Clear Cell Hidradenoma of the Breast Diagnosed on a Core Needle Biopsy
A case report and review of the literature

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Abstract: Clear cell hidradenoma (CCH) is a tumour originating from the eccrine sweat glands. It usually presents in the limbs, axilla or trunk. CCH of the breast is rare and can present as a cystic lesion in the breast that can be easily misdiagnosed as malignancy. We report a 36-year-old female patient who presented at the Sultan Qaboos University Hospital Breast Clinic, Muscat, Oman, in 2018 with a lump in her left breast. Ultrasound examination reported a complex cystic lesion with a solid, vascular component. An ultrasound-guided core needle biopsy was suggestive of clear cell hidradenoma. Surgical excision was performed and histopathology confirmed the diagnosis of CCH of the breast. This is the first ever case of a diagnosis of CCH made using core needle biopsy. CCH can be challenging to diagnose; therefore, awareness of its histopathological and ultrasonographic features are essential to avoid misdiagnosis and over treatment.

Keywords: Eccrine Glands; Breast; Acrospiroma; Sweat Gland Adenoma; Sweat Gland Neoplasms; Case Report; Oman.

Case Report
A 36-year-old female patient presented to the One-Stop Breast Clinic at the Sultan Qaboos University Hospital, Muscat, Oman, in 2018 with a four-month history of a painless lump in her left breast. She denied any history of pain, fever, nipple discharge or trauma.

the best of the author’s knowledge, this is the first case report to describe clear cell hidradenoma (CCH) of the breast diagnosed using core needle biopsy. Only four other reports have been able to diagnose this condition on cytological examination prior to excision with the aid of a fine needle aspiration. In addition, this report presents a review of the existing literature on this rare entity.
Her mother had been diagnosed with breast cancer at the age of 45.

Clinical examination revealed a single, firm, non-tender, mobile lump measuring 2 × 2 cm in the left breast at the three o’clock position. It was not fixed to the skin. Overlying skin, nipple and areola were normal. Ipsilateral lymph nodes were not enlarged.

An ultrasound of the breast revealed a complex cystic mass with a solid, vascular component seen in the posterolateral border, characteristic of a clear cell hidradenoma of the breast [Figure 1]. The lesion was classified as Breast Imaging Reporting and Data System category 4. The patient underwent ultrasound-guided 14 gauge core needle biopsy, targeting the solid component. The cystic component was completely collapsed after the fourth pass.

Microscopic examination of the biopsy showed nodules formed of sheets of uniform cells traversed by fibrovascular septa. The cells had round nuclei with even chromatin. Some cells had intracytoplasmic vacuoles containing mucin. The cytoplasm varied from eosinophilic to clear. There was no nuclear pleomorphism, mitosis or necrosis [Figure 2]. The cells were diffusely positive for p63 and negative for androgen receptor, oestrogen receptor, gross cystic disease fluid protein 15 and carcinoembryonic antigen [Figure 3]. The pathological diagnosis was consistent with clear cell hidradenoma.

Surgical excision of the tumour was recommended and was performed six months later. Ultrasound of the breast before the surgery showed the cystic component had reaccumulated and become larger than indicated in the previous scan. Microscopic examination of the resected specimen revealed breast tissue with well-circumscribed but unencapsulated multinodular lesion, formed by sheets of uniform cells and fibrovascular septa [Figure 4]. The cytomorphology of the cells and the immunoprofile was similar to the biopsy, confirming the diagnosis of clear cell hidradenoma. The postoperative course was uneventful. The patient has been disease free during the follow-up period of 18 months.

