

## A benign lesion similar to breast cancer

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*To the Editor:* We here reported a case of a breast lesion found by rapid pathological examination of frozen sections on February 2, 2018. The lesion was very similar to breast cancer in terms of gross observation and histological features. Immunohistochemistry and phosphatidylinositol-3-kinase (*PIK3CA*) gene sequencing were performed. The clinicopathological features of the lesion were reported in detail.

A 60-year-old woman stumbled upon a painless, inactive small mass on her left breast with no other symptoms. The B-ultrasound showed a round hypoechoic nodule in the left breast associated with structural distortion [Figure 1A]. She had no history of diseases. The patient underwent a lumpectomy on her left breast and specimen was obtained for pathological examination of rapidly frozen sections.

Macroscopically, the removed breast solid nodule was 1.0 cm × 1.0 cm × 0.6 cm in size, with a gray-yellow appearance and a hard touch. On the cut surface, the nodule had a dense texture and fine white asterisk-like fibers in the interior with burrs on the edges, whose level was significantly lower than that of the surrounding breast tissue [Figure 1B]. A 5- $\mu$ m thick tissue was cut for frozen section examination and stained with hematoxylin and eosin (H & E).

Microscopically, there was a radial star-shaped lesion with a central fibrous scar, where the mammary ducts were squeezed with vigorously proliferating cells, and the surrounding glands had different proliferation states. They were arranged radially outward and gradually transitioned to the surrounding normal tissue [Figure 1C and 1D]. A high-power microscope revealed myoepithelial cells surrounding the hyperplastic ductal epithelial cells. Given the presence of myoepithelial cells, the patient was not diagnosed with malignancy by the frozen section

examination, and instead a radial sclerosing lesion (RSL) was considered.

The lesion displayed in the conventional pathology was similar to that seen in frozen section. There were twisted glands and hyperplastic epithelial nests in the hardened fibrous tissue interstitium. Radially arranged mammary ducts and lobules could be seen around the lesion. Apocrine glandular metaplasia and a small amount of calcium deposits were observed in the hyperplastic catheter lumens [Figure 2A and 2B].

Immunohistochemical analysis showed that cytokeratin 5/6 exhibited a mottled positive expression in the proliferating cells in the duct [Figure 2C]. Positive expression of P63 and calponin protein indicated the presence of myoepithelial cells [Figure 2D]. We cut 8- $\mu$ m thick sections from paraffin-embedded tissue for *PIK3CA* sequencing, and no *PIK3CA* mutation was found. The patient was completely cured and the final diagnosis was breast RSL.

In addition to RSL, similar terms, such as radial scars and complex sclerosing adenosis, are also used. They are usually characterized by a group of sclerotic lesions with a central sclerotic lesion where the ducts and leaflets are radially distributed. They are benign entities in radiology and histology, but most easily mimic breast cancer. These lesions are rare and have a high risk of developing breast cancer. The relevant risk factors include age over 50 years and lesions >4 mm in diameter, especially atypical hyperplasia of ductal epithelial cells,<sup>[1]</sup> which will potentially increase the risk of developing invasive cancer. When there are no myoepithelial cells surrounding the atypical hyperplasia of the ductal epithelial cells, the invasive breast cancer can be diagnosed. Wilsher *et al*<sup>[2]</sup> reported in two articles that RSL may be a neoplastic precursor lesion of low-grade adenosquamous

