The iris in Williams syndrome

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Abstract

Forty three children with Williams syndrome and 124 control subjects had their eyes photographed. The photographs were examined by three ophthalmologists and four geneticists of varying experience. A stellate pattern was noted more often in the irides of patients with Williams syndrome (51%) than in those of the control subjects (12%), and was more difficult to detect, or was absent, in heavily pigmented irides. We conclude that the stellate pattern is of diagnostic importance, particularly if the pattern is carefully defined and the clinician is experienced.

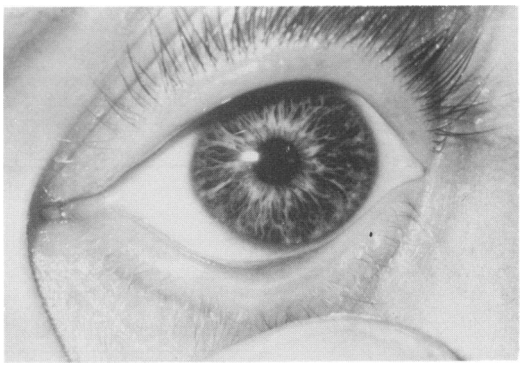

Figure 1 Stellate pattern of iris in a patient with Williams syndrome.

In 1961 Williams *et al* described a syndrome that included mental deficiency, characteristic elfin facies, and supravalvular aortic stenosis.[1] The same syndrome was also described by Beuren *et al* in 1962; they included peripheral pulmonary stenosis and dental anomalies among the features.[2] Further reports in 1963 noted the association with infantile hypercalcaemia and the phenotype has gradually been expanded.[3 4] Given the variability of the clinical picture the diagnosis can be difficult, and no single feature must always be present.

The most characteristic features of Williams syndrome are early feeding difficulties, mild growth retardation and mental deficiency, friendly and outgoing personality, hoarse voice, small widespaced teeth, and variable cardiovascular anomalies, usually including supravalvular aortic stenosis. The facies are characterised by malar flattening, full cheeks and lips with open mouth, long philtrum, depressed nasal bridge, short palpebral fissures, periorbital fullness, and epicanthic folds.[5]

Previous studies of ocular anomalies in Williams syndrome have described a characteristic pattern on the iris, strabismus, hypermetropia, and tortuousity of the retinal vessels.[6–9] The characteristic pattern (fig 1) has been described as 'stellate' or 'lacy and radial', and is thought to be caused by hypoplasia of the stroma of the iris.[10] A lateral displacement or absence of the anterior iris collarette has also been described.[9] Neither of these findings is pathognomonic for Williams syndrome and can be seen as normal variations in the general population, although the incidence of a stellate pattern in a normal population is unknown.

Most reports of Williams syndrome describe a stellate pattern of the iris as a characteristic sign. Incidences of 69%,[9] 74%,[6] and even 100% in a small group,[8] have been mentioned, and a high incidence of blue irides has also been reported—64%,[9] and 79%.[6] Williams noticed blue eyes in all four patients in his original report,[1] but did not mention any unusual pattern on the iris.

To find out if the iris has a characteristic colour in Williams syndrome patients the colour of irides in a normal population must be described. This was done in 1984 and 1986 by two groups of authors who examined 690 and 70 subjects, respectively; 55% were thought to have light irides and 45% dark irides.[11 12]

The intention of this study was to find out if a stellate pattern on the iris is a useful diagnostic marker in patients with Williams syndrome compared with a control group. We also wanted to compare the colours of irides of patients with Williams syndrome with those of the controls to see if we could correlate the stellate pattern with the colour of the irides.

Patients and methods

Through the parents' association of the Infantile Hypercalcaemia Foundation (Williams syndrome) we met 37 families with their children at their annual summer picnic in Hyde Park, London. We photographed each of their eyes separately. Another six children with Williams syndrome were photographed in our hospital, and so we obtained useful slides of 80 eyes. As a control group we took photographs of 124 children attending different clinics in the hospital, and of these 240 slides were useful.

All photographs were taken in the same way and by the same photographer (GA). A Nikon FM2 camera, with a Micro Nikkor 105 mm lens and a PN 11 extention ring, was used and gave a magnification on the film of 1:1. We used an Ektachrome 100 daylight balanced film and a portable, electronic Metz CT – 32 flash. For the photographs taken in Hyde Park we used a

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Table 1 Percentage of eyes showing stellate pattern in patients with Williams syndrome and in control subjects judged by seven observers

Observer	Stellate pattern in patients with Williams syndrome	Stellate pattern in control subjects	p Value	Unable to tell
1	64	1	<0·001	3
2	24	16	>0·05	14
3	28	6	<0·001	4
4	61	8	<0·001	15
5	59	25	<0·001	9
6	43	13	<0·001	15
7	80	16	<0·001	6
Mean (range)	51 (24–80)	12 (1–25)	<0·001	10 (3–15)

Table 2 Mean (range) percentage of eyes showing stellate pattern in patients with Williams syndrome and in control subjects as judged by experienced and less experienced observers

	Experienced observers (Nos 1 and 7)	Less experienced observers (Nos 2–6)
Stellate pattern in patients with Williams syndrome	72 (64–80)*	43 (24–61)**
Stellate pattern in control subjects	9 (1–16)*	14 (6–25)**
Unable to tell	5 (3–6)	11 (4–15)

*p<0·001; **p<0·001.

