SCIENTIFIC LETTERS

TTRs achieved were significantly improved compared to the previous period, which led to a positive evaluation of the self-monitoring programme.

Since we compared a single group of patients at 2 different times, we cannot rule out the possibility that all or some of the observed improvement in outcomes was due to other causes. However, both previous literature¹⁻⁶ and our results suggest that the increased monitoring frequency and the empowerment of patients and their parents to assume the management of treatment were the most likely causes of the observed changes.

References

- 1. Jones S, McLoughlin S, Piovesan D, Savoia H, Monagle P, Newall F. Safety and efficacy outcomes of home and hospital warfarin management within a pediatric anticoagulation clinic. J Pediatr Hematol Oncol. 2016;38:216–20.
- Murray JM, Hellinger A, Dionne R, Brown L, Galvin R, Griggs S, et al. Utility of a dedicated pediatric cardiac anticoagulation program: The Boston Children's Hospital experience. Pediatr Cardiol. 2015;36:842-50.
- Faircloth JM, Miner KM, Alsaied T, Nelson N, Ciambarella J, Mizuno T, et al. Time in therapeutic range as a marker for thrombotic and bleeding outcomes in Fontan patients. J Thromb Thrombolysis. 2017;44:38–47.
- Thrombolysis. 2017;44:38–47.

 4. Bauman ME, Massicotte MP, Kuhle S, Siddons S, Bruce AAK. EMPoWARed: Edmonton pediatric warfarin self-management study. Thromb Res. 2015;136:887–93.

 Christensen TD, Larsen TB, Hjortdal VE. Self-testing and selfmanagement of oral anticoagulation therapy in children. Thromb Haemost. 2011;106:391–7.

 Wong C, Batchelor K, Bua J, Newal F. Safety and efficacy of warfarin in paediatric patients with prosthetic cardiac valves: a retrospective audit. Thromb Res. 2011;128:331-4.

Rubén Berrueco^{a.b.d.*}, Cristina Benedicto^b, Anna Ruiz-Llobet^{a.b}, Susanna Gassiot^{a.c}, Albert Català^{a.b.d}

^a Institut de Recerca Pediàtrica, Hospital Sant Joan de Déu (IRP-HSJD), Barcelona, Spain

b Servicio de Hematología Pediátrica, Hospital Sant Joan de Déu, Universitat de Barcelona, Barcelona, Spain ^c Laboratorio de Hematología, Hospital Sant Joan de Déu, Universitat de Barcelona, Barcelona, Spain ^d Instituto Nacional de Investigación Biomédica en Enfermedades Raras (CIBERER), Instituto de Salud Carlos

*Corresponding author.

E-mail address: rberrueco@sjdhospitalbarcelona.org

(R. Berrueco).

2341-2879/

© 2017 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Giant breast fibroadenomas in adolescents: Diagnostic and therapeutic procedures*

Fibroadenoma gigante de mama en adolescentes: procedimientos diagnóstico-terapéuticos

יבמו במונטו.

Breast masses are rare in girls and female adolescents, and they exceptionally have a malignant aetiology. The most frequent diagnosis in these masses is juvenile fibroadenoma. When its size exceeds 5 cm, it is called giant fibroadenoma (GFA), a large-sized benign tumour with rapid growth. The differential diagnosis of GFA includes inflammatory processes, benign proliferative lesions and phyllodes tumour. Due to the lack of specific clinical guidelines for its correct diagnosis and treatment, the management of breast masses may pose difficulties.

We conducted a retrospective study of the breast masses larger than 5 cm managed between 2000 and 2017 in a paediatric hospital. We collected data on the clinical characteristics and the diagnostic tests and treatment used in

We present 4 cases of macromastia in patients with a median age of 15.3 years (range, 11.9–16.2), at Tanner stage 5 of pubertal development that sought care after developing a unilateral breast mass that was painless and growing quickly. On physical examination, the masses were painless, mobile, unattached to deeper tissues and with hypervascularization at the skin level (Fig. 1A). None of the patients had nipple discharge or local lymphadenopathy.

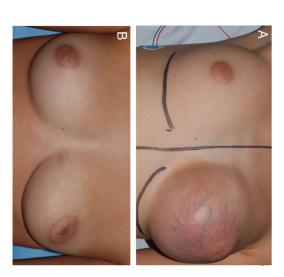


Figure 1 (A) Breast tumour in case 1 before surgery. (B) Outcome after simple excision of the tumour.

each case. The data was retrieved from the health records adhering to the protocols established by the hospital.

[☼] Please cite this article as: Corredor Andrés B, Márquez Rivera M, Lobo Bailón F, González Meli B, Azorín Cuadrillero D, Muñoz Calvo MT, et al. Fibroadenoma gigante de mama en adolescentes: procedimientos diagnóstico-terapéuticos. An Pediatr (Barc). 2018;89:383-385.

