CASE REPORT

Cylindroma of the breast in a 72-year-old woman with fibrocystic disease first misdiagnosed as a malignant lesion in imaging studies

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SUMMARY

Cylindroma is a benign skin adnexal tumour with apocrine and trichoepitheliomatous differentiation that is rarely seen in the breast. Here, we report a case of cylindroma in the subareolar region of the left breast in a 72-year-old woman who presented with a palpable mass .Ultrasound and mammographic reports of the lesion were considered probably malignant. An ultrasound-guided core needle biopsy was performed and the patient underwent wide local excision with axillary lymph nodes biopsy. Immunohistochemistry and histopathological studies confirmed cylindroma with fibrocystic changes in uninvolved parenchyma.

BACKGROUND

Cylindroma is a benign skin adnexal tumour with apocrine and trichoepitheliomatous differentiation. Most often, they occur in a single form, but multiple variants may be found in patients with the Brooke-Spiegler syndrome, which is an autosomal dominantly inherited disorder located on the CYLD1 gene on chromosome16.[1] Multiple cylindromas are mostly located on the head, neck or scalp and sometimes coalesce with each other to produce turban tumour. Malignant transformation may occur rarely in a multiple tumour variant.[2 3] Until now, only a few breast cylindromas have been reported (11 cases); therefore, the rarity of this tumour could cause misdiagnosis and would be improper in performing invasive procedures. We report this case because of its rarity and unusual mammographic and ultrasound findings with difficulties in initial diagnosis and briefly discuss its histopathological findings with important differential diagnosis.

CASE PRESENTATION

A 72-year-old woman presented with a mass in her left breast of 2-month duration. In the medical history of the patient, no skin tumour or breast lesion was reported. On physical examination, a firm, non-tender mass in the subareolar region of the left breast without abnormality of the overlying skin was identified. There was no associated axillary lymphadenopathy.

INVESTIGATIONS

On screening craniocaudal (CC) and mediolateral oblique (MLO) mammographies in the central position of the patient's right breast, a macrocalcification with a benign appearance was seen. Also seen were a lobulated mass with a curvilinear calcification adjacent to the left nipple and multiple small lymph nodes in both the axillary areas with normal morphology (figure 1). On ultrasonography, a lobulated heterogeneous mass (20×10 mm) of notably increased echogenicity, containing an area of calcification and posterior acoustic enhancement in the superior portion of the left nipple, was detected (figure 2). The lesion was considered to be probably malignant (BIRADS: IV) and thus corresponded to a radiological grading (NHS breast screening system) score of M4 and U4 on mammographic and ultrasonic imaging, respectively. An ultrasound-guided core needle biopsy was performed. The received specimen consisted of one piece of a cylindrical cream-coloured tissue M 1×0.1 cm. Microscopic examination revealed small uniform cells with a fairly granular cytoplasm and oval nuclei arranged around cylinders of dense acellular hyaline material, which had a positive reaction in Periodic Acid Schiff (PAS) staining (figure 3A,B). The first pathological diagnosis was

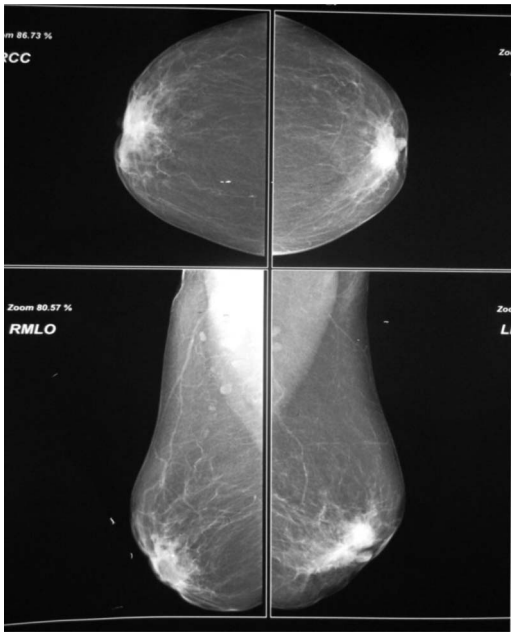

Figure 1 Screening mammography craniocaudal and mediolateral oblique views. A macrocalcification with a benign appearance in the right breast and a lobulated mass with a curvilinear calcification adjacent to the left nipple and multiple small lymph nodes in both the axillary areas.