Discussion

CCH is an uncommon benign adnexal skin tumour, originating from eccrine sweat glands of the superficial and deep layers of the dermis. Other names include
Table 1: Details of cases of clear cell hidradenoma published between 1968–20191–26

| Author and year of publication | Gender | Age in years | Breast side | Location               | Size of largest diameter in cm | Presenting complaint                      |
|-------------------------------|--------|--------------|-------------|------------------------|--------------------------------|------------------------------------------|
| Finck et al.1 (1968)          | F      | 46           | NS          | Upper inner quadrant   | 4                              | Nipple discharge                         |
|                               | F      | 61           | Right       | Upper outer quadrant   | 3                              | Breast mass                              |
|                               | M      | 42           | Left        | Subareolar             | 2                              | Nipple enlargement                       |
|                               | F      | 42           | Left        | Nipple                 | 0.7 (multiple)                 | Nipple discharge                         |
|                               | F      | 60           | NS          | Subareolar             | NS                             | Breast mass                              |
|                               | F      | 30           | Right       | Nipple                 | 1.5                            | Breast mass                              |
| Hertel et al.2 (1976)         | F      | 57           | NS          | Subareolar             | 2                              | Nipple discharge                         |
| Kobayashi et al.3 (1994)      | M      | 63           | Left        | Nipple                 | 3                              | Nipple discharge                         |
| Cyrlak et al.4 (1995)         | F      | 25           | Right       | Inner quadrant         | 7                              | Breast mass and nipple discharge         |
| Kumar and Verma5 (1996)       | F      | 75           | Left        | Upper inner quadrant   | 3                              | Breast mass                              |
| Kaise et al.6 (1996)          | F      | 52           | NS          | Upper inner quadrant   | NS                             | NS                                       |
| Domoto et al.7 (1998)         | F      | 58           | Left        | Outer lower quadrant   | 3                              | Breast mass                              |
|                               | M      | 44           | Left        | Subareolar             | 2                              | Nipple discharge                         |
| Shimizu et al.8 (1999)        | M      | 60           | Right       | Upper inner quadrant   | 3.5                            | Breast mass                              |
| Yamada et al.9 (2001)         | F      | 41           | Left        | Outer upper            | 2                              | Breast mass                              |
| Kosugi et al.10 (2002)        | F      | 25           | Right       | Axillary tail          | 2                              | Breast mass                              |
| Honnma et al.11 (2002)        | M      | 77           | NS          | Subareolar             | NS                             | NS                                       |
| Ghai and Bukhanov12 (2004)    | F      | 77           | Left        | Axillary tail          | 2.5                            | Breast mass                              |
| Kim et al.13 (2005)           | F      | 41           | Right       | NS                     | NS                             | Breast mass                              |
| Kazakov et al.14 (2007)       | F      | 55           | Left        | Upper outer quadrant   | 1.6                            | Breast mass                              |
| Ohi et al.15 (2007)           | F      | 55           | Left        | Upper inner quadrant   | 0.8                            | Breast mass                              |
| Girish et al.16 (2007)        | F      | 49           | Left        | Subareolar             | 3                              | Recurrent breast mass                    |
| Dhingra et al.17 (2007)       | F      | 60           | Right       | Upper outer quadrant   | 4.5                            | Breast mass                              |
| Mote et al.18 (2009)          | F      | 40           | Left        | Outer quadrant         | 5                              | Breast mass                              |
| Cho et al.19 (2010)           | F      | 56           | Left        | Axillary tail          | 3                              | Breast mass                              |
| Grampurohit et al.20 (2011)   | M      | 18           | Left        | Subareolar             | 4                              | Breast mass and nipple discharge         |
| Orsaria and Mariuzzi21 (2013) | M      | 39           | Left        | Upper outer quadrant   | 1                              | Recurrent breast mass                    |
| Ogata et al.22 (2013)         | M      | 38           | Right       | NS                     | 1.8                            | Breast mass and nipple discharge         |
| Sehgal et al.23 (2014)        | F      | 30           | Left        | Upper outer quadrant   | 2.5                            | Breast mass                              |
| Kashyap and Jyoti24 (2015)    | F      | 23           | Left        | Subareolar             | 4.5                            | Breast mass                              |
| Ano-Edward et al.25 (2018)    | M      | 62           | Left        | NS                     | 6                              | Breast mass                              |
| Jaitly et al.26 (2019)        | F      | 20           | Right       | Upper outer quadrant   | 5                              | Breast mass                              |
| Current case                  | F      | 32           | Left        | Upper outer quadrant   | 3                              | Breast mass                              |

F = female; NS = not specified; M = male.
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...clear cell hidradenoma.7,12,23 CCH may be associated with sporadic or hereditary genetic mutations.14,27,28 It is mostly observed in the age group of 20–50 years, and is twice as common among women than men.19 It is known to commonly occur in the scalp, face, upper extremity, axilla, trunk and pubic region.

