The surgical treatment of benign breast lesions in young adolescents

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Pasquale Petronella*, Fulvio Freda*, Andrea Fiore**, Vincenzo Sorrentino Padovano*, Marco Scorzelli*, Silvestro Canonico*

Second University of the Study of Naples, School of Medicine
**Department of Gerontology, Geriatry and Metabolic Diseases, O.U. of General and Geriatric Surgery*
***Department of Anaesthetic, Surgical and Emergency Science*

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AIM: *There is much controversy surrounding the treatment of benign breast lesions in young adolescents: on one side the need for surgical treatment and on the other doubts in regard to operating on young patients with a benign disease. Another element sparking the debate is the correlation between the appearance of fibroadenomas and the presence of elevated prolactin levels in the blood.*
MATERIAL OF STUDY: *42 patients between the ages of 14 and 21 being treated at the General surgery and Geriatrics Unit of the Department of Gerontology, Geriatrics and Metabolic Diseases at the Second University of Naples between 2001 and 2004. In addition, blood prolactin levels were measured in 24 patients.*
RESULTS: *Only 4.76% of the patients examined (2 cases) had a family history of breast tumours. Out of a total of 42 adolescent patients that were operated on, we detected fibroadenomas in 35 (83.34%), fibrocystic disease in 3 (7.14%), adenosis in 3 patients (7.14%) and a phylloid tumour in 1 (2.38%). Blood prolactin was measured in 24 patients and in 17 cases we detected increased plasmatic levels of this hormone; in addition, anamneses revealed that of these 17 patients, 9 were using oral contraceptives.*
DISCUSSION: *The most common cause of palpable breast masses in adolescents under 21 years of age are fibroadenomas. The connection to hormonal, genetic and family factors is still unknown, both during the genesis of this pathology and as concerns an increased risk of possible malignant development. The correlation between fibroadenomas and elevated prolactin serum levels still remains controversial today. Various studies, measuring the blood concentration of prolactin in many patients have demonstrated that both elevated blood levels of this hormone and the use of oral contraceptives play a role in the development and growth of benign breast lesions.*
CONCLUSION: *Fortunately, breast disease is rare in adolescents; these patients do not often develop nodules and where these do occur the vast majority of cases involve benign lesions. A thorough follow-up on patients with nodular breast lesions is thus useful. As concerns the connection between prolactin and fibroadenomas, we also reported interesting data; this represents 70.83% of our subjects.*

KEY WORDS: Blood prolactin levels, Fibroadenomas, Surgical treatment.

Introduction

Fortunately, breast disease is rare in adolescents; patients in this age range do not often develop nodules and where these do occur the vast majority of the cases involve benign lesions [1].
The incidence of breast tumours in adolescent patients is less than 0.1% out of 100,000 women under 20 [2,3]. The surgeon must evaluate the neoplastic risk for each individual patient, in accordance with previously established information.
Fibroadenomas are certainly the most frequent occurrences, but must be carefully differentiated from phylloid tumours, which also display localized opacity and possibly gross internal calcifications; only the growth curve can point towards a diagnosis [4,5].

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Correspondence to: Prof. Dott. Pasquale Petronella, Seconda Università degli Studi di Napoli, Facoltà di Medicina e Chirurgia, U.O. di Chirurgia Generale e Geriatrica, Piazza Miraglia 5, 80138 Naples, Italy (E-mail: pasquale.petronella@unina2.it)

There is much controversy surrounding the treatment approach with different schools of thought on the possibility of a malignant transformation from a benign neoformation [6,7]. Surgical intervention is not unanimously accepted as these cases involve young women. This is another element sparking the debate: on one side the need for surgical treatment and on the other doubts in regard to operating on young patients with a benign disease [6,8-10].
Some authors have suggested a correlation between the appearance of fibroadenomas and the presence of elevated prolactin levels in the blood; we will also examine this possibility in the discussion.

