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## CASE REPORT

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# Giant Fibroadenoma Presenting as an Axillary Mass in a Young Renal Transplant Recipient on Long-term Cyclosporine A Therapy

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### ABSTRACT

*We report on a young female renal transplant recipient on long-term cyclosporine A therapy who developed a giant fibroadenoma presenting as a rapidly enlarging solitary left axillary mass, with a background history of recurrent smaller fibroadenomas. A brief discussion of the clinical and imaging features, pathology, and treatment approaches follows with a short review of the literature. The importance of a multidisciplinary approach is also demonstrated.*

*Key Words:* Cyclosporine; Fibroadenoma; Kidney transplantation; Mammography; Ultrasonography

## 中文摘要

### 長期服用環孢素A的一名年輕腎移植患者在腋下窩出現巨大纖維腺瘤

薛靜雯、倪韻碧、蔡綺琪、陳永昌、周海倫

本文報告一名長期服用環孢素A的腎移植年輕女性患者。患者左腋下窩出現一個快速增大的孤立性腫塊，後被證實為一個巨大纖維腺瘤。患者的既往病史含復發性較小纖維腺瘤。本文簡短討論此症的臨床和成像特徵、病理學和治療方法，並簡短回顧文獻。這病例證明同時闡述多學科方法的聯合運用重要性。

### CASE REPORT

A 33-year-old female with recurrent immunoglobulin A nephropathy despite undergoing a renal transplant presented to our unit in the New Territories East Cluster in August 2013, complaining of a left axillary mass that had enlarged over a 9-month period. She had been taking long-term cyclosporine A therapy for 8 years following her renal transplant in 2005. Since then

she had been diagnosed with fibroadenomata at L1H, L3H and L7H, all treated by lumpectomy in 2008 and 2011. At the current presentation she was first assessed by the breast team at North District Hospital and then referred for breast imaging studies at Prince of Wales Hospital.

Breast examination showed a large lobulated axillary

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Submitted: 2 Oct 2015; Accepted: 5 Jan 2016.

Disclosure of Conflicts of Interest: All authors have no relevant conflicts of interest to disclose.

mass that was confirmed on ultrasound to be a highly vascularised lobulated mass (Figure 1a). Supplementary radiograph showed a well-lobulated non-calcified mass measuring up to 7 cm long (Figure 1b). Physical and ultrasound examinations were otherwise unremarkable. No other breast mass, enlarged cervical or axillary lymph node was present.

With the initial suspicion of an enlarged axillary node, and a particular concern about transplant-related lymphoproliferative disease, we performed an ultrasound-guided core needle biopsy of the mass. Biopsy revealed a fibroepithelial lesion with expansion of the specialised stroma. The benign ductal elements formed intracanalicular and pericanalicular patterns (Figure 2a). No stromal hypercellularity, atypia, or mitotic figures were identified (Figure 2b). The features were those of a fibroadenoma.

