The Denys-Drash syndrome

R F Mueller

Drash et al. described two unrelated children who presented with ambiguous genitalia, both of whom had a unilateral Wilms’ tumour, and subsequently developed progressive renal failure. Denys et al. had previously described a child with male pseudohermaphroditism, Wilms’ tumour, and a nephropathy in association with sex chromosomal mosaicism. Review of published reports shows 150 cases of what has subsequently been called the Drash or, more correctly, the Denys-Drash syndrome.

Clinical features

GENITALIA
The classical presentation of the Denys-Drash syndrome is in the newborn period as a child with ambiguous genitalia. Although some of the cases of the Denys-Drash syndrome present with normal male external genitalia, the vast majority will appear phenotypically female or have ambiguous genitalia (table 1). The majority of cases of the Denys-Drash syndrome with any one of these three phenotypes of their external genitalia will have a normal male karyotype. The relative paucity of cases with a female karyotype may be because of underdiagnosis of the syndrome in phenotypic females with the nephropathy or as a result of underascertainment because of the previous poor survival of children with renal failure in infancy or early childhood.

The findings in the internal genitalia in the Denys-Drash syndrome are extremely variable (table 2). While the internal genitalia in some of the cases will be appropriate for their external genitalia, it is much more common for the internal genitalia to be inappropriate, that is, Wolffian structures to be present in a phenotypic female, or for both Müllerian and Wolffian structures to be present. In addition, the gonads are often dysgenic (streak gonads or immature, infantile, or rudimentary testicular tissue) or both testicular and ovarian tissue are present or inappropriate for the external genitalia and the chromosomal sex, that is, male pseudohermaphroditism or true hermaphroditism.

RENALE FEATURES
The renal involvement in the Denys-Drash syndrome is classically two fold; the development of a progressive nephropathy and Wilms’ tumour (table 3). The age of presentation of the nephropathy is usually in the first year. The nephropathy is a primary feature as part of the syndrome and not secondary to other mechanisms as previously suggested, such as

<table>
<thead>
<tr>
<th>Table 1</th>
<th>External genitalia findings and chromosomes in the Denys-Drash syndrome</th>
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<tbody>
<tr>
<td>External genitalia</td>
<td>Chromosomes</td>
</tr>
<tr>
<td>Male (19-150)</td>
<td>46,XY 7.19</td>
</tr>
<tr>
<td>Female (65-150)</td>
<td>46,XX 1.19</td>
</tr>
<tr>
<td>ND</td>
<td>1.65</td>
</tr>
<tr>
<td>Female (50)</td>
<td>46,XY 25.63</td>
</tr>
<tr>
<td>ND</td>
<td>1.65</td>
</tr>
<tr>
<td>Ambiguous (65-150)</td>
<td>46,XY 42.65</td>
</tr>
<tr>
<td>ND</td>
<td>1.65</td>
</tr>
<tr>
<td>ND</td>
<td>1.65</td>
</tr>
</tbody>
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Table 1: External genitalia findings and chromosomes in the Denys-Drash syndrome.

<table>
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<tr>
<th>Table 2</th>
<th>Internal genitalia findings in the Denys-Drash syndrome</th>
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<tr>
<td>External genitalia</td>
<td>Internal genitalia</td>
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<tr>
<td>Male (19-19)</td>
<td></td>
</tr>
<tr>
<td>Female (65-73)</td>
<td></td>
</tr>
<tr>
<td>Ambiguous (62-65)</td>
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</table>

Table 2: Internal genitalia findings in the Denys-Drash syndrome.

* Dysgenic includes immature, infantile, rudimentary, and dysgenic testes, ovotestis, and fibrous streak.
> no details, W = Wolffian derived structures, M = Müllerian derived structures, W+M = both, N = neither present.
= not reported.
irradiation to normal kidneys, haemodynamic injury, or hyperfiltration after nephrectomy. If the nephropathy is absent, one might consider the diagnosis of the WAGR syndrome (see below). If, however, the external genitalia are female and the internal genitalia consist of both Müllerian and Wolffian derived structures, or if there are male chromosomes, one can be certain of the diagnosis of the Denys-Drash syndrome.

