

## Unilateral juvenile (virginal) hypertrophy of the breast

Dilek Güneş<sup>1</sup>, Kamer Mutafoğlu-Uysal<sup>1</sup>, Tülay Canda<sup>2</sup>, Serdar Saydam<sup>3</sup>

Ayşe Pınar Cemeroğlu<sup>4</sup>, Nur Olgun<sup>1</sup>

<sup>1</sup>Department of Pediatric Oncology, Dokuz Eylül University Institute of Oncology, and Departments of <sup>2</sup>Pathology, and <sup>3</sup>General Surgery, Dokuz Eylül University Faculty of Medicine, Izmir, Turkey, and <sup>4</sup>Department of Pediatric Endocrinology, Spectrum Health, DeVos Children's Hospital, Grand Rapids, Michigan, USA

**SUMMARY:** Güneş D, Mutafoğlu-Uysal K, Canda T, Saydam S, Cemeroğlu AP, Olgun N. Unilateral juvenile (virginal) hypertrophy of the breast. *Turk J Pediatr* 2008; 50: 278-281.

Juvenile hypertrophy of the breast (JHB) is an uncommon, benign disorder and typically occurs in peri-pubertal females. The etiology of JHB is uncertain. It may represent an end-organ hypersensitivity of the breast to normal levels of sex steroids. Clinically, it is characterized by rapid enlargement of breasts, either unilateral or bilateral. The definitive diagnosis is made by histopathologic examination. Treatment recommendations include surgery and hormonal therapy, although hormonal manipulation is still controversial in pediatric patients. Here we report a 13-year-old girl with unilateral JHB who did not require surgery or medical treatment.

**Key words:** juvenile hypertrophy of breast, adolescent, management.

Juvenile hypertrophy of the breast (JHB, synonyms: virginal hypertrophy of the breast, juvenile gigantomastia) is an uncommon, benign disorder and typically occurs in peri-pubertal females<sup>1-5</sup>. This entity was first described by Durston in 1669, although the patient reported was more consistent with the diagnosis of gravid hypertrophy instead of JHB<sup>1,2,6</sup>. The etiology of JHB is uncertain<sup>1-5</sup>. JHB usually develops sporadically, but familial cases have also been reported<sup>1,9</sup>. It occurs more commonly in girls between 8 to 16 years of age, and is clinically characterized by rapid enlargement of the breast<sup>1-3</sup>. The overgrowth of the breasts is usually bilateral, although unilateral JHB has been described<sup>4,5,10,11</sup>. It can cause several clinical problems such as breast pain, back and neck pain, dilatation of superficial veins, and skin ulcerations. It may also cause some serious psychological and cosmetic disturbances. We present a patient with unilateral JHB who did not require any treatment.

### Case Report

A healthy, postmenarchal 13-year-old girl was seen in our Pediatric Hematology-Oncology clinic with a chief complaint of rapid enlargement

of the right breast for the last two months. In addition to the breast enlargement, she noticed erythema and tenderness of her right breast. Her past medical history was unremarkable and she was not on any medications or oral contraceptive pills. Her family history was unremarkable with the exception of her brother having hemophilia A. On physical examination, the patient was a well-developed girl with a weight and height at 75<sup>th</sup> percentile. The right breast was markedly enlarged, and the left breast appeared normal (Fig. 1). The skin over the right breast was hyperemic, tender and warm. Palpation of the right breast revealed a uniformly firm texture without any discrete mass. Complete blood count, erythrocyte sedimentation rate, peripheral smear and chest radiography were normal. Ultrasonographic examination of the right breast showed an abnormal hyperechoic mass lesion that suggested a giant fibroadenoma of the breast.

An incisional biopsy was performed from the right breast for definitive diagnosis. Histopathological examination demonstrated proliferation of both stromal and ductal epithelial elements. There was also myoepithelial proliferation with budding in ductal structures with normal tubular

structures in some areas, which were compatible with JHB. Regular lobular structure was not yet formed. Dense fibrocollagenous tissue and myxoid connective tissue with vascular sections were seen in stroma (Fig. 2).



Fig. 1. Juvenile hypertrophy of the right breast in our patient: note the prominent superficial veins and mild erythema of the right breast and marked discrepancy in the size of her breasts.

