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Familial polythelia over three generations with polymastia in the youngest girl

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Abstract Supernumerary nipples or polythelia are developmental abnormalities located along the embryonic mammary lines. It is the most common form of accessory breast tissue malformation and usually occurs sporadically but familial aggregation has been reported. Polythelia has been reported in association with congenital malformations, in particular with renal anomalies. Polymastia in female patients has been reported to manifest usually during pregnancy or lactation. We report on a pedigree with six cases of polythelia over three generations and one case of polythelia and polymastia in the youngest member of this family. The girl (11 years old) had in addition to six supernumerary nipples, an accessory breast gland located under the normal left breast. No other congenital malformations could be detected. This girl will remain under follow-up until the end of puberty when the accessory breast gland will be removed. Manifestation of polymastia during puberty rarely has been reported.

Conclusion Polymastia may appear with familial polythelia even without renal anomalies.

Key words Familial history · Polymastia · Polythelia · Renal anomalies

Abbreviation *AMT* accessory mammary tissue

Introduction

Supernumerary nipples or polythelia are the most common form of the accessory mammary tissue (AMT) malformations. Supernumerary nipples have been found within the milk line extending from the axilla to the pubic region. The frequency of this condition ranges from 0.22% to 5.6% depending on various factors such as sex, ethnic group and geographical area [1, 12, 17]. The association between AMT and renal malformations has been repeatedly investigated but the results are still controversial. Many authors suggest that a supernumerary nipple/renal field defect exists [5]. Polythelia usually occurs sporadically but familial aggregation has been reported [7, 13]. We report on a girl who, in addition to familial polythelia with five affected members over three generations, presented with polymastia.

Case report

The index case is an 11-year-old girl (III:2) (Fig. 1) with polythelia and an uneventful medical history; especially no urinary tract infections. Polythelia consisted of three nipples with middle sized areolas on the left thoracic wall and three nipples with middle-sized areolas on the right thoracic wall. The classification of polythelia was performed according to Schmidt's criteria [12]. Additionally there was an accessory breast gland on the left side under the

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normal breast gland (Fig. 2). Pubertal development at presentation was PH2-3, B2-3 according to Tanner standards. On ultrasound examination the accessory breast gland had a diameter of 0.7 cm compared with the normal left breast gland measuring 2.5 cm. Urine analysis, urine cultures as well as a complete ultrasound examination of the urinary tract were normal.

The detailed family history revealed supernumerary nipples in the brother (III:1), the father (II:2), the aunt (II:3) (father's sister), the aunt's daughter (III:3) and the grandfather (I:2) (Fig. 1). All these relatives had only one middle-sized nipple (diameter $< 50\%$ of normal areola) on the left thoracic wall except the brother who had the supernumerary nipple on the right side. No urinary tract infections or malformations were reported in the above-mentioned relatives.

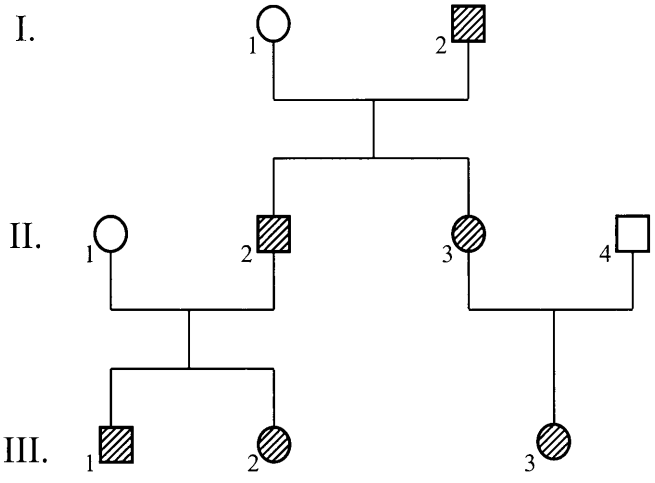

Fig. 1 Pedigree of the affected family. The index case is III:2 (polythelia and polymastia)