Renal biopsy typically shows mesangial sclerosis which is classically diffuse but can be focal and is characterised by an expanded fibrillar increase in the mesangial matrix, an increase in the mesangial cells of the glomeruli with hypertrophied vacuolised podocytes, thickened glomerular capillary basement membranes, dilated tubules, often containing hyaline casts, with tubulointerstitial infiltrate and fibrosis. 47-48 (figs 1 and 2).

The Wilms' tumour frequently presents as an abdominal mass, but often presents concurrently in a confounding manner with the nephropathy owing to the similar age of onset. It is important to follow up children presenting with apparently isolated Wilms' tumour, especially if there are any abnormalities of the external genitalia, for the possibility of the nephropathy. 42 In the cases with unilateral Wilms' tumour for which information was available, the tumour occurred slightly more frequently on the right.

Not all cases of the Denys-Drash syndrome reported developed a Wilms' tumour. This can be accounted for, in part, by the age of onset of the nephropathy and progression to end stage renal failure in the first year, often before renal dialysis and transplantation was generally available in this age group. The diagnosis of the Denys-Dash syndrome will not be obvious in cases of Wilms' tumour with normal female external genitalia but if the internal genitalia include Wolffian derived structures or dysgenic gonads or both, especially with male chromosomes, one can be certain of the diagnosis of the Denys-Drash syndrome.

GONADAL MALIGNANIES (TABLE 4)
Six of the children with the Denys-Drash syndrome have developed gonadoblastoma. 29,35,41,51 In four of these the gonadoblastoma was bilateral. In addition, two of the cases with bilateral gonadoblastoma had an unilateral juvenile granulosa cell tumour. The risk for development of gonadal malignancies overlaps with the Frasier syndrome (see below).

Associated findings
There are other physical findings in a number of case reports, some of which are almost certainly incidental (for example, myotonia), others probably being part of the syndrome (for example, structural renal abnormalities) (table 5).

Natural history
For the cases where there is information available, just less than one third were alive at the time of the report, with a range from 3 months to 21 years (table 6). Of those who died, the average age of death was 2 years, with a range from 1 month to just over 7 years. The primary cause of death was renal failure owing to the

<table>
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<td>Gonadal malignancies</td>
</tr>
<tr>
<td>Type</td>
</tr>
<tr>
<td>Gonadoblastoma</td>
</tr>
<tr>
<td>Bilateral</td>
</tr>
<tr>
<td>Unilateral</td>
</tr>
<tr>
<td>JGCT*</td>
</tr>
<tr>
<td>Unilateral</td>
</tr>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Range</td>
</tr>
<tr>
<td>Average</td>
</tr>
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* JGCT = juvenile granulosa cell tumour.
The Denys-Drash syndrome

Table 5  Associated findings in the Denys-Drash syndrome

<table>
<thead>
<tr>
<th>Type</th>
<th>No</th>
<th>Ref</th>
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<tr>
<td>Renal</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unilateral hyronephrosis</td>
<td>12</td>
<td></td>
</tr>
<tr>
<td>Duplication renal pelvis/ureters</td>
<td>23</td>
<td></td>
</tr>
<tr>
<td>Double left kidney</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Horseshoe kidney</td>
<td>16</td>
<td></td>
</tr>
<tr>
<td>Cardiac</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ventricular septal defect</td>
<td>21</td>
<td></td>
</tr>
<tr>
<td>Miscellaneous isolated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intestinal hernia</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>Monorchyous twins</td>
<td>14</td>
<td></td>
</tr>
<tr>
<td>Contracures</td>
<td>15</td>
<td></td>
</tr>
<tr>
<td>Androgen receptor abnormality</td>
<td>40</td>
<td></td>
</tr>
<tr>
<td>Sensory/motor deafness</td>
<td>41</td>
<td></td>
</tr>
<tr>
<td>Congenital nystagmus</td>
<td>42</td>
<td></td>
</tr>
<tr>
<td>Multiple</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cleft palate, mental retardation, nystagmus</td>
<td>43</td>
<td></td>
</tr>
<tr>
<td>Aniridia, mental retardation (del 11p13)</td>
<td>44</td>
<td></td>
</tr>
<tr>
<td>Cerebral atrophy, mental retardation, chronic bronchiotic, low IgG</td>
<td>45</td>
<td></td>
</tr>
<tr>
<td>Craniosynostosis, mental retardation, horseshoe kidney</td>
<td>46</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>15/150 (10%)</td>
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</table>

nephropathy. It is likely that the prognosis for children with the Denys-Drash syndrome will improve because of increasing availability of renal transplantation.