Materials and methods

We performed a study on 42 patients between the ages of 14 and 21 (average age 17.3) being treated at the General surgery and Geriatric Unit of the Department of Gerontology, Geriatrics and Metabolic Diseases at the Second University of Naples between 2001 and 2004.
All the young patients were enrolled in a careful follow-up programme that involved ultrasonic and cytological examinations. Surgical treatment was recommended for lesions that underwent changes over time.

The inclusion criteria for treatment were:
– lesions with dimensions > 2 cm;
– rapidly growing lesions;
– FNAC showing atypical cells;
– tenderness;
– aesthetic damage.
A pre-surgical ultrasound was performed on all patients, which showed the presence of a formation that was located in the superior external quadrant in the majority of cases; a physical examination revealed lesions with a hard/elastic consistency, well-defined edges and that were movable over surface and deep tissues.
Multiple lesions were found in three patients, two of which had lesions located in different quadrants within the same breast, while only one patient had lesions in both breasts.
Patients discovered the neoformations by chance or as a result of pain.
Most young patients underwent surgical removal of the lesions under locoregional anaesthesia in an outpatient procedure, while three patients with multiple lesions underwent general anaesthesia as regular admissions.

TABLE I - *Family history*

Family history	Number of cases
Mother	1
Sister	1

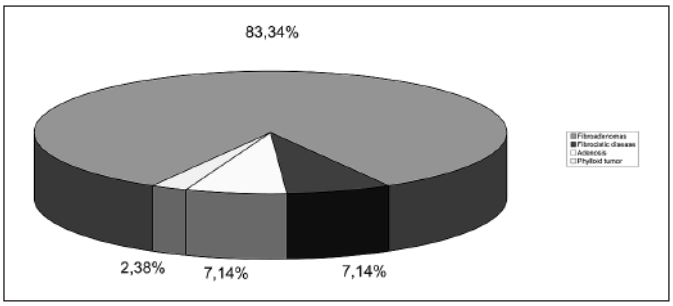

Fig. 1

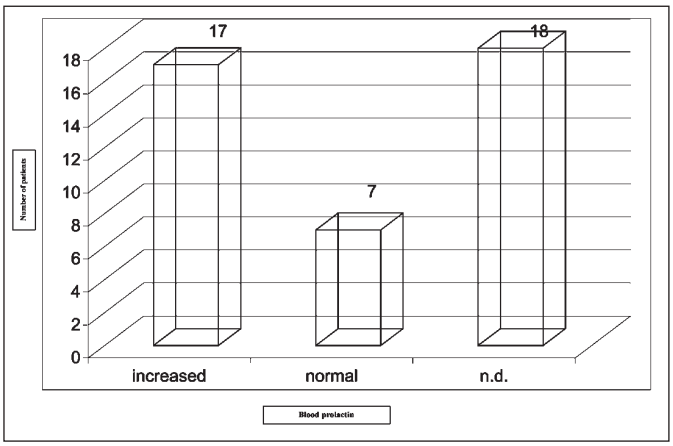

Fig. 2

The operative report was sent to the Anatomic Pathology Service for the identification of the lesion type.
In addition, blood prolactin levels were measured in 24 patients; 17 of these showed an increase in the plasmatic concentration of this hormone.

Results

Only 4.76% of the patients examined (2 cases) had a family history of breast tumours (Table I). The average age of menarche for patients was 12.2 years (range 10-14).
Removed lesions measured 2.3 cm on average (with a 2-3 cm variation); symptoms of pain during the initial visit were present in only 2 patients.
Out of a total of 42 adolescent patients that were operated on, we detected fibroadenomas in 35 (83.34%), fibrocystic disease in 3 (7.14%), adenosis in 3 patients (7.14%) and a phylloid tumour in 1 (2.38%) (Fig. 1).
Blood prolactin was measured in 24 patients and in 17 cases we detected increased plasmatic levels of this hormone (Fig. 2); in addition, anamneses revealed that of these 17 patients, 9 were using oral contraceptives.
To date none of the patients report a return of the disease.