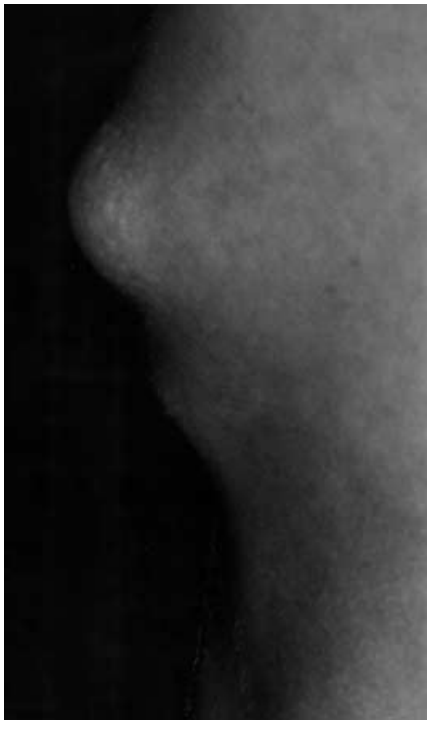

Fig. 2 Lateral view of the chest with the normal and the accessory mammary gland (below)

Discussion

Etymologically, the term polythelia or hyperthelia as well as polymastia or hypermastia comes from Greek and means "many nipples" and "many breast glands", respectively. Polythelia and polymastia represent a typical example of atavism in natural populations. Atavism, the spontaneous reappearance of ancestral characteristics in individual members of a species, serves to remind us that the genetic and developmental information originally used in the production of such characteristics has not been lost during evolution but lies quiescent within the genome and in the process of embryonic development [12]. Mammary glands develop from a pair of mammary ridges extending along the body wall [6].

There is a wide clinical spectrum, characterised by the presence of one or more anatomical mammary structures such as nipple, areola and glandular parenchyma. A simple classification of AMT has been proposed by Urbani et al. [19] (Table 1). Polythelia is much more common than polymastia. In women, polythelia has been reported in association with glandular tissue. Polymastia usually appears in pregnancy or during lactation and is rare before puberty. Polymastia may even appear without polythelia. An extensive range of congenital and hereditary anomalies have been reported in association with AMT including gonadal, cardiovascular, gastrointestinal and skeletal alterations [10, 11] as well as dysmorphic syndromes such as ectodermal dysplasia of Hay and Wells [4] or aplasia cutis congenita with syndactyly [3]. The association of AMT with congenital kidney and urinary malformations needs further investigation since contrasting results have been reported [5, 7–11]. In contrast, an interesting theory has been suggested by Urbani and Betti [15, 18] that the presence of familial history of AMT may be a protective factor against the development of congenital nephrourinary malformations.

The mode of inheritance of polythelia seems to be heterogeneous, since three modes have been suggested: autosomal dominant [12, 14], X-linked dominant [7] and recessive [13]. Urbani et al. [20] reported that the anomaly would be secondary to non-expression of a single major gene regulating the normal regression of redundant accumulations (or anlage) along the ectodermal mammary ridge which normally occurs during the 3rd month of embryonic development [2]. The genetic

Table 1 Classification of AMT adapted from [19]

Type	Glandular parenchyma	Subtypes
Aberrant mammary tissue type 1 (AMT 1)	+	–
Aberrant mammary tissue type 2 (AMT 2)	–	Only nipple (polythelia vera) Mammary areola only Nipple and areola

defect might be caused by a somatic mutation occurring early in embryogenesis, giving rise to a clone of mosaic cells that are homozygous or hemizygous for the mutation showing paradominant transmission [20]. In our pedigree, the grandfather was the first affected person suggesting autosomal dominant inheritance. This is in agreement with other reports suggesting that children of an affected male more often inherit AMT than children of an affected female [14, 16]. Additionally in our pedigree, it is noteworthy that in the third generation of a family with autosomal dominant simple polythelia, a girl shortly after onset of puberty, presented with an accessory mammary gland. From the therapeutic point of view, the girl will be kept under clinical follow-up during the further pubertal development. If no other accessory mammary breast tissue appears, surgical treatment will be performed as a prophylaxis against breast cancer which has a higher prevalence in polymastia [2, 21].

To our knowledge, such a pedigree with an autosomal dominant inheritance of supernumerary nipples and occurrence of a supernumerary breast tissue in the youngest generation without other associated malformations, in particular of the kidney and urinary tract, has never been reported.

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