Management

The management of children with the Denys-Drash syndrome can be likened to “walking a multidimensional tight rope”. Monitoring for the progressive nature of the nephropathy is essential. Treatment of renal failure is often determined by the practical difficulties of offering peritoneal dialysis, haemodialysis, or renal transplantation in infancy or early childhood.

Bilateral nephrectomy for children with end stage renal failure owing to the Denys-Drash syndrome has been suggested to obviate the risk of developing Wilms’ tumour. More recently it has been suggested that, in children with the syndrome who are hypertensive at the time of instituting dialysis, unilateral nephrectomy should be carried out with the second kidney being removed at the time of transplantation. If the child is not hypertensive, ipsilateral nephrectomy should be carried out at the time of transplantation, screening the remaining kidney with six monthly ultrasound.69

Owing to the possible associated risk of gonadal malignancy in some of the cases of the Denys-Drash syndrome, elective gonadectomy should be seriously considered as an option because of the difficulty in effective screening for gonadal malignancies. This is important to keep in mind in the future with the likelihood of improved long term survival as a result of the increasing availability of renal transplantation in the younger child.

Differential diagnosis

WAGR SYNDROME

There is phenotypic overlap with Wilms’ tumour in association with aniridia, genito-urinary abnormalities, and mental retardation (the WAGR syndrome)?-73 as evidenced by the occurrence of aniridia and mental retardation in one of the cases with the Denys-Drash syndrome.46 The diagnosis can be difficult in the cases with abnormalities of the external genitalia in association with a Wilms’ tumour but without the nephropathy, as previously mentioned.

FRASIER SYNDROME

Frasier et al.47 reported a pair of female monozygous twins, one of whom presented with abdominal pain and was subsequently found to have streak gonads with a teratoma, and went on to develop chronic renal failure. Her twin was also found to have streak gonads with a gonadoblastoma in situ. Both twins had a normal male karyotype. Moorthy et al.26 suggested that this and subsequent similar reports48-53 represented a separate syndrome, the Frasier syndrome. The nephropathy is similar to that seen in patients with the Denys-Drash syndrome but is usually of a later age of onset.

The reports of occasional gonadal malignancies in a small proportion of the case reports of the Denys-Drash syndrome (see above) suggest that if patients with the Denys-Drash syndrome survive long enough they could be at risk of developing a gonadal malignancy.

NEPHROTIC SYNDROME IN THE FIRST YEAR OF LIFE

In children presenting with nephrotic syndrome in the first year of life, one should consider in the differential diagnosis congenital nephropathy of the Finnish type, idiopathic nephrosis, diffuse mesangial proliferation, minimal change or focal segmental sclerosis, and isolated diffuse mesangial sclerosis.64-66

DIFFUSE MESANGIAL SCHLEORSIS

Isolated diffuse mesangial sclerosis occurs as a possible autosomal recessive disorder on the basis of a report of five affected persons in an Arab-Israeli family. In addition, it has been reported in a male and female sib pair with associated ocular findings, consisting of nystagmus and absent foveal reflection in the male with mental retardation, while his sister had nystagmus, bilateral optic atrophy, and abnormal maculae.85
Aetiology and genetics

The Denys-Drash syndrome usually occurs sporadically. There are, however, reports of one affected male and female sib pair as well as an affected male twin pair.22

The demonstration of constitutional deletions of 11p13 as the smallest region of overlap in persons with the WAGR syndrome, and the loss of constitutional heterozygosity of this region, led to the isolation of candidate cDNA sequences and the tumour suppressor gene, WT1, and identification of mutations within it being responsible for the development of Wilms' tumour.86-89

The WT1 gene has 10 exons producing four distinct mRNAs owing to two alternative splice sites in exons 5 and 9 encoding a protein of 45–49 kDa, with features including nuclear localisation, four contiguous Cys–His, zinc finger domains, and an amino-terminus rich in proline and glutamine, suggestive of its function as a DNA binding protein.90 The zinc finger domains of the WT1 polypeptide are active during the G, to G, transition of the cell cycle in cultured cells. The WT1 gene also shows considerable homology to and recognises similar binding sites to the epidermal growth receptor and the Krox family, which are important nuclear intermediates in signal transduction expression.90

The WT1 gene is expressed during nephrogenesis in condensed renal mesenchyme, specifically the renal vesicle, and glomerular epithelial cells and would therefore appear to have a role in glomerular development during kidney organogenesis.91 In addition, high levels of WT1 mRNA expression are observed in developing gonads in early fetal development. In mature gonads, WT1 expression is restricted to the Sertoli cells of testes and granulosa and epithelial cells of ovaries.91 These findings made the WT1 gene an obvious candidate gene for the Denys-Drash syndrome.

