Case reports

Many large and smaller arteries in the body, particularly the arcuate vessels in the kidney, the coronary arteries, the aorta, and the carotid vessels, showed intimal thickening. In the aorta, the elastic tissue was somewhat fragmented. In a section through a costochondral junction the growing zone was absent and the bony trabeculae thickened. Samples of muscle showed atrophy and partial replacement by fat. In the skin of the scalp, the hair follicles appeared to be in the resting phase, with little evidence of new hair shaft formation. The epidermis itself seemed inactive. The pituitary gland had a large posterior lobe with mucous inclusions.

In the brain, the layering of the cerebral cortex was normal. The white matter was diminished and the corpus callosum was thin and poorly myelinated. The lateral geniculate bodies were severely hypoplastic and the optic radiations virtually absent. The cerebellar cortex was severely hypoplastic (Fig. 3), showing thinning of the molecular layer and a very sparsely populated granule cell layer. The Purkinje cells were best preserved but were frequently displaced out of line and displayed occasional dendritic stars and axonal torpedoes. The inferior olives were normal. The central grey masses in the cerebrum and cerebellum were normally formed. The pyramidal tracts in the brainstem and spinal cord were small and poorly myelinated. A striking feature in the cerebrum and cerebellum was extensive calcification. This was patchy and involved capillaries, the walls of the larger arteries within the brain, and interstitial tissues. The larger arteries often showed narrowing or occlusion of the lumen by fibrous tissue. However, no infarcts had occurred. The calcific deposits were present in cerebrum and cerebellum and were particularly heavy, though in a patchy fashion, in the basal ganglia, cerebellar cortex, and dentate nucleus. In the eyes, the retinae were severely atrophic and disorganised.

Discussion

Microcephaly with atrophy of the cerebellar cortex may occur in several conditions. It is the significant lesion in viral diseases such as feline panleucopenia and rat virus infections but may also be a nonspecific finding resulting from unknown causes. Some of the features present in this girl have been reported in Cockayne’s syndrome, such as dwarfism, kyphosis, microcephaly with atrophy of the cerebellar granule cell layer, retinitis pigmentosa, prognathism of the maxilla, beaked nose, and atrophy of the ovaries. However, other features are quite different. For example, Cockayne’s dwarfs never look so bizarre, do not show symptoms until 6 months of age, and survive for decades. Indeed, a comparison of the present case with some of those available in the published reports (Moossy, 1967) emphasises the differences. We feel, therefore, that one is justified in continuing to recognise the present patient and her brother as having a distinct disease entity, possibly of genetic origin.

We owe the clinical details to Drs B. R. Lowry and B. Tischler. Dr J. Rootman opened the eyes.

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Late discovery of a case of testicular feminisation

SUMMARY The accidental discovery, in an inguinal hernia, of a male gonad in a 67-year-old woman is reported. The association of an unambiguous female phenotype with a purely male karyotype and a male gonad suggests the diagnosis of testicular feminisation. The differential diagnosis, particularly of testicular feminisation with true hermaphroditism, is discussed.

The accidental discovery of a testis during an inguinal hernia repair in a phenotypically female patient raised the differential diagnosis between true hermaphroditism, mixed gonadal dysgenesis, and testicular feminisation. The case is further unusual by its late discovery at the age of 67 years.

Case report

This 67-year-old woman had been raised as a girl. Her phenotype was female without ambivalence of her external genitalia. At age 22, she had consulted a
gynaecologist for primary amenorrhoea and was told she had no uterus and could, therefore, have no children. This prompted her to remain single, but did not keep her from experiencing a normal sexual life as a woman. She was the second of five children, and was born when her father was 25 and her mother 27 years old. There was no family history of sexual ambivalence or sterility. Her two brothers were married and had three and two children, respectively. One sister, who menstruated normally, was divorced soon after marriage and had no children. Another sister died, unmarried, of tuberculosis at the age of 26. The proposita is the only survivor of the family. At the age of 55, she again consulted a gynaecologist who stated absent axillary and scanty pubic hair, impalpable mammary glands in otherwise well-developed breasts, and a short vagina.

At the age of 67, while repairing a right inguinal hernia, the surgeon found a mass in the hernia sac, apparently attached to the round ligament. On palpation, a similar but smaller mass was felt in the opposite inguinal canal.

Examination of the excised multinodular mass, weighing 55 g, showed it to be composed of testicular tissue and of smooth muscle with a cystic area lined with somewhat papillary, cubic epithelium. The testis was of the fetal type, with normally structured but small seminiferous tubules, lined with immature Sertoli cells (Fig. 1). Spermatogonia were totally lacking. The interstitium contained numerous Leydig cells without Reinke crystals. Testicular tissue was found in several separate nodules. One nodule resembled ovarian stroma, but contained no follicular cells or any corpora albicantia (Fig. 2). On a Masson stain, the cytoplasm remained unstained.

Serum testosterone, 10.7 nmol/l (308 ng/100 ml), and dihydrotestosterone, 4.64 nmol/l (135 ng/100 ml), levels were in the range of normal adult males.

A lymphocyte culture from the peripheral blood showed a normal male karyotype. No mosaicism was detected in over 120 mitoses analysed. Q-banding did not reveal any chromosomal rearrangement; all of 55 mitoses observed contained a fluorescent Y chromosome.