Discussion

The most common cause of palpable breast masses in adolescents under 21 years of age are fibroadenomas, benign stromal tumours of polyclonal origin characterised by a focal hyperplasia of the lobular stroma [11-13]. These appear as a mobile mass that can, in a very small percentage of cases, reach diameters up to 10 cm. This type of lesion is quite often located in the superior external quadrant of the breast [14]. A physical examination of these masses generally shows them to be well-defined, hard/elastic nodules that show no variations during menstruation [15]. The connection to hormonal, genetic and family factors is still unknown, both during the genesis of this pathology and as concerns an increased risk of possible malignant development [8,16]. Fibroadenomas are thus sometimes treated with hormone therapy in Europe. This type of treatment is based on the use of progesterone and tamoxifen and results are currently limited and unconfirmed and have not provided statistically significant data; surgery still represents the gold standard [17]. The role of diet has been examined in various studies, hypothesizing a positive association between the consumption of saturated fats and the risk of atypias or proliferative forms of benign breast disease [18]. Other more recent studies have shown little support for this connection [19,20]. Adolescents with proliferative or non-proliferative fibroadenomas are, in any case, at a lower risk of developing carcinoma than older women [21]. A histological classification of lesions and the classification of patients depending on a positive family history of breast cancer are still essential [22].
These classifications are also controversial and not universally accepted [23]. We believe the classification suggested by the WHO [24] can be useful (Table II).

TABLE II - *Who classification of benign breast lesions*[24]

1. Benign epithelial neoplasms:	intraductal papilloma; adenoma (tubular and lactiferous);
2. Myoepithelial lesions: myoepithelioma;	adenomyoepithelioma;
3. Mesenchymal tumours:	hemangioma; lipoma and angiolipoma; leiomyoma; others;
4. Fibroepithelial tumours:	fibroadenoma; phylloid tumour (benign, malignant or borderline);
5. Nipple tumours:	nipple adenoma; syringomatous adenoma.

In 95% of cases the microscopic examination of fibroadenomas reveals a mixed fibroepithelial tumour that represents a hyperplastic reaction to the lobular stroma, with myxoid tissue, muscle fibres and sclerotic tissue [2]. There is also the possibility, based on an excisional biopsy, of a post-operative diagnosis of carcinoma within the fibroadenoma, a rare occurrence but not to be underestimated; this carcinoma is generally classified as DCIS [25]. More frequently, however, extremely large fibroadenomas are found; these tumours are characterised by fast growth and can double the size of the relative breast in 3-6 months [26,27]. Large fibroadenomas often have a dense stroma and cells characterized by ductal epithelial atypias, unlike phylloid tumours [22].
Ultrasonography has become the first choice for diagnosis and, in fact, mammography is not capable of distinguishing between the different formations due to the high density of mammary glands in young women [28]. In evaluating solid masses FNAC provides a high degree of specificity and sensitivity in benign or malignant diagnoses; this is thus a quick and accurate diagnostic test [29]. Generally, fibroadenomas appear to be well-defined grey or white masses. They can be directly removed from normal breast tissue using a capsule [14]. The formation is removed through a periareolar incision if there are no specific complications; furthermore, no supplemental procedures are generally required, such as mastopexy or additive or reductive mammoplasty, with a good final aesthetic outcome [24].
The correlation between fibroadenomas and elevated prolactin serum levels still remains controversial today. Various studies, measuring the blood concentration of prolactin in many patients have demonstrated that both elevated blood levels of this hormone and the use of oral contraceptives play a role in the development and growth of benign breast lesions [30,31]. It has also been inferred that elevated blood concentration of prolactin causes, through a link with its receptors (also found within glandular breast tissue, which is quite abundant in adolescents), an abnormal activation of these receptors that, in turn, produces cellular "up regulation" thus initiating a series of intracellular reactions that eventually lead to the development and growth of fibroadenomas [32-34]. Our data appear to confirm this correlation but our small sample size prevents us from taking a specific position.