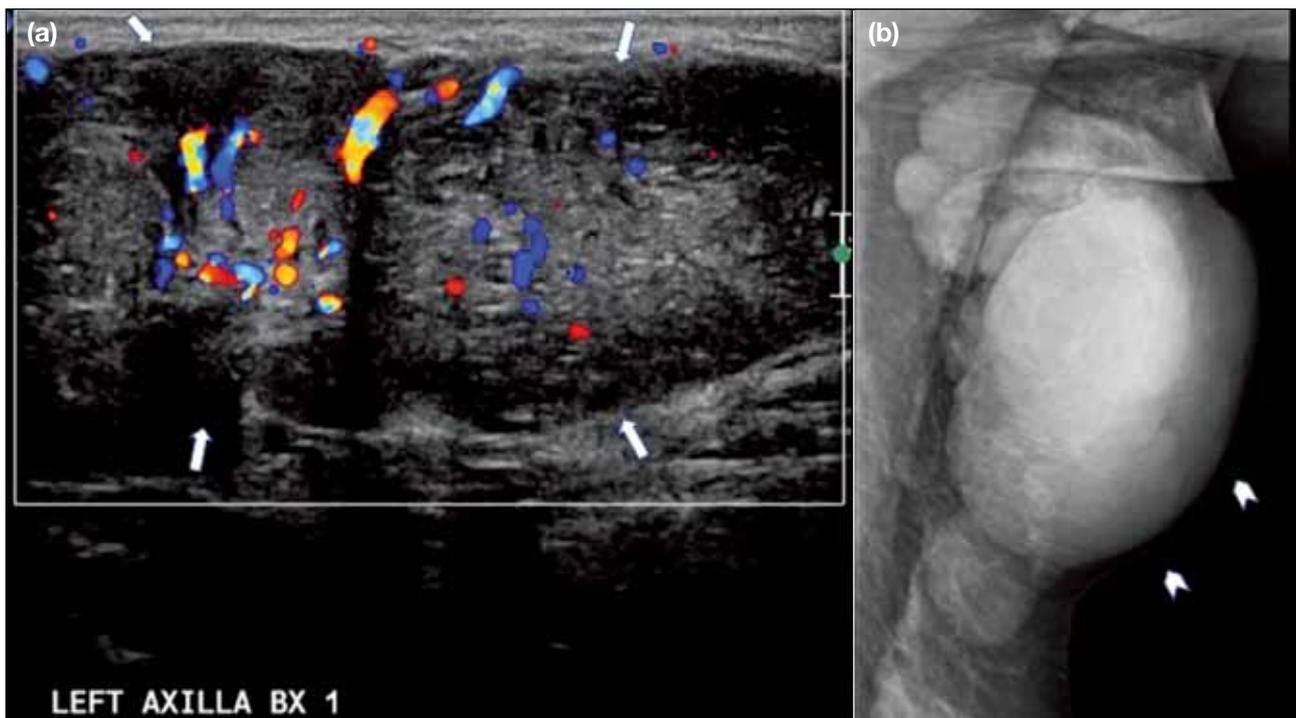
Multidisciplinary team review concluded that the unusual presentation of a rapidly enlarging axillary giant fibroadenoma against a background of multiple fibroadenomatosis in this young renal patient was likely related to the chronic prescription of cyclosporine A therapy. Treatment options of excision versus conservative management were offered to the patient

who opted for surgical excision of the mass rather than a reduced dose of cyclosporine A and watchful waiting. Wide local excision of the axillary mass was performed and histological examination confirmed fibroadenoma.