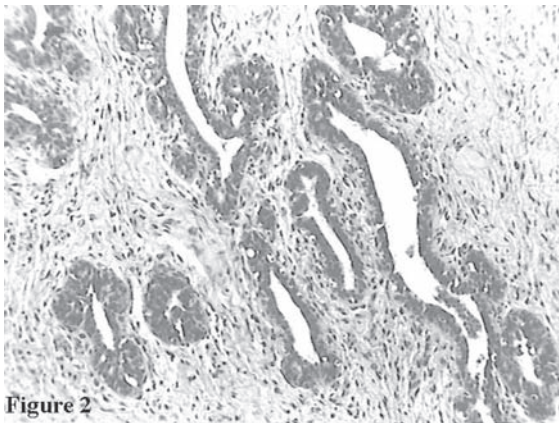


Figure 2  
Fig. 2. Histopathologic appearance of the right breast biopsy of the patient with juvenile hypertrophy of the breast: the proliferation of both tubular ductal structures and stromal connective tissue is present in hematoxylin and eosin stain (x100).

Since her unilateral breast enlargement did not cause any severe clinical, psychological, or cosmetic problems, we decided to follow her periodically without any surgical or medical intervention. During the four years of follow-up, her breast size remained stable.

### Discussion

In most girls, thelarche is usually the first sign of puberty. Complex hormonal influences affect breast development, which continues about

three to five years during pubertal development in girls. Ductal and lobular-alveolar development is mainly influenced by estrogen and progesterone, respectively<sup>3-5</sup>. The presence of estrogen receptors in the stroma and progesterone receptors in ductal epithelium confirms their effect on breast tissue<sup>5</sup>. Corticosteroids, thyroxine and prolactin seem to have a role in breast development as well<sup>3-5</sup>. This period of development in breast tissue is followed by reproductive phase (cyclic activity), and then involution. What stops the breast from continuous growth is not clear. The normal range for the breast size is arbitrary and therefore difficult to define accurately. In one categorization, ideal breast size was reported as 250 mm<sup>3</sup> to 300 mm<sup>3</sup>, and the size between 400 mm<sup>3</sup> to 600 mm<sup>3</sup> was considered as moderate hypertrophy and more than 1500 mm<sup>3</sup> as gigantomastia<sup>4</sup>.

Juvenile hypertrophy of the breast is a very uncommon disorder that occurs near the time of menarche and results in pathologic overgrowth of the breasts<sup>1,7</sup>. Bauer et al.<sup>2</sup> reviewed all pediatric breast pathologies over an 11-year period and found only five cases (12.5%) with the diagnosis of JHB among 40 adolescent patients. In JHB, the overgrowth of the breasts is usually bilateral, although unilateral JHB has been described, as in our patient<sup>4,5,10,11</sup>. Initially, rapid enlargement of the breast occurs for about three to six months followed by continuous but slow growth of the breast<sup>1,3</sup>. The breast can grow to weigh as much as 13.5 kg to 22.5 kg<sup>4,12</sup>. In our patient, the growth rate was slow for the past four years and the terminal breast size was not massive. In JHB, the breasts are usually pendulous and diffusely firm, without any discrete mass lesions, but ropelike thickenings may develop. It can cause breast pain, and back and neck pain. Dilatation of superficial veins or skin ulcerations may be present. Physical and psychological problems may develop.

The etiology of JHB is uncertain. In these individuals hormonal studies are normal<sup>1-5</sup>, and the number of estrogen receptors is not different from healthy adolescents<sup>1,5,13</sup>. Some authors have suggested that JHB may develop due to an end-organ hypersensitivity and exaggerated response to normal levels of sex steroids<sup>1,3-5,13</sup>.

The differential diagnosis of abnormal breast enlargement during childhood includes pseudo-gigantomastia associated with obesity,

fibroepithelial tumors of the breast such as juvenile phyllodes tumor and fibroadenomas, gravid hypertrophy of the breast, malignant tumors such as lymphomas<sup>14</sup> and sarcomas, breast hypertrophy secondary to endocrine disorders such as true precocious puberty resulting from hypothalamic lesions, constitutional precocity, polyostotic fibrous dysplasia, pseudoprecocious puberty resulting from ovarian granulosa cell tumors, follicular cysts, adrenocortical tumors, and exposure to a variety of hormones, including gonadotropins, estrogens, testosterone, and corticosteroids<sup>1,3</sup>.

Ultrasonographic (US) examination of the breasts is rarely useful for differential diagnosis. Magnetic resonance imaging (MRI) may be more useful for defining breast architecture and pathologic lesion<sup>3</sup>. US breast examination of our patient showed a regular, hyperechoic, giant mass in the right breast, which suggested a giant fibroadenoma. Fibroadenomas should be considered in the differential diagnosis of JHB. Especially juvenile and giant forms of fibroadenomas are more likely to mimic JHB<sup>2,3</sup>. Both entities result from end-organ hypersensitivity to normal levels of hormones. Fibroadenomas are neoplasms of the mammary glands, and histological examination of the breast tissue is required for differential diagnosis. Although histological findings are similar in these two entities, tumor capsule is not present, stroma is less organized and ductal proliferation is more prominent in JHB than in fibroadenomas<sup>1,3</sup>.

