Sultan Qaboos University Med J, August 2020, Vol. 20, Iss. 3, pp. e357–361, Epub. 5 Oct 20
Submitted 3 Jan 20
Revision Req. 1 Mar 20; Revision Recd. 30 Mar 20
Accepted 27 Apr 20
https://doi.org/10.18295/squmj.2020.20.03.017

CASE REPORT

Clear Cell Hidradenoma of the Breast Diagnosed on a Core Needle Biopsy

A case report and review of the literature

*Sara S. H. Al-Adawi,[1] Badriya Al-Qasabi,[2] Maiya Al-Bahri,[3] Adil Aljarrah,[4] Suad Al-Aghbari[4]

تشخيص ورم غدي عرقي صافي الخلايا في الثدي بإستخدام خزعة الإبرة اللبية

تقرير حالة ومراجعة الأدبيات

سارة العدوية، بدرية القصابية، ميا البحرية، عادل الجراح، سعاد الأغبرية

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.

الملخص: الورم الغدي العرقي صافي الخلايا هو ورم مصدره الغدد العرقية الناتحة، يظهر عادة في الأطراف أو الإبط أو الجذع. يعتبر هذا الورم نادرا وقد يظهر على شكل آفة كيسية في الثدي والذي يمكن تشخيصه بشكل خاطئ وبسهولة على أنه ورم خبيث. نعرض هنا حالة مريضة تبلغ من العمر 36 عاما قدمت إلى عيادة الثدي في مستشفى جامعة السلطان قابوس في مسقط، سلطنة عُمان في سنة 2018 وكان لديها كتلة في ثديها الأيسر. أظهر جهاز الموجات فوق الصوتية وجود آفة كيسية معقدة ذات مكون وعائي صلب. كانت خزعة الإبرة اللبية الموجهة بالموجات فوق الصوتية توحي بوجود ورم غدي عرقي صافي الخلايا. تم إجراء الاستئصال الجراحي وأكد التشريح المرضي النسيجي تشخيص ورم غدي عرقي صافي الخلايا في الثدي. تعتبر هذه الحالة الاولى على الإطلاق التي يتم فيها تشخيص هذا الورم باستخدام خزعة الإبرة اللبية. يشكل تشخيص هذا الورم تحديا لذلك فإن الوعي بخصائص التشريح المرضي النسيجي والموجات فوق الصوتية للورم مهم جدا لتفادي التشخيص الخاطئ والمبالغة في العلاج.

الكلمات المفتاحية: غدد ناتحة؛ ثدي؛ ورم نهايات الغدد العرقية ؛ ورم الغدة العرقية الحميد؛ أورام الغدة العرقية؛ تقرير حالة؛ عُمان.

Clear cell hidradenoma (CCH) is a rare benign tumour of the eccrine glands. It is commonly observed in the face and upper extremities. CCH of the breast is extremely rare and only 33 cases have been reported worldwide at the time of this report.[1–26] CCH has been classified by Hertel *et al*. as a type of true adenoma of the breast.[2] The diagnosis can be challenging as its radiological and cytological findings can mimic other conditions of the breast. In addition, the breast is a modified apocrine gland; therefore histogenetically, CCH of the breast can arise from both eccrine glands and mammary ducts.[7] Finck *et al*. suggested that CCH of the breast is a form of mammary ductal papillomatosis, thus explaining why CCH may present as a mass in the deep tissues of the breast with no apparent relation to the skin.[1] To 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.

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.

[1]*Department of General Surgery, Oman Medical Speciality Board, Muscat, Oman; Departments of* [4]*General Surgery,* [2]*Radiology and* [3]*Pathology, Sultan Qaboos University Hospital, Muscat, Oman*

**Corresponding Author's e-mail: sara93916@gmail.com*

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

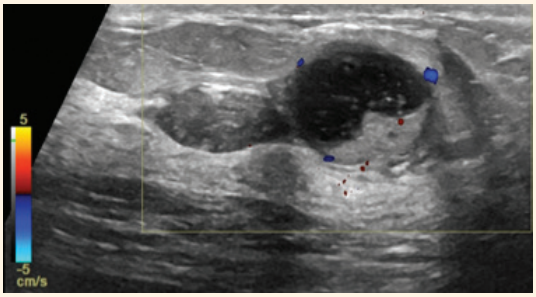

Figure 1: Ultrasound of a lesion in the left breast of a 36-year-old female patient demonstrating a cystic mass with solid, vascular component in the posterolateral border.