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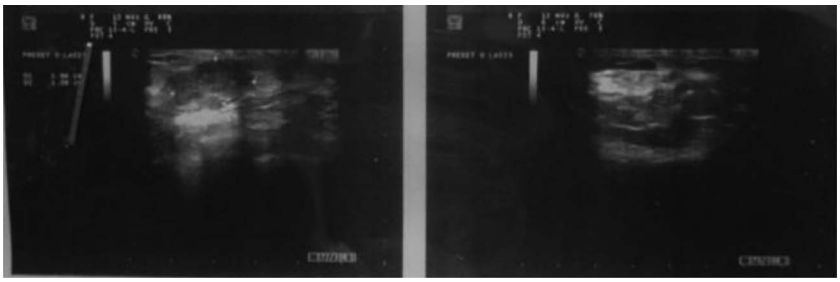

Figure 2 Ultrasonography of the right and left breasts of the patient. A lobulated heterogeneous mass of notably increased echogenicity containing an area of calcification and posterior acoustic enhancement in the superior portion of the left nipple.

intraductal papillomatosis, but after reviewing the literature, cylindroma of the breast was suggested. In order to attain definitive and differential diagnosis, Immunohistochemical (IHC) studies of the lesion were carried out. Neoplastic cells were immunoreactive for p63 (especially the outer myoepithelial cells), cytokeratin7 (the inner larger cells), anti smooth muscle actin (peripheral myo epithelial cells) and for S-100 protein (Langerhans cells), were immunoreactive to P63 (figure 4A–D); however, they were negative for the oestrogen, progesterone and Her2neu receptors. Thus, based on the histopathological and IHC studies, cylindroma was reported, but because of the probably malignant findings of mammography, ultrasound and the patient's age, the possible coexistence underlying malignancy of the frozen section was considered. The received frozen section specimen consisted of one piece of a creamish-yellow coloured tissue measuring 5×2×1.5 cm. On cut section tumoral lesion was appeared M 2 cm in largest diameter. Microscopic examination revealed a non-encapsulated but well-demarcated tumoral area composed of solid nests, trabeculae and lobules of neoplastic epithelial basaloid cells, which had small hyperchromatic nuclei arranged in a palisading pattern in the periphery in some areas admixed with larger cells having an eosinophilic cytoplasm and pale staining nuclei. In some foci, the tumour filled the large lactiferous ducts lumina with areas of calcification in the periphery. The nests, trabeculae and lobules were surrounded by a thickened, continuous hyaline basement membrane, which in a low power view produces a 'jigsaw' or mosaic pattern. Cytological atypia, pleomorphism and mitotic figures were not seen. Some small tubular formations filled with hyaline globules were also noticed. Fibrocystic changes were seen in the uninvolved breast parenchyma (figure 5A,B). There was no epidermal connection. The frozen section was suggestive of a benign lesion, but definitive diagnosis was deferred for permanent. A wide local excision with two enlarged axillary lymph nodes excisional biopsy was performed. The received specimen consisted of a yellowish-grey-coloured tissue M 8×7×2 cm. On the cut section, small cystic spaces appeared. Light microscopic examination revealed breast tissue without residual tumour and in some areas glands were cystically dilated lined by double to pseudostratified columnar epithelial cells. Axillary lymph nodes had a reactive pattern. Cylindroma without any underlying malignancy with areas of fibrocystic changes in the adjacent parenchyma was reported.

DIFFERENTIAL DIAGNOSIS

Two main tumours that should be differentiated from cylindroma are adenoid cystic carcinoma (solid variant) and basal cell carcinoma. Adenoid cystic carcinoma is differentiated from cylindroma by its nuclear hyperchromasia, atypism, mitotic figures and discontinuous hyaline membrane. Basal cell carcinoma is differentiated from cylindroma by its characteristic histopathological findings such as solid nests with a peripheral palisading pattern and connection to the overlying epidermis and absence of the thick hyaline basement membrane around the neoplastic nests. Intraductal papillomatosis also could have areas mimicking cylindroma but differentiated from it by its papillary pattern and lack of hyaline basement membrane and positive reaction to estrogen receptor and progestron receptor in IHC studies.

TREATMENT

Wide local excision with a few (two) axillary lymph nodes excisional biopsy were performed.

OUTCOME AND FOLLOW-UP

Seven months after diagnosis, no recurrence was detected and the general condition of the patient was good.