In our patient, the final diagnosis of JHB was made by histopathological examination. Histologically, this condition is an exaggeration of the normally developing breast. Characteristically the breast tissue shows varying degrees of stromal and ductal hyperplasia, often with dilatation and cystic degeneration of the ducts, and interstitial and periductal edema<sup>1-3</sup>. Glandular-alveolar development is markedly overshadowed by ductal proliferation and stromal changes are also prominent<sup>1</sup>.

Four modalities of treatment have been recommended in JHB, including reduction mammoplasty, mastectomy with implantation of prosthesis, hormonal manipulation, and combination of surgery and medications<sup>1-5</sup>.

Appropriate surgical intervention should be performed in late adolescence or early adulthood when breast growth rate stabilizes

and ideally when no change in size is detected over the last 12 months<sup>1-5</sup>. Breast reduction surgery is usually the treatment choice. The most commonly applied procedure is reduction mammoplasty with sparing of the nipple areola complex<sup>3,9</sup>. The recurrence of breast hypertrophy requiring additional surgery is a major problem.

Hormonal manipulation remains controversial because of unknown long-term effects. Antiestrogen drugs such as medroxyprogesterone, dydrogesterone, and tamoxifen citrate have been shown to be useful. Tamoxifen citrate is an antiestrogen drug that can cause a regression in the size of the breast. Several cases with JHB who were treated successfully with tamoxifen citrate have been reported in the literature and it was found to be the most effective agent for preventing recurrence<sup>3,9,15</sup>. However, potential side effects of tamoxifen citrate limit its use in children.

In conclusion, JHB is a rare benign disorder that should be kept in mind during the differential diagnosis of abnormal breast enlargement in pubertal girls. Diagnosis can be challenging especially when it is unilateral. Definitive diagnosis can be made by histopathologic examination. The treatment of choice for this disorder is still controversial. Optimal treatment strategy should be based on the patient's clinical and psychological features, and unnecessary aggressive interventions should be avoided.

#### REFERENCES

1. Kupfer D, Dingman D, Broadbent R. Juvenile breast hypertrophy: report of a familial pattern and review of the literature. *Plast Reconstr Surg* 1992; 90: 303-309.
2. Bauer BS, Jones KM, Talbot CW. Mammary masses in the adolescent female. *Surg Gynecol Obstet* 1987; 165: 63-65.
3. Baker SB, Burkey BA, Thornton P, et al. Juvenile gigantomastia: presentation of four cases and review of the literature. *Ann Plast Surg* 2001; 5: 517-526.
4. Neinstein LS. Breast disease in adolescents and young women. *Pediatr Clin North Am* 1999; 46: 607-629.
5. Templeman C, Hertweck SP. Breast disorders in the pediatric and adolescent patient. *Obstet Gynecol Clin North Am* 2000; 27: 19-34.
6. Durston W. Concerning a very sudden and excessive swelling of a woman's breast. *Philosophical Transactions for Anno 1669*; 4: 1047-1049. London: Royal Society; 1970 (Cross reference).
7. Albert H. Diffuse idiopathic hypertrophy of the mammary glands in the female. *JAMA* 1910; 55: 1339 (Cross reference).

8. Dehner LP, Hill DA, Deschryver K. Pathology of the breast in children, adolescents, and young adults. *Semin Diagn Pathol* 1999; 16: 235-247.
9. Govrin-Yehudain J, Kogan L, Cohen HI, et al. Familial juvenile hypertrophy of the breast. *J Adolesc Health* 2004; 35: 151-155.
10. Netscher DT, Mosharafa AM, Laucirica R. Massive asymmetric virginal breast hypertrophy. *South Med J* 1996; 89: 434 (Abstract).
11. Agaoglu G, Ozgur F, Erk Y. Unilateral virginal breast hypertrophy. *Ann Plast Surg* 2000; 45: 451-453.
12. Oberman HA. Breast lesions in the adolescent female. *Ann Pathol* 1979; 1: 175 (Cross reference).
13. Jabs AD, Frantz AG, Smith-Vaniz A, et al. Mammary hypertrophy is not associated with increased estrogen receptors. *Plast Reconstr Surg* 1990; 86: 64-66.
14. Di Noto A, Pacheco BP, Vicala RE. Two cases of breast lymphoma mimicking juvenile hypertrophy. *J Pediatr Adolesc Gynecol* 1999; 12: 33-35.
15. Kucukaydin M, Kurtoglu S, Okur H, et al. Virginal hypertrophy. Case report. *Turk J Pediatr* 1994; 36: 243-248.