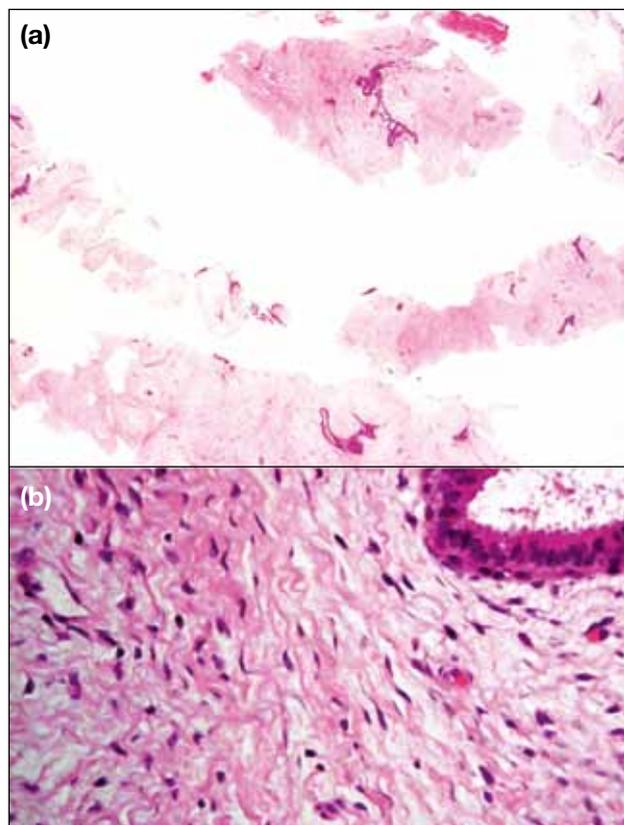
## DISCUSSION

First reported in 1980, the incidence of fibroadenoma among renal transplant recipients prescribed cyclosporine A therapy was reported to be one in 9.4 patients, far higher than in the general population.<sup>1</sup> Postulated mechanisms include: (1) a direct effect of the drug on breast fibroblasts; (2) an endocrine effect mediated via the hypothalamic-pituitary axis, as evidenced by higher oestrogen and lower follicle-stimulating hormone levels; and (3) increased synthesis and expression of transforming growth factor  $\beta$  (pro-fibrotic cytokine), also believed to be the cause of gingival hypertrophy.<sup>1,2</sup> There is a consequently higher chance of developing multiple, bilateral, and recurrent fibroadenomata, an uncommon entity in the general population.<sup>3</sup> These lesions are usually 1 to 5 cm in diameter, and many will double or triple in size within 2 to 3 years.<sup>3</sup> The breast parenchymal density of these patients are also noted to be higher on mammograms.

‘Giant fibroadenoma’ refers to a fibroadenoma that



**Figure 1.** Imaging findings for the work-up of a large left axillary mass. (a) Transverse ultrasound image of the left axilla showing a well-defined lobulated mass with significant vascularity (arrows). (b) Supplementary radiograph of the left axilla showing a large multilobulated radiopaque mass (arrowheads).



**Figure 2.** Histological examination of the left axillary mass core biopsy specimen. (a) Cores of breast tissue showing fibroepithelial lesion with expansion of the specialised stroma and ductal element forming intracanalicular and pericanalicular patterns (H&E; original magnification, x 20). (b) Stroma of the lesion showing bland spindled stromal cells. There is no hypercellularity, atypia, or mitotic activity (H&E; original magnification, x 400).

measures more than 5 cm and weighs more than 500 g.<sup>3</sup> Fibroadenoma is common among the general female population but its presentation as a giant axillary mass is not. Although there is no malignant degeneration, adenoma can mimic phyllodes tumour or lymphoma on mammogram and ultrasound, especially in patients who are immunosuppressed. Such imaging appearances can be anxiety provoking for the patient who is often a young individual in otherwise good health. Tissue diagnosis should therefore be obtained for clarification if there are unusual features or risk factors, for example, the rapidly enlarging nature of the mass and the potential risk of development of lymphoproliferative disease in our patient.<sup>3</sup>

Clinicians may face a dilemma when considering treatment options for this patient. First, it has been reported that upon stopping cyclosporine A therapy, some fibroadenomata will regress in size, and there

will be a decrease in breast density on mammograms.<sup>4</sup> There is, however, no statistically significant correlation between cyclosporine A dosage or blood level and the subsequent development of fibroadenoma. In addition, the risk of breast cancer in renal transplant patients does not appear to be increased relative to the general population.<sup>1,5</sup>

Although reducing the dose of cyclosporine A may not be the most optimal solution, we believe that changing to an immunosuppressant regimen that excludes cyclosporine A may be a possible option that prevents the need for more surgery, and also serves to reduce the chance of fibroadenoma recurrence. This course of action must nonetheless be balanced against the risk of graft failure. Management of these patients should therefore adopt a multidisciplinary approach, where treatment options should be thoroughly discussed with the patient as well as radiologists, pathologists, breast surgeons and renal physicians, with particular attention paid to the dosage of cyclosporine A or use of a drug combination devoid of cyclosporine A.<sup>3</sup> Watchful waiting for potential regression of the fibroadenomata should also be discussed as an alternative to surgical excision and potential avoidance of unnecessary invasive procedures.<sup>4,5</sup>

This case illustrates the importance of an awareness of the role of cyclosporine A in inducing fibroadenoma in renal transplant recipients that will help in achieving a correct and timely diagnosis. Good communication within a multidisciplinary team together with thorough discussion with the patient about surgical and non-surgical options underlie the key to successful management of these lesions.

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