DISCUSSION

Cylindroma is a benign skin adnexal tumour mostly seen sporadically in a single pattern in the head and scalp, but multiple cylindromas may occur in hereditary forms.[2–4] Malignant transformation is rare in single forms and has been reported in multiple tumour variants. Cylindroma of the breast is a very rare lesion and was first described by Gokastan *et al*[4] in 2001; incidentally, it was found in a lumpectomy specimen for infiltrating lobular carcinoma. Solitary cylindromas affect middle-aged and elderly persons with a female preponderance.[4] In literature

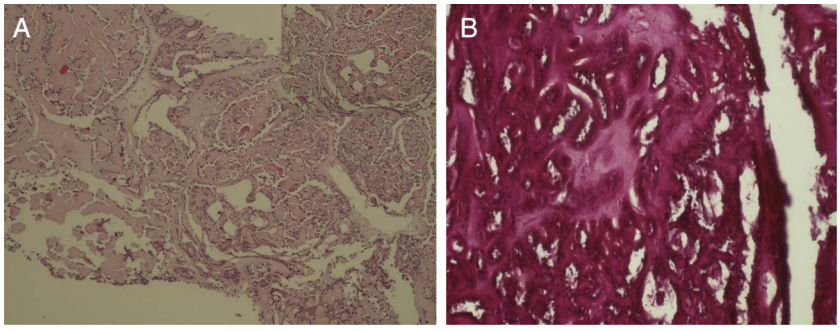

Figure 3 (A) Core needle biopsy showed a tumoral lesion composed of small round hyper chromatic cells arranged around cylinders of dense acellular hyaline material (H&E staining ×20). Inset (H&E ×40). (B) Hyaline membrane had a positive staining in Periodic Acid Schiff staining (objective ×20).

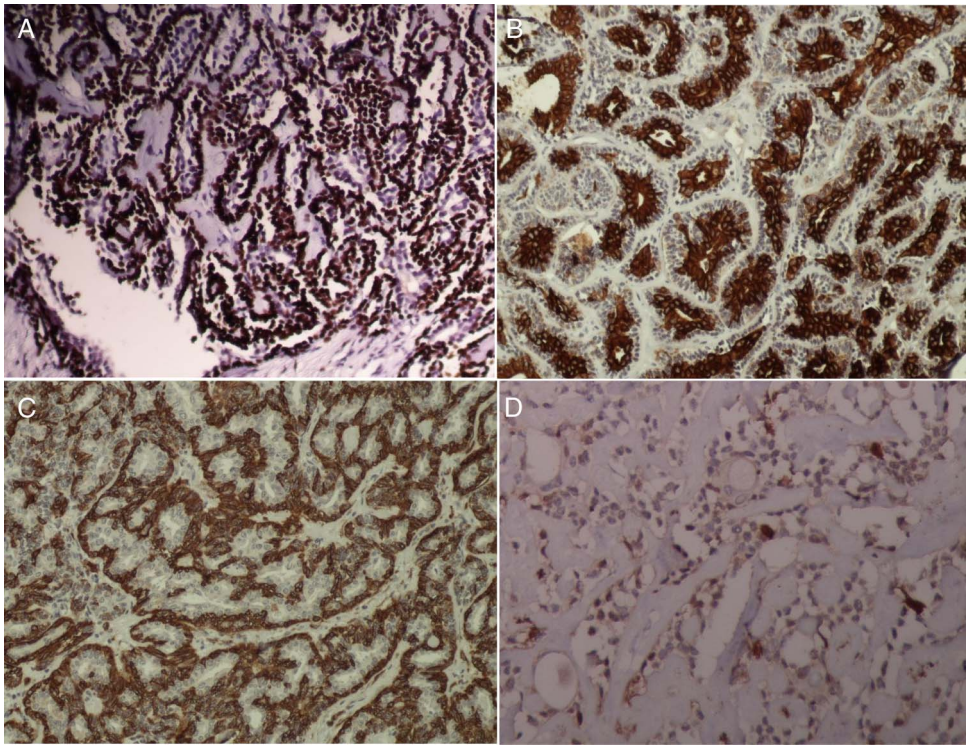

Figure 4 (A) By immunohistochemistry, the tumour cells were strongly positive for P63, especially the outer myoepithelial cells (objective ×20); (B) cytokeratin 7 was positive especially in the inner larger cells (objective ×20); (C) positive reaction of peripheral myoepithelial cells to antismooth muscle actin (objective ×20) and (D) positive reaction of Langerhans cells to S-100 protein (objective ×40).