Conclusion

Fortunately, breast disease is rare in adolescents; these patients do not often develop nodules and where these do occur the vast majority of cases involve benign lesions. The incidence of breast cancer in adolescents is very low, but the possibility of borderline lesions should not be excluded. A thorough follow-up on patients with nodular breast lesions is thus useful including an ultrasound and possible FNAC.

If, however, lesions measure over 2 cm, display rapid growth, cellular atypias, tenderness and aesthetic alternation surgical intervention is necessary to completely remove the lesions and ensure the best aesthetic outcome.
As concerns the connection between prolactin and fibroadenomas, we also reported interesting data; we tested 24 patients and 17 of these displayed an increase in the blood concentration of prolactin. This represents 70.83% of our subjects. However, since our data are numerically limited, they cannot confirm with certainty the existence of a causal nexus between the two factors examined and are merely indicative.

Riassunto

Obiettivo: Ci sono molte controversie che interessano il trattamento delle lesioni mammarie benigne nelle giovani adolescenti: da un lato la necessità di un trattamento chirurgico e dall'altro i dubbi in merito ad intervenire su giovani pazienti con malattia benigna. Un altro elemento causa di dibattito è la correlazione fra la comparsa di fibroadenomi e la presenza di elevati livelli di prolattina nel sangue.
Materiali e metodi: 42 pazienti di età compresa tra i 14 ed i 21 anni sono state operate presso l'unità di Chirurgia Generale e Geriatrica del Dipartimento di Gerontologia, Geriatria e Malatie del Metabolismo della Seconda Università degli Studi di Napoli. In 24 pazienti, inoltre, è stata dosata la concentrazione ematica della prolattina.
Risultati: Solo il 4,76% delle pazienti prese in esame (2 casi) avevano una storia familiare positiva per tumore mammario. Su un totale di 42 pazienti adolescenti operate, abbiamo riscontrato in 35 presenza di fibroadenoma (83,34%), in 3 malattia fibrocistica (7,14%), in 3 pazienti presenza di adenosi (7,14%), in 1 presenza di tumore filloide (2,38%). In 24 pazienti si è dosata la concentrazione ematica della prolattina ed in 17 casi abbiamo evidenziato un aumento dei livelli plasmatici di tale ormone; inoltre si è evinto dall'anamnesi che di queste 17 pazienti, 9 facevano uso di contraccettivi orali.
Discussione: La causa più comune di massa palpabile della mammella nelle adolescenti fino a 21 anni è rappresentata dal fibroadenoma. Rimane dubbia l'associazione con fattori ormonali, genetici e familiari, sia nella genesi di tale patologia sia nell'aumentato rischio di possibile evoluzione maligna. Per quanto riguarda la correlazione tra fibroadenoma ed elevati livelli sierici di prolattina, ancora oggi ci sono delle controversie a riguardo. Diversi studi, dosando la concentrazione ematica della prolattina in numerose pazienti, hanno dimostrato che sia gli elevati livelli ematici di tale ormone sia l'assunzione dei contraccettivi orali giocano un ruolo nello sviluppare ed accrescere tale lesione benigna della mammella.
Conclusioni: La patologia mammaria nelle adolescenti è fortunatamente rara; tali pazienti non sviluppano frequentemente noduli ed inoltre nella quasi totalità dei casi si tratta di lesioni benigne. È utile, quindi, uno stretto follow up delle pazienti che mostrano lesioni nodulari della mammella. Per quanto concerne l'associazione tra prolattina e fibroadenoma, anche noi abbiamo rilevato dati interesanti; siamo di fronte ad una percentuale del 70,83%.

References

1. Musella M, Renne M, Colacino MR, Carrano A, Castaldo P, Cimmino G, Musella S: *Clinical manifestations in benign breast diseases. The surgeon's role in the evaluation of signs and diagnostic work-up*. Ann It Chir, 1997; 68(2):167-71.