384 SCIENTIFIC LETTERS

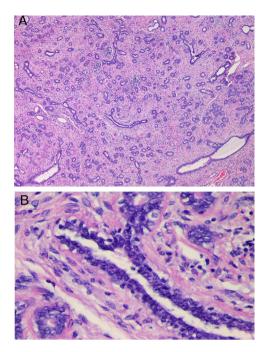


Figure 2 (A) Histological examination in case 3. Fibroepithelial proliferation with areas of pericanalicular and intracanalicular growth. No evidence of marked stromal growth, fat infiltration or cleft-like spaces. (B) Detail of Fig. 2A (H&E stain, $4\times$), showing a mildly hyperplastic epithelium and a stroma without cytological atypia or mitotic activity.

Sonographic examination of the breast revealed hypoechoic, lobulated masses with well-defined margins, in cases 1 and 3 with superficial hypervascularization. The findings in all patients were compatible with GFA or phyllodes tumour. The assessment of cases 1 and 4 included an MRI examination that revealed heterogeneous lesions that appeared isointense and hypointense on T1-weighted images and hyperintense on T2-weighted images, with no signs of infiltration. The radiological findings were not conclusive.

The diagnosis of GFA was confirmed after excision of the masses (Fig. 2); the maximum tumour diameter ranged between 5 and 14.5 cm and the mean weight was 1500 g. The surgical technique used in cases 1, 2, and 3 was simple excision (Fig. 1B). In case 4, excision was followed by placement of a filled tissue expander that was emptied gradually with the purpose of helping the skin recover its elasticity progressively. We ought to mention that none of the patient experienced postoperative complications and all had good outcomes.

Table 1 presents the clinical characteristics, radiological and pathological findings and final diagnosis for each case.

Giant fibroadenomas are masses characterised by a diameter of more than 5 cm and rapid growth, and they are an infrequent type of fibroadenoma that accounts for 0.5–2% of the total cases. ^{1–3} Their aetiology is unknown, although it has been hypothesised that they may be caused by increased sensitivity to oestrogen. ¹ In most cases, the mass develops during pubertal development around the time of menarche. This could be explained by the high cellular activity of the

Table	1 Clinical, ra	adiological	Table 1 Clinical, radiological and gross and histological or	ological characte	characteristics of the cases.				
Case	Case Race	Age (years)	Time elapsed from onset (months)	Localisation	Suspected diagnosis after ultrasound	Diagnosis after FNAB ^a /CNB ^b Excisional biopsy ^c	Type of surgery	Gross tumour volume (cm)	Final diagnosis after analysis of specimen
-	Caucasian	11.9	7	Unilateral	GFA/phyllodes tumour	Virginal breast hypertrophy ^c	Simple excision	14.5 × 11.5 × 7	GFA
7	Caucasian	16.2	Not documented	Unilateral	GFA/phyllodes tumour	GFAa	Simple excision	$5 \times 4 \times 2$	GFA
3	Caucasian	14.9	_	Unilateral	GFA/phyllodes tumour	GFA ^b	Simple excision	$10\times8\times8.5$	GFA
4	Black	15.7	24	Unilateral	GFA/phyllodes tumour	GFAª	Simple excision + tissue expansion	$12 \times 10 \times 3$	GFA
CNB, c	ore needle biop	ısy; FNAB, fii	CNB, core needle biopsy; FNAB, fine needle aspiration biopsy;	n biopsy; GFA, gia	GFA, giant fibroadenoma.				

SCIENTIFIC LETTERS 385

lobules from the onset of puberty to approximately age 25 years. 4,5 The patients in our study were aged less than 17 years, which was consistent with the description of Sosin et al. 2

The differential diagnosis of GFA includes inflammatory processes, benign proliferative lesions (hamartoma, lipoma, virginal or juvenile hypertrophy of the breast and pseudoangiomatous stromal hyperplasia [PASH]) and phyllodes tumour.^{2,3} The main diagnosis that needs to be excluded is phyllodes tumour, which corresponds to fewer than 1% of all breast tumours. Its clinical and sonographic features may be indistinguishable from those of GFA and even virginal hypertrophy or PASH. Virginal hypertrophy is characterised by a rapid growth of breast tissue due to hypersensitivity to estrogens. In very rare cases, breast masses correspond to lipoma, hamartoma or PASH. 4-6 The histological differential diagnosis includes virginal hypertrophy of the breast, breast hamartoma and, most importantly, phyllodes tumour. Fine-needle puncture aspiration biopsy is not useful to discriminate between these diseases. It is extremely difficult to distinguish GFA and phyllodes tumour in a core needle biopsy (CNB), and one study found that up to 25% of phyllodes tumours had initially been classified as fibroadenomas based on the CNB histology. Some authors have proposed histological features that would indicate surgical excision: increased stromal cellularity compared to a conventional fibroadenoma in more than 50% of the submitted tissue sample, stromal overgrowth viewed in a 10× microscopic field, stromal fragmentation and entrapment of fat in the lesion.⁶