Table 3 Colour of irises in 43 patients with Williams syndrome and 124 control subjects

Colour group	Mean value of observers as percentage of patients with Williams syndrome	Mean value of observers as percentage of control subjects
1 (light blue)	12	23
2 (darker blue)	38	28
3 (green)	33	20
4 (light brown)	8	21
5 (dark brown)	9	8

black umbrella to exclude superfluous daylight. The power of the flash is such that any ambient light is completely negated, ensuring that the indoor and outdoor photographs are comparable.

The 320 slides were mixed and were shown in random order to seven observers, three ophthalmologists and four geneticists. The observers were asked to say 'yes' if they noticed a stellate pattern, 'no' if they did not, and 'do not know' if they were unable to give an answer. They were also asked to score the colour of the irides with the help of a five number scale: 1=light blue, 2=darker blue, 3=green, 4=light brown, and 5=dark brown.

Results

The results of the study are seen in table 1. The mean incidence of stellate patterns of the irides in patients with Williams syndrome was 51% (range 24–80) among the seven observers. The mean incidence of stellate patterns among the control subjects was 12% (range 1–25). The incidence of irides in which the observers were unable to tell varied between 3% and 15%, with a mean value of 10%. A χ^2 analysis was done to see if there were significantly more stellate patterns in the patients than in the control subjects. The results were significant ($p<0·001$) for all but one of the observers. There was a difference between 'experienced' and less experienced observers. The experienced clinicians found stellate patterns in 72% (range 64–80) of patients with Williams syndrome and in 9% (range 1–16) of the control subjects. The results for the less experienced were 43% (range 24–61) and 14% (range 6–25%), respectively (table 2).

We found great discrepancies among the observers concerning the colour scoring. The mean values among all the observers are shown in table 3. Of the patients with Williams syndrome, 50% were found to have blue irides (colour group 1 and 2) compared with 51% of those of the controls (table 3).

Discussion

There are problems in comparing the incidence of stellate patterns on the irides in patients with Williams syndrome in different studies as a definition of the pattern is difficult, and there are even greater problems in comparing the colour of the irides as objective definitions of the different colours vary from study to study. We did not find any significant differences in colour of the irides between patients and control subjects. There were, however, considerable problems with interobserver differences. It was also noted that the detection of a stellate iris pattern was much more difficult in dark irides than in light ones. Figure 1 shows a 'typical' stellate pattern on the iris of a patient with Williams syndrome. In fig 2, however, the features of the pattern are less obvious and thus more difficult for the observers to score.

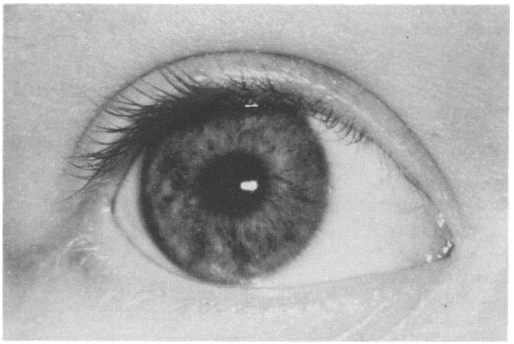

Figure 2 Iris of a patient with Williams syndrome in which features of the stellate pattern are less obvious.

The patterns on the irides in patients with Williams syndrome are described as stroma hypoplasia,[10] abnormality anterior to the iris,[6] and lateral displacement or absence of the iris collarette.[9] We believe that the irides in this syndrome are characterised by a normal pigmentary frill and a normal pupillary portion central to the collarette. There is variable peripheral displacement of the collarette, often giving it a sinous appearance, and peripheral to the collarette there are raised trabeculas anterior to the usual stroma of the iris. These trabeculas seem to be more radial than in normal irides and there are prominent crossings of the trabeculas. The far periphery of the iris seems normal.

We conclude that Williams syndrome does have a characteristic iris pattern that can be described as stellate, and which occurs in at least half of the patients. We believe that the stellate pattern is a sign of diagnostic importance provided that care is taken to define the features of the pattern accurately. Finally, increased clinical experience seems to make the stellate pattern of the iris a more useful tool in discriminating patients with Williams syndrome from a group of control subjects.

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