<table>
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<tr>
<th>Author</th>
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<th>Location</th>
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<tr>
<td>Pelletier et al91</td>
<td>C to T missense transition G to A missense transition G to A missense transition G to A missense transition</td>
<td>Arg to Trp Exon 9–Zn finger III Arg to Gly Exon 9–Zn finger III Asp to Asn Exon 9–Zn finger III Arg to His Exon 8–Zn finger II</td>
<td>7</td>
</tr>
<tr>
<td>Bruening et al92</td>
<td>C to T missense transition G to A missense transition G to A missense transition G to C missense to transversion C to T missense transition C to T missense transition</td>
<td>Arg to Trp Exon 9–Zn finger III + 5 of splice donor site within intron 9 Cys to Tyr Exon 7–Zn finger I Arg to Pro Exon 9–Zn finger III Arg to Trp Exon 9–Zn finger III</td>
<td>1</td>
</tr>
<tr>
<td>Coppes et al93</td>
<td>C to T missense transition C to T missense transition C to T missense transition</td>
<td>His to Tyr exon 8–Zn finger II</td>
<td>1</td>
</tr>
<tr>
<td>Baird et al94</td>
<td>C to T missense transition G to A missense transition G to A missense transition G insertion generates stop codon C to T missense transition</td>
<td>Arg to Trp Exon 9–Zn finger III Asp to Asn Exon 9–Zn finger III Arg to His Exon 8–Zn finger II</td>
<td>3</td>
</tr>
<tr>
<td>Poulak et al95</td>
<td>C to T missense transition G to A missense transition</td>
<td>Arg to Trp Exon 9–Zn finger III</td>
<td>1</td>
</tr>
<tr>
<td>Little et al96</td>
<td>C to T missense transition G to A missense transition C to T missense transition C to T missense transition</td>
<td>Arg to Trp Exon 9–Zn finger III Asp to Asn Exon 9–Zn finger III Arg to Stop Exon 9–Zn finger II His to Cys Exon 8–Zn finger II</td>
<td>1</td>
</tr>
<tr>
<td>Ogawa et al97</td>
<td>A insertion Generates stop codon</td>
<td>Position 1534</td>
<td>1</td>
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<td>Konig et al98</td>
<td>C to T missense transition G to A missense transition C to T missense transition C to T missense transition G to A missense transition</td>
<td>Arg to Trp Exon 9–Zn finger III Cys to Gly Exon 8–Zn finger II Arg to Stop Exon 9–Zn finger II Cys to Tyr Exon 8–Zn finger II</td>
<td>2</td>
</tr>
<tr>
<td>Sakai et al99</td>
<td>C to T missense transition G to A missense transition</td>
<td>Arg to Trp Exon 9–Zn finger III Cys to Tyr Exon 8–Zn finger II</td>
<td>1</td>
</tr>
<tr>
<td>Clarkson et al100</td>
<td>C to T missense transition G to A missense transition</td>
<td>Cys to Tyr Exon 9–Zn finger II</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 7** Findings in the WT1 gene in the Denys-Drash syndrome

**TYPES OF MUTATION**

All of the constitutional mutations so far reported in the Denys-Drash syndrome have been near or within the zinc finger coding region of the WT1 gene51 54 55 57 59 64–68 (table 7). The same C to T transition missense mutation at amino acid 394 in exon 9 involving the third zinc finger of the WT1 gene has been reported in 17 of the 34 cases of the Denys-Drash syndrome in which a molecular defect has been identified.

The G to A transition at + 5 of the splice donor site within intron 9 is the only other mutation reported more than once in the Denys-Drash syndrome.54 62 This mutation would prevent the production of WT1 isoforms containing exon 9.