2. Shannon C, Smith J: *Breast cancer in adolescent and young women.* Eur J Cancer, 2003; 39:2632-42.

3. Courtillot C, Plu-Bureau G, Binart N, Balleyguier C, Sigal-Zafrani B, Goffin V, Kuttenn F, Kelly PA, Touraine P: *Benign breast diseases.* J Mammary Gland Biol Neoplasia, 2005; 10:325-35.

4. Agarwal P, Sparnon AL: *Benign breast lesions in adolescent girls: An overview with a case report.* Pediatr Surg Int, 2005; 21:381-82.

5. Tomimaru Y, Komoike Y, Egawa C, Motomura K, Inaji H, Kataoka TR, Koyama H: *A case of phyllodes tumor of the breast with a lesion mimicking fibroadenoma*. Breast Cancer, 2005; 12:322-26.

6. Connolly JL, Schnitt SJ: *Benign breast disease: Resolved and unresolved issues.* Cancer, 1993; 71:1187-89.

7. Muy-Kheng MT, Asseryanis E, Kroiss R, Kubista E, Wagner T: *Surgical breast lesions in adolescent females.* Pediatr Surg Int, 2009; 25:73-75.

8. Petrella G, Miro AG, Musella M, Formisano C: *Benign breast diseases: The surgeon's role in its treatment.* Ann It Chir, 1997; 68(2): 187-92.

9. Munshi A, Hsueh NL, Tiwana MS: *Complementary and Alternative Medicine in present day Oncology care: Promises and pitfalls*. Jpn J Clin Oncol, 2008; 38:512-20.

10. Thangapazham RL, Gaddipati JP, Rajeshkumar NV, Sharma A, Singh AK, Ives JA, Maheshwari RK, Jonas WB: *Homeopathic medicines do not alter growth and gene expression in prostate and breast cancer cells in vitro.* Interg Cancer Ther, 2006; 5:356-61.

11. Kuijper A, Preisler ASS, Rahusen FD, Gille JJ, Van Der Wall E, Van Diest PJ: *Multiple fibroadenomas harbouring carcinoma in situ in a woman with a family history of breast/ovarian cancer.* J Clin Pathol, 2002; 55:795-97.

12. Sklair-Levy M, Sella T, Alweiss T, Craciun I, Libson E, Mally B: *Incidence and management of complex fibroadenomas.* AJR Am J Roentgenol, 2008; 190:214-18.

13. Foxcroft LM, Evans EB, Hirst C, Hicks BJ: *Presentation and diagnosis of adolescent breast disease.* Breast, 2001; 10:399-404.

14. Pettinato G, Panico L, de Rosa N, D'Antonio A, Bifano D, Avallone M: *Benign lesions of the breast*. Ann It Chir, 1997; 68(2): 151-66.

15. Rego MF, Navarrete MA, Facina G, Falzoni R, Silva R, Baracat

EC, Nazario AC: *Analysis of human mammary fibroadenoma by Ki-67 index in the follicular and luteal phases of menstrual cycle.* Cell Prolif, 2009; 42:241-47.

16. Collins LC, Baer HJ, Tamimi RM, Connolly JL, Colditz GA, Schnitt SJ: *The influence of family history on breast cancer risk in women with biopsy-confirmed benign breast disease: Results from the Nurses' Health Study.* Cancer, 2006; 107:1240-47.

17. Mauvais-Jarvis P: *Le traitement hormonal des mastopathies bénignes.* Bull Cancer, 1991; 78:365-71.

18. Baer HJ, Schnitt SJ, Connolly JL, Byrne C, Cho E, Willet WC, Colditz GA: *Adolescent diet and incidence of proliferative benign breast disease.* Cancer Epidemiol Biomarkers Prev 2003; 12:1159-67.

19. Rohan TE, Negassa A, Caan B, Chlebowski RT, Curb JD, Ginsberg M, Lane DS, Neuhouser ML, Shikany JM, Wassertheil SS, Page DL: *Low-fat dietary pattern and risk of benign proliferative breast disease: A randomized, controlled dietary modification trial.* Cancer Prev Res (Phila Pa), 2008; 1:275-84.