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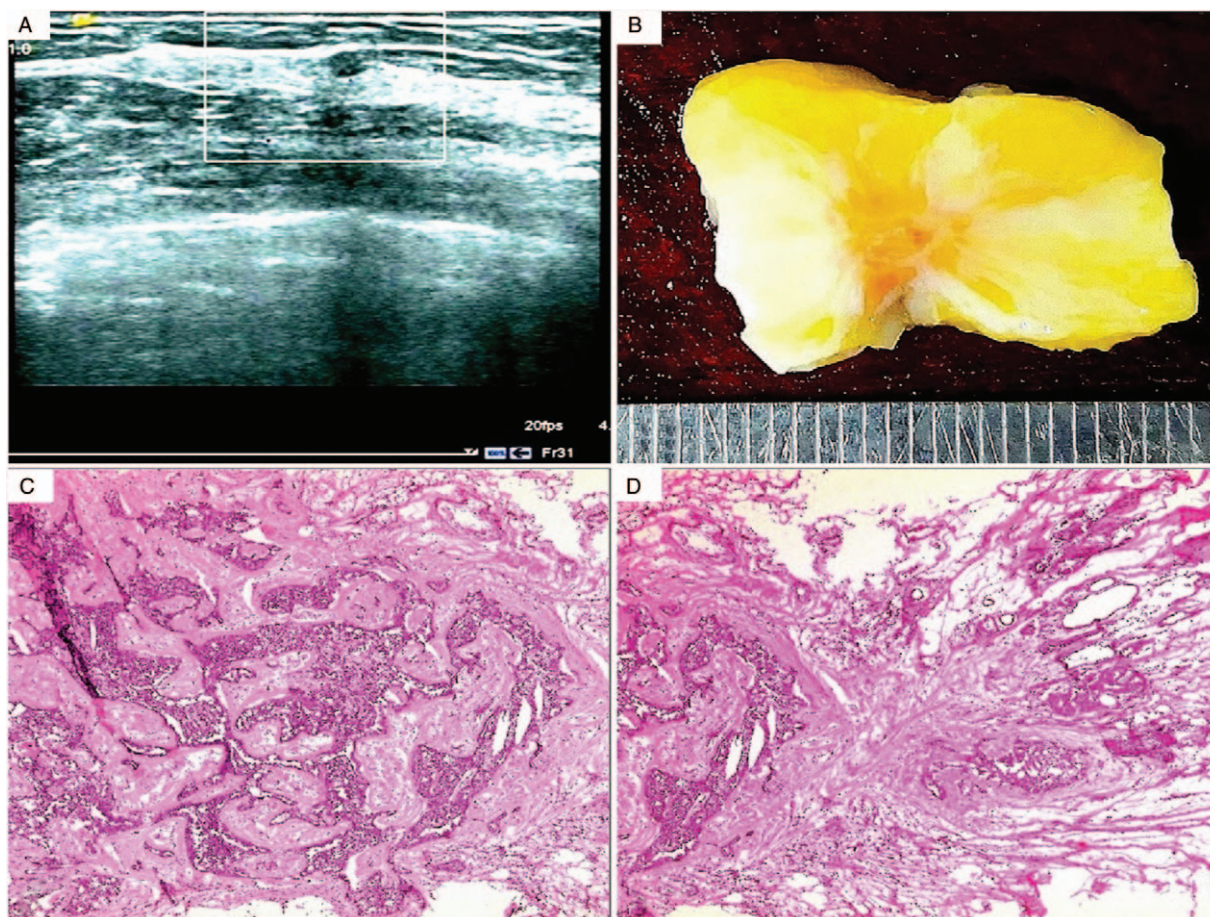
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**Figure 1:** B-scan, gross cut and frozen section pathological images of RSL. (A) B-ultrasound showed a round hypoechoic nodule associated with structural distortion. (B) The grayish yellow nodule with a dense texture had fine white asterisk-like fibers inside with burrs on the edges. (C) Significantly proliferating ductal epithelial cells in the central fibrous scar area (H & E, original magnification  $\times 100$ ). (D) The lesion was radially aligned and gradually transitioned to the surrounding normal tissue (H & E, original magnification  $\times 100$ ). H & E: hematoxylin and eosin; RSL: radial sclerosing lesion.

carcinoma (LGASC). They may form a continuous morphological spectrum with benign sclerosing lesions at one end and LGASCs at the other end, which are usually more extensive and have prominent connective tissue stroma.

The activated point mutations in *PIK3CA* were found in 25%–30% of invasive breast cancers.<sup>[3]</sup> Interestingly, *PIK3CA* mutations also existed in RSL. Wilsher *et al*<sup>[2]</sup> detected hot spot mutations of *PIK3CA* in 10 (77%) of 13 cases of RSL. Wolters *et al*<sup>[3]</sup> detected *PIK3CA* mutations in 14 (63.6%) of 22 RSLs, and found that the remaining 8 cases of RSL were wild-type for all of the screened genes. Our case was a wild-type of *PIK3CA*. Due to the small number of reported RSL cases, the frequency of such mutations needs to be confirmed by a larger number of cases. However, these studies have indeed helped us understand the pathogenesis of RSL and its relationship with breast cancer.

