cells, while lacking a medium sized chromosome, had a small ring chromosome. It was not possible to decide whether the ring was derived from X or Y chromosome material. Hormone replacement therapy was not instituted. She subsequently remained well but was found dead in bed at the age of 30 years. Following a necropsy and a coroner's inquest death was attributed to a haemopericardium, owing to a dissecting aneurysm of the aorta, due to Erdheim's medial necrosis.

Discussion

The mortality each year from dissection of the aorta among Scottish women aged 15 to 55 years is of the order of 1 to 2 per 100 000. It is very improbable, therefore, that three deaths from dissection of the aorta among 157 women with TS in this age group have occurred by chance. Also there are at least seven previously reported cases. It is true that five of these had an associated coarctation of the aorta, an

anomaly that is not uncommon in TS and one that is not infrequently complicated by dissection.⁸ However, only three of these had a haemodynamically significant coarctation²⁻⁴ and none of the three women described in this paper had any evidence of coarctation. Dissection of the aorta appears, therefore, to be a particular hazard for TS patients and although the risk is probably accentuated by coarctation it is greatly increased even when the aorta appears normal beforehand. The immediate cause of dissection of the aorta in young people is often cystic medial necrosis.⁹ This histological appearance has been described in at least four of the previously reported cases^{1 3-5} and in two of the patients described in this paper. Cystic medial necrosis may also be associated with the condition of bicuspid aortic valve which was noted in three of the reported TS cases,³⁻⁵ and with aortic dilation and regurgitation.¹⁰ In two of our patients and in at least one of the reported cases⁷ there was no evidence of either an aortic coarctation or of an aortic valve abnormality. Systemic hypertension was noted in four of the reported cases,^{2 5-7} but was not recorded in any of the three patients described in this paper.

In Marfan's syndrome (MS) and Ehlers-Danlos syndrome (EDS), both of which have a greatly increased risk of dissection of the aorta usually attributed to degenerative changes in the aortic wall,¹¹ the underlying defect is believed to be a disorder of collagen biosynthesis.¹² Attention was drawn to similarities between EDS and TS as long ago as 1951 by Rossi and Cafilisch¹³ and Rossi and Angst,¹⁴ but we know of no report of a collagen abnormality in TS.

An increased risk of dissection renders TS patients more than usually susceptible to the abnormal haemodynamic stresses of aortic valve disorder and coarctation. It would seem advisable, therefore, to intervene promptly and perhaps earlier than might otherwise seem necessary to correct such abnormalities. Regular monitoring of the diameters of the aortic root in TS patients would also seem a reasonable precaution.

We are grateful to numerous consultants and general practitioners who have referred patients with Turner's syndrome to the Edinburgh MRC Unit

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susceptibility to a particular disorder. The data presented here on PGM and tuberculosis lead one to suspect that discovery of true associations of gene markers and disease must await establishment of more refined techniques of gene identification, such as that of isoelectric focusing used here or of DNA probes currently in process of development.

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Correction

In the paper by Price and Wilson on "Dissection of the aorta in Turner's syndrome" which was published in the February 1983 issue of the Journal (20:61-3), the last sentence of the first column on the first page should have read: "They all had the clinical features of TS and the following chromosome abnormalities: 45,X (83); 46,X,i(Xq) (12); 45,X/46,X,i(Xq) (19); 45,X/46,XY (13); 46,X,del(X)(p) (5); 45,X/46,X,+r (7); 45,X/46,X,mar(X) (4); 45,X/46,X,r(X) (5); other mosaics (9)".