Histological sexing on interphase nuclei was performed on tissue sections after paraffin-embedding and on buccal smears. Quinacrine-mustard-fluorescence revealed Y-bodies in all tissues studied, but in various proportions. Sertoli cells and buccal mucosa cells showed a frequency in the range of normal males (60%), while interstitial cells from the testis, smooth muscle, and ovarian stroma showed a much lower frequency varying from 15 to 25%.

Blood grouping did not detect a double cell population.

**Discussion**

In the presence of a female phenotype, a male karyotype, and a predominantly male gonad, one is con-
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Fig. 2 Ovarian-like stroma. (x 480.)

fronted with the differential diagnosis of mixed gonadal dysgenesis, true hermaphroditism, and testicular feminisation.

Mixed gonadal dysgenesis cannot be formally ruled out since the nature of the opposite gonad is unknown. However, it is the least likely diagnosis in the presence of an unambiguous female phenotype with breast development (Federman, 1967). Furthermore, the as yet unexplored mass in the left inguinal canal, present since childhood, suggests an undescended testis rather than a streak gonad. This mass has not changed in size and is, therefore, unlikely to be a tumour (a frequent occurrence in gonadal dysgenesis).

The diagnosis of a true hermaphrodite is more difficult to discard; though associated with a pure male karyotype it is not very common. In a survey of the published material of all cytogenetically examined true hermaphrodites, we found a total of 143 cases, 108 of which had been collected by Polani (1970), another 11 cases by Benirschke et al. (1972), the last 24 having appeared since 1971 (list of references obtainable from the author on request). Of these 143 cases, 26 (18%) have an apparently purely male karyotype. Nearly half of all cases present with a female karyotype and another third with a mosaic or chimeric karyotype.

We have searched for a second cell line by blood typing and by the study of interphase nuclei. No double population of red blood cells could be detected. Quinacrine studies on interphase nuclei showed a male pattern in buccal smear and in Sertoli cells, with over 60% positive nuclei. The frequency was much lower in other tissues studied (such as testicular interstitium, smooth muscle, fibroblasts), varying between 15 and 25% positive cells. This selective positivity of Sertoli cells has been noticed before (Palutke et al., 1973). In Palutke's case, Sertoli cells were the only brightly fluorescent cells in a true hermaphrodite with a 46,XX karyotype. Therkelsen (1964), in another 46,XX hermaphrodite, found that Sertoli cells were the only cells lacking the Barr body. The low frequency of Y-bodies in most tissues besides Sertoli cells suggests either an XO- or an XX-line or a technical artefact. In the absence of a mosaic pattern on chromosome analysis of peripheral blood leucocytes, we think that technical difficulties are the most likely explanation, though a mosaic cannot be excluded. In the absence of a positive indication of a mosaic, we consider this patient's karyotype as purely male.

A male genotype, associated with a female phenotype, suggests therefore testicular feminisation as the most likely diagnosis.

The familial element is totally lacking in this case. The proposita had two younger sisters, one of whom menstruated normally. Menstrual history is unknown in the other one who died at the age of 26 of tuberculosis. No amenorrhoeic aunts are known on either the paternal or the maternal side of the patient's family.

Clinically, the absence of axillary hair, the very sparse pubic hair, as well as the hypoplastic vagina are
all features of this disorder (Naftolin and Judd, 1973). The histological findings also are in favour of this diagnosis. The gonadal structure of an immature testis lacking spermatogonia and presenting with Leydig cell hyperplasia is consistent with the findings in testicular feminisation (Ferenczy and Richart, 1972).

The nature of the tissue resembling ovarian stroma is not clear. This feature has been described before (Stenchever et al., 1969). A Masson stain did not reveal any smooth muscle characteristics. The age of the patient precludes the presence of functional gonadal tissue. Ghosn et al. (1971), in a similar case of a 25-year-old woman, classified their patient as atypical testicular feminisation, hesitating to identify ovarian stroma as such when present without follicles. Pfeiffer (1974) prefers to classify cases without functional ovarian tissue as pseudohermaphrodites. Polani (1970), however, states that the absence of functional gonadal tissue does not eliminate true hermaphroditism.

The nodules of smooth muscle found in the inguinal canal could represent either remnants of Mullerian or Wolffian origin: cases of partial suppression of the Mullerian system have been described in testicular feminisation. The gonadal structure of an immature testis lacking spermatogonia and presenting with Leydig cell hyperplasia is also consistent with the findings in testicular feminisation.

Finally, normal levels, for an adult male, of testosterone and dehydrotestosterone in a perfectly female looking patient are hallmarks of testicular feminisation, where peripheral target organs are resistant to androgens. This finding correlated well with the well-developed Leydig cells in the testis and with the sparsity of pubic hair.

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Inconsistent expression of both centromeres of a dicentric Y chromosome in a child with ambiguous external genitalia 1

SUMMARY A newborn child with ambiguous external genitalia had evidence of internal female development on the left and internal male development on the right. Blood chromosome analysis showed three cell types: 45,X; 46,XY with the Y being submetacentric and about twice the usual size with two 'centromeric' C bands; and 46,X, dic(Y). Chromosome studies from the skin, uterus, and Fallopian tube showed almost exclusively 45,X cells. This represents the second reported patient in whom two centromeres are inconsistently expressed though present as showed by two 'centromeric' C bands.

That human dicentric Y chromosomes are not rare is indicated by the review of 16 cases by Cohen and coworkers in 1973. However, none of these or

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Late discovery of a case of testicular feminisation.

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