reviews, six cases presented with symptomatic lesions, two cases on screening mammography, and three cases incidentally were found in the specimens of the removed breast tissues of suspicious infiltrating carcinoma.[1–6] Our case presented with a palpable mass lesion in the subareolar region of the left breast. The histopathological characteristic feature of cylindroma is similar to its dermal counterpart composed of nests of small hyper chrome cells and larger clear cells inside the nests surrounded by thick hyaline bands that are positively stained by PAS and immunoreactive for collagen IV. Neoplastic cells diffusely stained for pan cytokeratin and inner larger cells have a positive reaction for cytokeratin 7. Dendritic Langerhans cells between the tumour cells have a positive reaction to the S-100 protein. All the tumour cells are negative for the ER, PR and Her2 neu receptors. Peripheral myoepithelial cells are positive for p63 and antismooth muscle actin and have a main role in the secretion of mucopolysaccharide that surrounds the nests.[5] Mahmoud *et al*[2] reported cylindroma in a 62-year-old woman, which was discovered by a screening mammogram, without a family history and no underlying breast disease of the patient, but our case had fibrocystic changes in the uninvolved breast parenchyma. None of the reported cases in the literature had calcification, whereas our case had a crescent form calcification that produced malignant features in both the ultrasound and mammographic findings. In 2004, Wang *et al*[3] reported a case of breast cylindroma in a 54-year-old woman who had a family and personal history of dermal cylindroma on the head and neck, but our patient did not have any family or medical history. Albores Saavedra *et al* reported four breast cylindromas; one of them was located in the proximal part of the large lactiferous duct. They found that, in the retroalveolar cylindromas, several ductal-lobular involvements may be detected.[4] Similarly, the lesion in our patient was located in the subareolar area with large ducts involvement and fibrocystic changes in the adjacent parenchyma. The two main differential diagnoses of cylindroma are adenoid cystic carcinoma, especially solid form, and basal cell carcinoma and should be excluded in all suspected cylindroma of the breast lesions. Adenoid cystic carcinoma (ACC) is

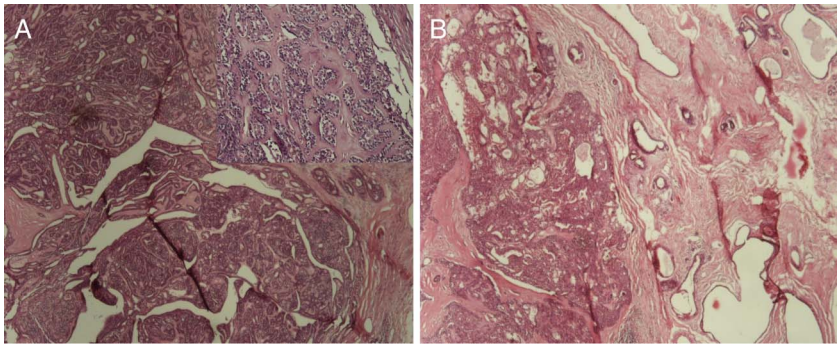

Figure 5 (A) Tumoral lesion filled the lactiferous duct (H&E ×20) and (B) fibrocystic changes in uninvolved parenchyma (H&E objective ×20).

an uncommon malignant tumour that arises within secretory glands most commonly seen in the major and minor salivary glands of the head and neck regions. Other uncommon areas involved by this neoplasm are the trachea, lacrimal gland, skin, vulva and is also a very rare tumour in the breast that only consist of 1% of all breast carcinoma with a good prognosis and rarely metastasis to other organs.[2 4 6] Histologically, ACC is composed of epithelial and myoepithelial cells arranged in cribriform, tubular and solid growth patterns. Some of the tubules contain mucin inside their lumina and the neoplastic cells have a nuclear pleomorphism, cytologic atypia and conspicuous mitotic figures. Lack of a surrounding thickened, band like hyaline basement membrane and absence of Langerhans cells are the clues for differentiating it from cylindroma.[7 8] Basal cell carcinoma is differentiated from cylindroma by its characteristics features composed of islands of basaloid cells with a peripheral palisading pattern, retracted stroma from the islands and no surrounding thick hyaline basement membrane.[7 8] In basal cell carcinoma, involvement of the overlying skin tissue with epidermal connection is seen, which differentiates it from cylindroma. Our case was first misdiagnosed as intraductal papillomatosis which inside the large duct's epithelial cells are proliferated and arranged in papillary formations without surrounding by thick hyaline basement membrane and cells are positive for ER and PR. Also, in the frozen section, it caused difficulty in diagnosis because of an intraductal component with calcifications in the periphery and hyperchromasia of the neoplastic cells nuclei. All the reported cases of breast cylindroma did not relapse and were treated by local excision. Only in the cases of associated infiltrating carcinomas were mastectomy recommended. The prognosis of cylindroma without recurrence in the breast was excellent.

Learning points

- Although cylindroma is a rare benign tumour in old age patients with a breast mass, it should be considered as a differential diagnosis especially when the lesion is located in the retroareolar area or inside the lactiferous ducts.
- Cylindroma may occur in a breast with fibrocystic changes and areas of calcification that mimic a malignant lesion.
- Adenoid cystic carcinoma (especially solid variant) and basal cell carcinoma should be considered as two main differential diagnoses plus breast cylindroma and for differentiation of these tumours from each other beyond histopathological criteria, such as mitosis, pleomorphism and atypism. Immunohistochemical studies are necessary.

Competing interests None.

Patient consent Obtained.

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