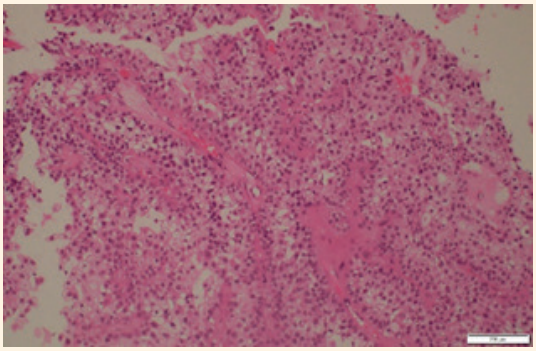

Figure 2: Haemotoxylin and eosin stain at x20 magnification of the core needle biopsy demonstrating sheets of apocrine cells with clear cytoplasm, separated by fibrous *septa*.

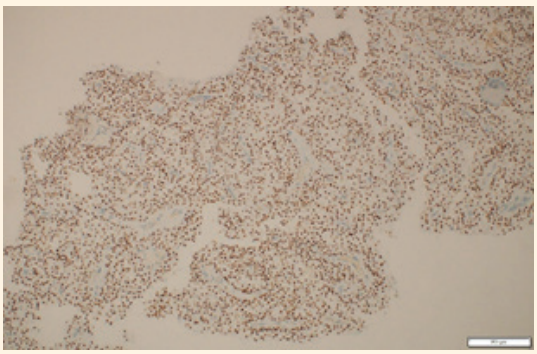

Figure 3: p63 immune stain at x20 magnification showing diffuse nuclear positivity in tumour cells.

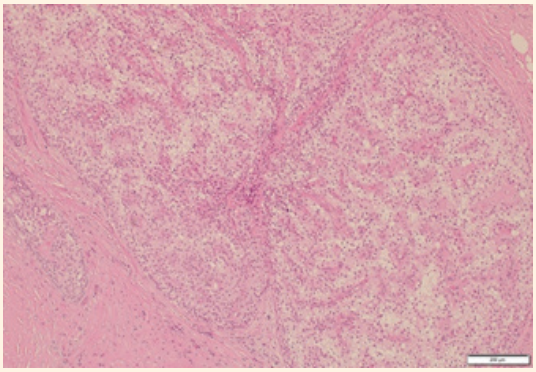

Figure 4: Haematoxylin and eosin stain at x20 magnification of the resected specimen revealing a lesion with nodules formed of sheets of uniform cells traversed by fibrovascular *septa*. The cytomorphology of the cells is bland.

Table 1: Details of cases of clear cell hidradenoma published between 1968–2019[1–26]

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 Verma[5] (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 Bukhanov[12] (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 Mariuzzi[21] (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 Jyoti[24] (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.

eccrine acrospiroma, nodular hidradenoma and solid-cystic 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.[17] 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 discolouration 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 Vimetin 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.

References

1. Finck FM, Schwinn CP, Keasbey LE. Clear cell hidradenoma of the breast. Cancer 1968; 22:125–35. https://doi.org/10.1002/1097-0142(196807)22:1<125::aid-cncr2820220115>3.0.co;2-3.

2. Hertel BF, Zaloudek C, Kempson RL. Breast adenomas. Cancer 1976; 37:2891–905. https://doi.org/10.1002/1097-0142(197606)37:6<2891::aid-cncr2820370647>3.0.co;2-p.

3. Kobayashi T, Miyake Y, Shinagawa M, Maeda Y, Tsujimoto S, Miura M. Clear cell hidradenoma of the male breast nipple. J Jpn Soc Clin Cytol 1994; 33:745–6. https://doi.org/10.5795/jjscc.33.745.

4. Cyrlak D, Barr RJ, Wile AG. Malignant eccrine acrospiroma of the breast. Int J Dermatol 1995; 34:271–3. https://doi.org/10.1111/j.1365-4362.1995.tb01595.x.

5. Kumar N, Verma K. Clear cell hidradenoma simulating breast carcinoma: A diagnostic pitfall in fine-needle aspiration of breast. Diagn Cytopathol 1996; 15:70–2.

6. Kaise H, Sakamoto G, Akiyama F, Iwase T, Yoshimoto M, Tsuzuku M, et al. Clear cell hidradenoma of the breast-A case report. Nyuugann no Rinsyou 1996; 11:113–16.

7. Domoto H, Terahata S, Sato K, Tamai S. Nodular hidradenoma of the breast: Report of two cases with literature review. Pathol Int 1998; 48:907–11. https://doi.org/10.1111/j.1440-1827.1998.tb03860.x.

8. Shimizu K, Nishikawa M, Sasaki H, Misaka K, Ueda Y, Fujimori T, et al. Cytologic findings of clear cell hidradenoma in the male breast skin: A case report. J Jpn Soc Clin Cytol 1999; 38:342–7. https://doi.org/10.5795/jjscc.38.342.

9. Yamada M, Miyata A, Kawai K, Kawano H. Clear cell hidradenoma associated with hemartoma of the breast - report of a case. J Jpn Surg Assoc 2001; 62:53–7. https://doi.org/10.3919/jjsa.62.53.

