Paper

Female karyotype (XX) in patients with ambiguous genitalia does not guarantee the absence of intra-abdominal testes

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Abstract

We report three patients with ambiguous genitalia and 46 XX karyotype who had intra-abdominal testes. The mechanism for the development of testes in such patients, the risk of malignancy and value of histological assessment of intra-abdominal testes are discussed.

Introduction

The intra-abdominal testis is 30 to 50 times more likely to become malignant than a normally placed testis (1). When patients with ambiguous genitalia have a female (XX) karyotype, the intra-abdominal gonads are often presumed to be ovaries, with a lesser malignant potential. We report 3 patients with ambiguous genitalia and female (XX) karyotype who had intra-abdominal testes. One patient had a gonadoblastoma developing in this testis.

Case reports

The clinical features are summarised in the Table. The presenting features of each patient were different. Case 1, with abnormal genitalia from birth was referred to us for further management after clitoroplasty by a paediatric surgeon; case 2, for investigation of primary amenorrhoea and ambiguous genitalia from birth; and case 3 with hirsutism. All had been brought up as girls.

Genetic studies confirmed a female (46XX) karyotype in all three. All had laparoscopic gonadectomy following confirmation of testicular tissue by laparoscopic biopsy. The second patient who had a small gonadoblastoma did not have tumour dissemination.

Discussion

Traditional teaching is that the presence of the Y chromosome determines the maturation of undifferentiated gonads into testes (2). This leads to the assumption that gonads of individuals with XX karyotype would be ovaries.

Table. Clinical and histological features

Case	*Age*	*Presentation*	*Breast development*	*External genitalia*	*Hair pattern*	*Vagina*	*Uterus*	*Gonads (macroscopy)*	*Histology*
1	12	Ambiguous genitalia	Absent	Labia +, no scrotum	Female	Present, narrow	Central nodule	Bilateral testes	Testis
2	15	Primary amenorrhoea	Absent	Labia +, no scrotum	Scanty axillary and pubic hair	Present, narrow	Rudimentary	Streak left gonad, right testis	Testis + Gonadoblastoma (streak gonad, fibrous tissue)
3	18	Virilisation	Absent	Labia +, no scrotum	Male	Present, narrow	Small	Streak right gonad, left testis	Testis (streak gonad, fibrous tissue)

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Influence of the Y chromosome on gonadal differentiation is mediated *via* a gene sequence located on its short arm, which codes for TDF, the testicular determining factor[3]. Koopman and co-workers showed that this is most probably a single gene, referred to as SRY (4). Translocation of the SRY gene to the paternal X chromosome could therefore cause development of testes in an XX individual, termed XX sex reversal. This usually produces unambiguous genitalia (5). More recently, male gonadal development has been demonstrated in individuals with XX karyotype, who are also negative for the SRY gene (6,7). Male sexual differentiation in such patients may be due to alteration of one or more downstream Y, X or autosomal testis determining genes (6). It has been suggested also that male sex differentiation may be due to a downstream gene on the X chromosome, in which expression is influenced by X inactivation (6). Thirdly, XX sex reversal may occur as the result of low grade mosaicism undetected by cytogenetics (8).

Our report confirms the value of biopsy of intra-abdominal gonads by laparoscopy in people with ambiguous genitalia. Karyotyping, or even the exclusion of male genetic material by gene probing, would guarantee that such a gonad is an ovary. The fact that one of our patients had a tumour in an intra-abdominal testis emphasises the value of early detection and removal of such testes in patients with ambiguous genitalia.

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Preventing stroke

Preventing stroke is the most important strategy for reducing the cost of this disease. Management of modifiable risk factors, especially hypertension and cigarette smoking, has the greatest impact on prevention of first stroke.

T J Ingall. Preventing ischaemic stroke. *Postgraduate Medicine* 2000; **107**: 34-50.