#### Declaration of patient consent

We have obtained patient consent form. In the form the patient has given her consent for her images and other clinical information to be reported in the journal. She understand that her name will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

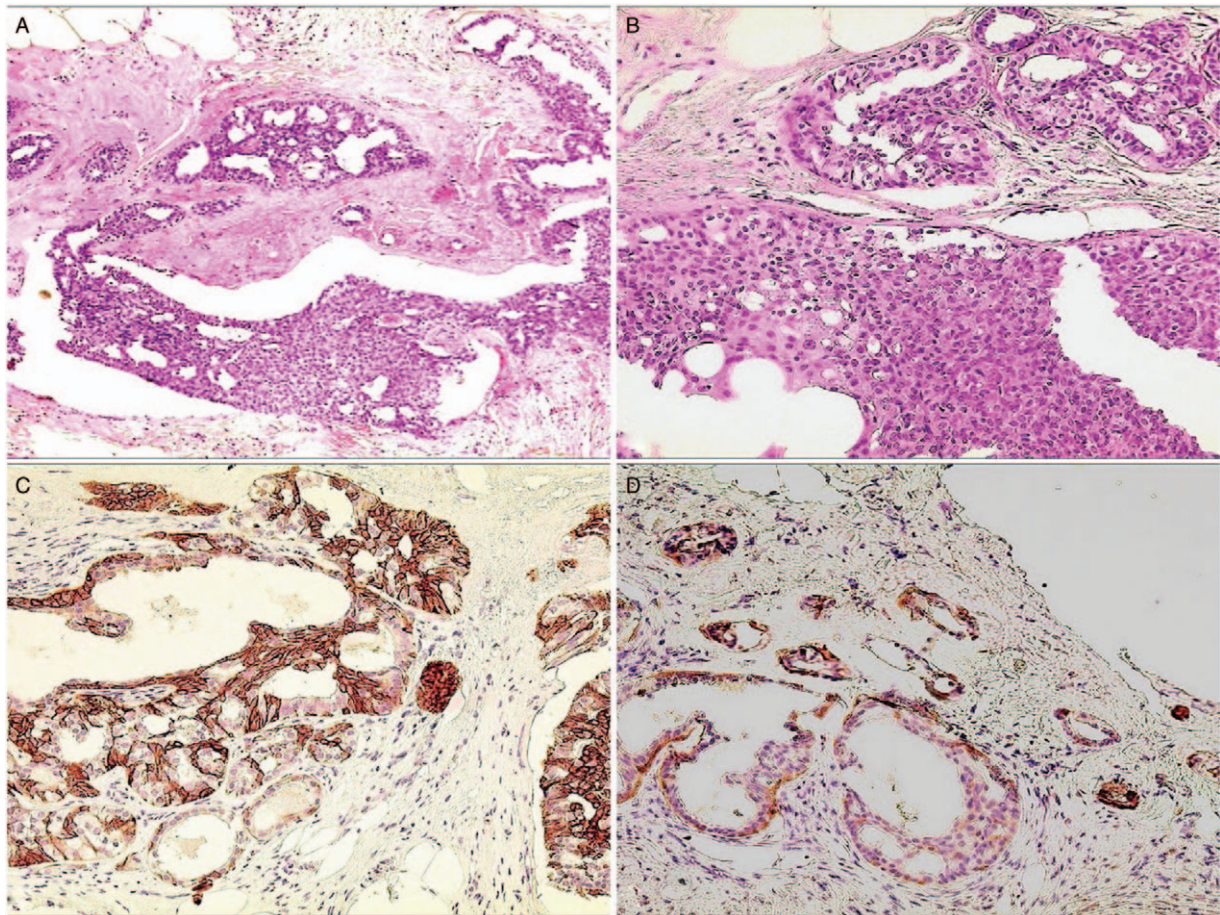
#### Conflicts of interest

None.

#### Author contributions

Zhao Y was responsible for study conception, design and drafted the manuscript. Wang WC performed the data analysis, summarized the clinical data. Lu T performed molecular investigation and performed pathological investigation.





**Figure 2:** Conventional pathological and immunohistochemical images of RSL. (A): There were distorted glands and hyperplastic epithelial nests in the sclerotic stroma (H & E, original magnification  $\times 200$ ). (B): A high-power microscope showed ductal hyperplasia (H & E, original magnification  $\times 400$ ). (C) Immunohistochemical staining of CK5/6 showed a mottled positive expression (original magnification  $\times 400$ ). (D): Immunohistochemical staining of calponin showed positive expression of myoepithelial cells (original magnification  $\times 400$ ). H & E: hematoxylin and eosin.

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