10. Kosugi I, Kasahara Y, Tatsuzawa A. A case of clear cell hidradenoma mimicking a cystic tumor of the breast. J Jpn Surg Assoc 2002; 63:571–4. https://doi.org/10.3919/jjsa.63.571.

11. Honnma N, Takubo K, Kuroiwa K, Arai T, Sawabe M, Akiyama F, et al. Clear cell hidradenoma of the male breast – A case report. Nyuugann no Rinsyou 2002; 17:346–8.

12. Ghai S, Bukhanov K. Eccrine acrospiroma of breast: Mammographic and ultrasound findings. Clin Radiol 2004; 59:1142–4. https://doi.org/10.1016/j.crad.2004.05.002.

13. Kim YO, Jeon CW, Chang HK. Fine needle aspiration cytology of eccrine acrospiroma of the breast: Report of a case misdiagnosed as ductal carcinoma. Korean J Cytopathol 2005; 16:31–5.

14. Kazakov DV, Vanecek T, Belousova IE, Mukensnabl P, Kollertova D, Michal M. Skin-type hidradenoma of the breast parenchyma with t(11;19) translocation: Hidradenoma of the breast. Am J Dermatopathol 2007; 29:457–61. https://doi.org/10.1097/DAD.0b013e318156d76f.

15. Ohi Y, Umekita Y, Rai Y, Kukita T, Sagara Y, Sagara Y, et al. Clear cell hidradenoma of the breast: A case report with review of the literature. Breast Cancer 2007; 14:307–11.

16. Girish G, Gopasetty M, Stewart R. Recurrent clear cell hidradenoma of the breast: A case report. Internet J Surg 2007; 10:1–3. https://doi.org/10.5580/1a7a.

17. Dhingra KK, Mandal S, Khurana N. An unusual case of nodular hidradenoma of breast. Iran J Pathol 2007; 2:80–2.

18. Mote DG, Ramamurti T, Naveen Babu B. Nodular hidradenoma of the breast: A case report with literature review. Indian J Surg 2009; 71:43–5. https://doi.org/10.1007/s12262-009-0010-y.

19. Cho KE, Son EJ, Kim JA, Youk JH, Kim EK, Kwak JY, et al. Clear cell hidradenoma of the axilla: A case report with literature review. Korean J Radiol 2010; 11:490–2. https://doi.org/10.3348/kjr.2010.11.4.490.

20. Grampurohit VU, Dinesh US, Rao R. Nodular hidradenoma of male breast: Cytohistological correlation. J Cytol 2011; 28:235–7. https://doi.org/10.4103/0970-9371.86364.

21. Orsaria M, Mariuzzi L. Recurrent eccrine hidradenoma of the breast in a male patient: Problems in differential diagnosis. Our Dermatol Online 2013; 4:215–17. https://doi.org/10.7241/ourd.20132.52.

22. Ogata H, Kanazawa S, Saito F, Kubota Y, Mitsuda A, Kaneko H. Male breast clear cell hidradenoma —A case report and literature review—. Nihon Rinsho Geka Gakkai Zasshi 2013; 74:1193–7. https://doi.org/10.3919/jjsa.74.1193.

23. Sehgal S, Goyal P, Ghosh S, Mittal D, Kumar A, Singh S. Clear cell hidradenoma of breast mimicking atypical breast lesion: A diagnostic pitfall in breast cytology. Rare Tumors 2014; 6:5343. https://doi.org/10.4081/rt.2014.5343.

24. Kashyap S, Jyoti K. Acrospiroma of breast: A rare clinically significant differential diagnosis in breast lump - A case report. J Evol Med Dent Sci 2015; 4:12614–17. https://doi.org/10.14260/jemds/2015/1817.

25. Ano-Edward GH, Amole IO, Adesina SA, Ajiboye OA, lasisi ME, Jooda RK. Nodular hidradenoma of the breast: A case report. Alex J Med 2018; 54:367–8. https://doi.org/10.1016/j.ajme.2018.04.004.

26. Jaitly V, Jahan-Tigh R, Belousova T, Zhu H, Brown R, Saluja K. Case report and literature review of nodular hiradenoma, a rare adnexal tumor that mimics breast carcinoma, in a 20-year-old woman. Lab Med 2019; 50:320–5. https://doi.org/10.1093/labmed/lmy084.

27. Behboudi A, Winnes M, Gorunova L, Oord JJ van den, Mertens F, Enlund F, et al. Clear cell hidradenoma of the skin—a third tumor type with a t(11;19)-associated TORC1–MAML2 gene fusion. Genes Chromosomes Cancer. 2005 Feb 23;43(2):202–5.

28. Kocjan G. Diagnostic Dilemmas in FNAC Cytology: Difficult Breast Lesions. In: Fine Needle Aspiration Cytology: Diagnostic Principles and Dilemmas. Heidelberg, Germany: Springer Verlag GmbH, 2006. Pp. 181–211. https://doi.org/10.1007/3-540-31412-1_9.