A further five have mutations within exon 9 affecting zinc finger III, seven have mutations within exon 8 affecting zinc finger II, and one each have mutations in exons 7 and 6; the former would affect zinc finger I. The latter mutation generates a premature stop codon owing to a frameshift which would result in a gene product without any of the zinc fingers. The adenosine insertion in exon 9 reported would result in an altered reading frame leading to an abnormal proline rich C-terminus of zinc finger III and a truncated gene product missing zinc finger IV owing to generation of a premature stop codon.61

Although 22 of the 34 mutations so far identified occur in exon 9 suggesting that mutations in the third zinc finger may be a "hot spot" for mutations leading to the Denys-Drash phenotype,10 there is no consistent pattern to the mutations reported in the Denys-Drash syndrome. There is, however, marked variation in the phenotypic features seen in the case reports with the most common
mutation, and the same mutation in tumour and constitutional DNA has been reported in a female with isolated Wilms' tumour without any genitourinary abnormalities. In addition, a variety of mutations in the WT1 gene have been reported in patients with isolated Wilms' tumour or with associated genital abnormalities, including deletions of the whole WT1 gene. The means by which mutations in the WT1 gene result in the phenotypic findings seen in the Denys-Drash syndrome could involve the role of the WT1 gene product as a DNA binding protein. Loss of the zinc fingers through generation of premature stop codons or alteration of their function through mutations within the zinc fingers would alter the DNA binding function of the WT1 gene product. It has been suggested that the development of Wilms' tumour occurs through the mechanism of a dominant gain of function or “dominant negative mutation”. While it has also been suggested that the renal and genital abnormalities may be the result of a change of function of the WT1 gene product. Alternatively, mutations involving the splice sites would result in alternative splicing of the WT1 gene producing an altered differential expression of the WT1 isoforms.

Suggestions that mutations in the WT1 gene may be responsible for other syndromes or developmental abnormalities have not been borne out by reports to date. Analysis of the WT1 gene in three patients with Frasier syndrome showed no evidence of any mutations in exon 9, although mutations elsewhere in the WT1 gene cannot be excluded. Analysis of the WT1 gene in 12 males with isolated genital abnormalities showed no evidence of mutations although, again, the techniques used for mutational identification cannot exclude the possibility of a mutation being responsible for isolated genital abnormalities. PARENTS Analysis of the WT1 gene in 27 parents of 14 cases showed no evidence of the mutation present in their offspring suggesting that in the majority of instances the Denys-Drash syndrome arises as a new mutation. The father of one case, although phenotypically normal, was shown to be constitutionally heterozygous for the same mutation as his affected child. This latter observation could be either because the father was a somatic mosaic for the mutation, or because of reduced penetrance of the WT1 gene or genomic imprinting. The latter explanation is unlikely as the WT1 gene has been shown to exhibit similar expression with both maternal and paternal transmission. TUMOUR FINDINGS Analysis of DNA from the Wilms' tumours from four of the cases showed that they were heterozygous for the same mutation identified constitutionally. In three of the patients with the Denys-Drash syndrome, analysis of the tumours showed loss of the normal WT1 allele and the tumours from two of the other cases were homozygous for the constitutional mutation.
31 Koyanagi T, Hirasa M, Taniguchi K, et al. Wilms tumor and nephrotic syndrome in male pseudohermaphrodi-
32 Kofuku A, Hansen MF, Lampkin BC, et al. Loss of alleles at loci on human chromosome 11 during genesis of
Wilms' tumor. Nature 1984;309:170-1. WTI, in males with genetic abnor-
33 Laitinen T. The pathogenesis of congenital nephrotic
34 Laforce RF. Wilms' tumor and nephrotic syndrome. Arch
35 Laforce RF, McCallum J, McLean C, et al. Further evidence of
Wilms' tumor in males with congenital nephrotic syn-
36 Laborit H. Tumor nephritis of the first year of life.
Cancer Res 1964;24:1547-51.
37 Lafontaine JL. Syndrome of Wilms' tumor in infants and
38 Lai T, Wright PA, Poston WS, et al. Variable expression of
the WT1 gene in patients with Wilms' tumor. Am J Med
39 Lai T, Wright PA, Poston WS, et al. Variable expression of
the WT1 gene in patients with Wilms' tumor. Am J Med
40 Lai T, Wright PA, Poston WS, et al. Variable expression of
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The Denys-Drash syndrome