However, CCH of the breast is extremely rare; only 33 cases have been reported [Table 1]. CCH can easily be confused with other causes of breast lumps and misdiagnosis can lead to unnecessary anxiety and over-treatment. Hertel et al. classified CCH of the breast as a type of true adenoma of the breast.2 It has two distinct histogenetic origins, one from skin adnexal glands and another from mammary ducts.7,20

CCH of the breast shows features similar to those occurring elsewhere in the body.11 A review of the 33 reported cases revealed that it has a female predominance in ages ranging from 18–77 years. There is a predominance of the left breast and it occurs in the nipple and subareolar region in more than 50% of cases.7,17 The size can range from 0.7–7 cm. The most common presenting complaint is a painless breast mass but some patients can also present with nipple discharge, bluish discoloration of the overlying skin or ulceration.5,26 CCH can easily be misdiagnosed preoperatively as a carcinoma of the breast.

To avoid misdiagnosis, the patient should undergo imaging after a breast mass has been identified. Radiological features of CCH are non-specific, but described as superficial, well circumscribed and consisting of a cystic and solid portion. The cystic portion may appear complex due to haemorrhage while the solid portion is typically hypervascular on Doppler examination. Aspiration of the lesion reveals clear or haemorrhagic fluid content.

In all reported cases, only one case correctly diagnosed CCH based on fine needle aspiration cytology.3 The remaining cases were diagnosed on histopathology of the excised specimen. One case reported that the initial cytology was suggestive of malignancy and the diagnosis of CCH was made only after mastectomy.5 In another case, the intraoperative frozen histopathology section was inconclusive, therefore surgery was abandoned until the permanent preparation reported CCH.9 The current case distinguishes itself from others as the diagnosis of CCH was based on a core needle biopsy of the solid component prior to offering treatment, thus sparing the patient from an unnecessary mastectomy or wide local excision.

On histopathology, the tumour is located in the dermis, lobulated and well circumscribed. The solid portion is vascular, consisting of round polyhedral cells that contain a round nucleus, eosinophilic cells with clear glycogen-rich cytoplasm and transitional cells in between.5,8,20,22,28 The clear cells are typically Periodic acid-Schiff diastase resistant and stain positive for p63, keratin, epithelial membrane antigen, carcinoembryonic antigen, s-100 and Vimentin but negative for alpha-smooth muscle actin, cluster of differentiation-10, oestrogen receptor and progesterone receptor.15,17,20 The only myoepithelial marker that stains positively is p63 and it is therefore an important marker to consider in the diagnosis of clear cell hidradenoma.15

Treatment of CCH in the breast is complete surgical excision of the tumour with safe margins. Incomplete excision may result in recurrence. Malignant transformation is reported in 5% and is difficult to predict because the clinical presentation and histology are similar.16,18,20

Awareness of this diagnosis and its characteristic histological and sonographic appearance is important. With correct diagnosis, the appropriate management can be undertaken, negating unnecessary over- or under-treatment. In the current case, the patient was successfully diagnosed with CCH at the One-Stop Breast Clinic using a 14 gauge core needle biopsy. With this diagnosis, the patient was offered complete excision with appropriate margins. By doing so, the risk of recurrence was minimised, while avoiding unwarranted breast resections, chemotherapy or radiotherapy.

Conclusion

This is the first case report that describes CCH of the breast diagnosed using core needle biopsy. Awareness of the radiological and histopathological appearance of this extremely rare benign tumour is important to reduce misdiagnosis and over-treatment. CCH should be suspected as a differential diagnosis of complex cystic breast lesions. It should be remembered that fine needle aspiration cytology and core needle biopsies play an important role in the pre-operative diagnosis.

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