20. Webb PM, Byrne C, Schnitt SJ, Connolly JL, Jacobs TW, Baer HJ, Willet WC, Colditz GA: *A prospective study of diet and benign breast disease.* Cancer Epidemiol Biomarkers Prev, 2004; 13:1106-13.

21. Worsham MJ, Raju U, Lu M, Kapke A, Botttrell A, Cheng J, Shah V, Savera A, Wolman SR: *Risk factors for breast cancer from benign breast disease in a diverse population.* Breast Cancer Res Treat, 2009; 118:161-68.

22. Hartmann LC, Sellers TA, Frost MH, Lingle WL, Degnim AC, Ghosh K, Vierkant RA, Maloney SD, Pankratz VS, Hillmann DW, Suman VJ, Johnson J, Blake C, Tisty T, Vachon CM, Melton LJ, Visscher DW: B*enign breast disease and the risk of breast cancer.* N Engl J Med, 2005; 353:229-37.

23. Cserni G, Orosz Z, Kulka J, Sapi Z, Kalman E, Bori R: *Divergences in diagnosing nodular breast lesions of noncarcinomatous nature.* Pathol Oncol Res, 2006; 12:216-21.

24. Tavassoli FA, Devilee P: *Tumours of the breast and female genital organs*. IARC Press 2003; 10.

25. Hemalatha AL, Raghupathi AR, Karthikeyan TM, Kumar DB, Shashidhar HB: *Carcinoma within a fibroadenoma: A case report,* Indian J Pathol Microbiol, 2006; 46:592-94.

26. Stehr KG, Lebeau A, Stehr M, Grantzow R: *Fibroadenoma of the breast in an 11-year-old girl.* Eur J Pediatr Surg, 2004; 14:56-59.

27. Gobbi D, Dall'Igna P, Alaggio R, Nitti D, Cecchetto G: *Giant fibroadenoma of the breast in adolescents: Report of 2 cases.* J Pediatr Surg, 2009; 44:39-41.

28. Garcia CJ, Espinoza A, Dinamarca V, Navarro O, Daneman A, Garcia H, et al: *Breast US in children and adolescents.* Radiographics, 2000; 20:1605-12.

29. Pacinda SJ, Ramzy I: *Fine-needle aspiration of breast masses.* J Adolesc Health, 1998; 23:3-6.

30. Courtillot C, Chakhtoura Z, Bogorad R, Genestie C, Bernichtein S, Badachi Y, Janaud G, Akakpo JP, Bachelot A, Kuttenn F, Goffin V, Touraine P: *Benign Breast Diseases Study Group. Characterization of two constitutively active prolactin receptor variants in a cohort of 95 women with multiple breast fibroadenomas*. J Clin Endocrinol Metab, 2010; 95(1):271-79.

31. Zubor P, Kajo K, Stanclova A, Szunyogh N, Galo S, Dussan CA, Minarik G, Visnovsky J, Danko J: *Human epithelial growth factor receptor 2[Ile655Val] polymorphism and risk of breast fibroadenoma.* Eur J Cancer Prev, 2008; 17(1):33-38.

32. Kang Y, Kim JH, Lee TH, Kim TS, Jung WH, Chung HC, Park BW, Sheen SS, Han JH: *Expression of anaphase-promoting complex7 in fibroadenomas and phyllodes tumors of breast.* Hum Pathol, 2009; 40(1):98-107.

33. Franco N, Arnould L, Mege F, Picard SF, Arveux P, Lizard-Nacol S: *Comparative analysis of molecular alterations in fibroadenomas associated or not with breast cancer.* Arch Surg, 2003; 138(3): 291-95.

34. Cericatto R, Pozzobon A, Morsch DM, Menke CH, Brum IS, Spritzer PM: *Estrogen receptor-alpha, bcl-2 and c-myc gene expression in fibroadenomas and adjacent normal breast: Association with nodule size, hormonal and reproductive features.* Steroids. 2005; 70(3):153-60.