X-Linked Ichthyosis and Cryptorchidism

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Sir,

In X-linked recessive ichthyosis (XLI), the incidence of various congenital defects is quite high [10]. Association of XLI with mental retardation [1,4], hypogenitalism [1, 3, 4, 7], cryptorchidism [1, 7, 8] and hypertrophic pylorus stenosis [2, 6] have been described. The most frequent association may be cryptorchidism as recently pointed out by Traupe and Ropers [7], Traupe and Happle [8] and Traupe et al. [9]. They suggested that birth complications and cryptorchidism are closely linked in XLI and should be considered as clinical manifestations of steroid sulfatase deficiency [7–9].

We surveyed some of our patients with regard to cryptorchidism and perinatal complications. Diagnosis of XLI relied on genetic, clinical and histopathological evidence and was confirmed by biochemical investigations (steroid sulfatase testing, lipoprotein mobility). 22 patients aged 3–15 years from 17 different families were studied and examined. 9 of them presented with bilateral cryptorchidism or had undergone previous hormonal or surgical treatment because of cryptorchidism. In Spain, the mean frequency of cryptorchidism in the normal population is 3^1% with a decrease to 1% at the age of 2, whereas in premature babies cryptorchidism occurs with a frequency of up to 20% [5].

It is difficult to assess, whether earlier perinatal complications had occurred in our patients. However, we believe this is quite likely since we recorded in our families a high rate of perinatal mortality (10 cases, number of cases presenting XLI unknown) and abortions (24 cases, number of cases presenting XLI unknown). 2 boys with XLI were born beyond term and 5 children were mentally retarded, 1 of whom was also affected by XLI. Steroid sulfatase testing and lipoprotein electro-phoresis could be carried out only in living family members (affected boys, or mothers and sisters); material from aborted fetuses or stillborn children could not be studied. Therefore, definite conclusions cannot yet be drawn. Our data, however, seem to confirm the hypothesis that perinatal complications and cryptorchidism are a direct result of lacking steroid sulfatase activity.

References


Letters to the Editor

The data of Unamuno et al. [8] on the high incidence of cryptorchidism in X-linked recessive ichthyosis are of considerable interest, in particular to those concerned with pediatric dermatology. For an affected boy the sequels of untreated cryptorchidism may be far more serious than the ichthyosis. Following our report [7] on this association dealing with seven instances of cryptorchidism out of a series of 25 patients with X-linked recessive ichthyosis, and a recent communication of Lykkesfeldt et al. [2] on 9 cases of testicular maldescent among 76 such patients and 3 additional affected patients with normally descended gonads who developed testis cancer, this is now the third study confirming a high frequency of cryptorchidism in X-linked recessive ichthyosis, reporting 9 cases out of a series of 22 patients [8].

How can the apparent association of cryptorchidism and X-linked recessive ichthyosis be explained? The simplest answer is to consider testicular maldescent a further manifestation of steroid sulfatase deficiency. Even in the absence of cryptorchidism patients with X-linked recessive ichthyosis exhibit an abnormal androgen and estrogen metabolism that is characterized by elevated levels of LH and estrone sulfate, a lack of decline of dehydroepiandrosterone sulfate in older age, and low androstenedione and estradiol levels [3]. Surprisingly, testosterone remains normal. This is probably due to the compensatory increase of LH [3]. LH plays an important role in normal testicular descent as is evidenced by the usual effectiveness of a HCG treatment. Therefore it is conceivable that testicular descent in X-linked recessive ichthyosis may require higher LH levels than in normal persons and that in some of the patients the LH levels will not be sufficient.
A second possible mechanism giving rise to cryptorchidism in X-linked recessive ichthyosis are cytoge-netic aberrations involving the short arm of the X-chromosome such as X-Y translocations [4,6] or the loss of the distal part of the short arm of the X-chromosome (Xp-) [1, 5]. In these cases, secondary steroid sulfatase deficiency occurs due to deletion of the steroid sulfatase gene. These deletions usually also involve genes in the neighborhood of the steroid sulfatase gene. Therefore patients with such a cytogenetic aberration present with a broad spectrum of associated symptoms such as cryptorchidism, hypogenitalism, mental retardation and even anosmia with hypogona-dotropic hypogonadism (Kallman syndrome). These deletions are inherited in a dominant pattern and their expressivity in female carriers is rather low [1, 4–6]. Due to a founder effect they are most likely not distributed evenly in larger populations, which could account for the observed differences in the percentage of patients affected with cryptorchidism in the various regions of Europe.

The two mechanisms discussed here to explain the association of cryptorchidism and X-linked recessive ichthyosis are not mutually exclusive, but rather may both contribute to this association.

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References