Ultrasound is the first-line imaging test for assessment of a breast mass during adolescence. Fibroadenomas appear as a round or oval mass, isoechoic or hypoechoic and with well-defined borders. Doppler ultrasound reveals hypervascularization in up to 80% of cases, and was found in 50% of our patients. The sonographic appearance may be the same in cases of virginal hypertrophy, PASH or phyllodes tumour, which calls for histological examination in masses larger than 5 cm or exhibiting rapid growth. 7-9 Magnetic resonance imaging of the breast is not used routinely. However, it may be useful to define the lesion better before surgery. 7

The treatment of fibroadenomas depends mainly on their size. For those with a diameter of less than 5 cm in adolescents, treatment is conservative, as the risk of malignancy is nearly non-existent in the group aged less than 20 years. In cases of suspected GFA, complete excision of the mass is indicated for gross and histological examination, as GFA cannot be differentiated from some other masses, mainly phyllodes tumour, based on the clinical presentation and radiological features.⁵

If possible, surgery must spare healthy breast tissue and the nipple-areolar complex. Based on our results and the evidence published in the literature, simple excision, where the case allows it, is the treatment of choice on account of the low rate of postsurgical complications and the excellent cosmetic outcomes.¹⁰

In conclusion, ultrasound is the first-line imaging test for assessment of a mass in the breast, and a full gross and histological examination is necessary in masses with diameters of more than 5 cm and/or exhibiting rapid growth, as fine needle aspiration and core needle biopsies are not useful in this type of lesion. The surgical treatment of choice is simple excision.

References

- Gao Y, Saksena MA, Brachtel EF, terMeulen DC, Rafferty EA. How to approach breast lesions in children and adolescents. Eur J Radiol. 2015;84:1350-64.
- Sosin M, Pulcrano M, Feldman ED, Patel KM, Nahabedian MY, Weissler JM, et al. Giant juvenile fibroadenoma: a systematic review with diagnostic and treatment recommendations. Gland Surg. 2015:4:312-21.
- 3. Rafeek N, Rangasami R, Dhanraj K, Joseph S. Multimodality approach in the diagnosis and management of bilateral giant juvenile breast fibroadenoma. BMJ Case Rep. 2016, http://dx.doi.org/10.1136/bcr-2016-217588.
- Kupsik M, Yep B, Sulo S, Memmel H. Giant juvenile fibroadenoma in a 9-year-old: a case presentation and review of the current literature. Breast Dis. 2017, http://dx.doi.org/10.3233/BD-160250.
- 5. Duflos C, Plu-Bureau G, Thibaud E, Kuttenn F. Breast diseases in adolescents. In: Sultan C, editor. Pediatric and adolescent gynecology. Evidence-based clinical practice. 2nd ed. Basel: Karger; 2012. p. 208–21.
- 6. Van Osdol AD, Landercasper J, Andersen JJ, Ellis RL, Gensch EM, Johnson JM, et al. Determining whether excision of all fibroepithelial lesions of the breast is needed to exclude phyllodes tumor: upgrade rate of fibroepithelial lesions of the breast to phyllodes tumor. JAMA Surg. 2014;149:1081-5.
- Ross DS, Giri DD, Akram MM, Catalano JP, Olcese C, Van Zee KJ, et al. Fibroepithelial lesions in the breast of adolescent females: a clinicopathological study of 54 cases. Breast J. 2017;23:182–92.
- Sanchez R, Ladino-Torres MF, Bernat JA, Joe A, DiPietro MA. Breast fibroadenomas in the pediatric population: common and uncommon sonographic findings. Pediatr Radiol. 2010;40:1681-9.
- Smith GE, Burrows P. Ultrasound diagnosis of fibroadenoma is biopsy always necessary? Clin Radiol. 2008;63:511–5.
- Ezer SS, Oguzkurt P, Ince E, Temiz A, Bolat FA, Hicsonmez A. Surgical treatment of the solid breast masses in female adolescents. J Pediatr Adolesc Gynecol. 2013;26:31–5.

Beatriz Corredor Andrés ^{a,b}, María Márquez Rivera ^{a,b}, Fernando Lobo Bailón ^c, Beatriz González Meli ^c, Daniel Azorín Cuadrillero ^d, María Teresa Muñoz Calvo ^{a,b,e,f,*}, Jesús Argente ^{a,b,e,f,g}

- ^a Servicio de Pediatría, Hospital Infantil Universitario Niño Jesús, Madrid, Spain
- ^b Servicio de Endocrinología, Hospital Infantil Universitario Niño Jesús, Madrid, Spain
- ^c Sección de Cirugía Plástica, Hospital Infantil Universitario Niño Jesús, Madrid, Spain
- ^d Servicio de Anatomía Patológica, Hospital Infantil Universitario Niño Jesús, Madrid, Spain
- ^e Departamento de Pediatría, Universidad Autónoma de Madrid, Madrid, Spain
- ^f CIBER Fisiopatología de la Obesidad y Nutrición, Instituto de Salud Carlos III, Madrid, Spain
- ^g IMDEA Instituto de Alimentación, CEI UAM + CSIC, Madrid, Spain
- * Corresponding author.

E-mail address: maitemunozcalvo@gmail.com (M.T. Muñoz Calvo). 2341-2879/

© 2017 Asociación Española de Pediatría. Published by Elsevier España, S.L.U. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).