International Journal of Research and Review
Vol. 10; Issue: 2; February 2023
Website: www.ijrrjournal.com
Case Report *E-ISSN: 2349-9788; P-ISSN: 2454-2237*

Autopsy Pathology of Invasive Lobular Carcinoma of the Breast: A Case Report

Offiah, A.U.[1], Amadi, A.N.[2], Azuamah, Y.C.[3], Igwe, F.E.[1], Onyesom, E.[1]

[1]College of Medicine and Health Sciences, Abia State University, Nigeria
[2]Department of Public Health, Federal University of Technology, Owerri, Nigeria
[3]Department of Optometry, Federal University of Technology, Owerri, Nigeria

Corresponding Author: Offiah, A.U.

DOI: https://doi.org/10.52403/ijrr.20230232

ABSTRACT

The cause of death can be determined by performing an autopsy. This study reviewed the autopsy pathology performed on a 54 year old woman who died of invasive lobular carcinoma of the breast. The autopsy was performed at Abia State University Teaching Hospital, Aba, Nigeria. She presented with fever and generalized body weakness of one week duration and was being treated for malaria and typhoid fever. Her condition deteriorated in two days of hospitalization despite the treatment given and she later passed away. Autopsy findings revealed that the breasts were symmetrical and the overlying skin was grossly normal. There was no area of ulceration or change in the skin. The nipples were not retracted. Cut sections of both breasts showed diffuse white fibrous tissue in areas and no obvious lymphadenopathy was noted. Histologic sections of the breast tissue showed uniform small bland cells with round nuclei and inconspicuous nucleoli invading a fibrotic fibrocollagenous stroma and adipocytes in single files. There was poor attempt at tubule formation. Histological section of the lungs showed infiltration by malignant epithelial cells similar to ones seen in the breast. There were haemorrhages, congestion and edema in the alveolar interstitium, and some of the alveolar were filled with fibrinous material. Also seen were numerous mixed inflammatory cell infiltrates. The final diagnosis was invasive lobular carcinoma of the breast, with widespread metastasis to the lungs, pleural and peritoneum. The cause of death was ruled as invasive lobular carcinoma of the breast. A thorough autopsy of deaths of women of postmenopausal age was recommended in other to identify associated pathologies.

Keywords: Breast cancer, Invasive lobular carcinoma, Invasive ductal carcinoma, Autopsy

INTRODUCTION

Invasive lobular carcinoma (ILC) is a type of breast cancer that begins in the milk-producing glands (lobules) of the breast. [1] Invasive cancer means the cancer cells have broken out of the lobule where they began and have the potential to spread to the lymph nodes and other areas of the body. Invasive lobular carcinoma makes up a small portion of all breast cancers. The most common type of breast cancer begins in the breast ducts (invasive ductal carcinoma). As it grows larger, invasive lobular carcinoma may cause an area of thickening in part of the breast, a new area of fullness or swelling in the breast, a change in the texture or appearance of the skin over the breast such as dimpling or thickening and a newly inverted nipple. Invasive lobular carcinoma begins when cells in one or more milk-producing glands of the breast develop mutations in their DNA. [2] The mutations lead to the inability to control cell growth, which results in the cells dividing and growing rapidly. Depending on the aggressiveness of the cancer type, the cancer cells can spread to other parts of the body. Lobular carcinoma cells tend to

invade breast tissue by spreading out in a distinct way rather than forming a firm nodule. The affected area may have a different feel from the surrounding breast tissue, more like a thickening and fullness, but it's unlikely to feel like a lump.

Women are more likely to develop breast cancer, but men also can develop breast cancer. The risk of breast cancer increases with age. Women with invasive lobular carcinoma tend to be a few years older than women diagnosed with other types of breast cancer. The use of the female hormones, estrogen and progesterone during and after menopause has been shown to increase the risk of invasive lobular carcinoma. [3] Women with a rare inherited condition called hereditary diffuse gastric cancer syndrome have an increased risk of both stomach (gastric) cancer and invasive lobular carcinoma. The risk of invasive lobular carcinoma is high in female mutation carriers, as about 50% are expected to develop the disease. [4] Carriers must therefore undergo intensive breast cancer screening, with, for example, yearly magnetic resonance imaging and mammogram starting at age 30 years. Invasive lobular carcinoma accounts for 5%–15% of all invasive breast cancers and is the second most common type of breast cancer behind invasive ductal carcinoma of no special type. [5]

Recently there has been a marked increase in the incidence of ILC, mainly among the post-menopausal population. This is likely the result of improved diagnostic techniques and the use of hormone replacement therapy. ILC has a distinct biological profile and thus presents unique challenges with regard to systemic treatment and management of the disease. Hallmark features of ILC include; the loss of cell-cell adhesion molecule E-cadherin, resulting in small, discohesive cells proliferating in single-file strands, positivity for both the estrogen and progesterone receptor, and human epidermal growth factor receptor 2 negativity. [6] These key pathological features alongside the diffuse growth pattern of ILC make establishing a diagnosis particularly challenging. ILC is difficult to detect both upon physical examination and with standard imaging techniques. However magnetic resonance imaging (MRI) has a reported greater sensitivity in the detection and characterization of ILC than "gold standard" mammography. [7] Systemic therapy is an integral part of the multidisciplinary approach to treating breast cancer and this often involves the use of chemotherapy. However, due to the unique molecular biology of ILC, treatment response to chemotherapy is often predictably poor, resulting in lower rates of complete pathological response thus leading to an increase in mastectomy rates in these patients. On the other hand, studies [8,9] have shown that ILC responds well to endocrine therapy, making it the optimal choice in the treatment of ILC. A deeper understanding of the unique molecular profile and alterations that define this breast cancer subtype will lead the way in improving diagnosis, management, and treatment outcomes for patients with ILC. This study reviews the autopsy pathology of a 54 year old woman who died of invasive lobular carcinoma of the breast.

MATERIALS AND METHODS

This study was a laboratory study in which a detailed autopsy was performed on a dead body at Abia State University Teaching Hospital, Aba, Nigeria. The autopsy includes external description, examination of internal organs and histological analysis. Clinical notes of the patient before her death were also reviewed.

RESULTS

Clinical Notes: A 54 year old multiparous woman was brought-in dead to the Accident and Emergency Unit of the Abia State University Teaching Hospital on referral from a peripheral center. She was said to have presented with fever and generalized body weakness of 1 week duration and was being treated for malaria and typhoid fever. She was given antimalarials, antibiotics and

intravenous fluid. Her condition deteriorated in 2 days of hospitalization despite the above treatment given and was referred to the accident and emergency unit of Abia State University Teaching Hospital for onward treatment. She later passed away.

Autopsy Findings

Reproductive System: The endometrial cavity showed three polypoid intramural fibroid nodules, aggregating to 6x4x3cm. Both ovaries and fallopian tubes were grossly normal. The cervix was grossly normal. The vagina wall was smooth and unremarkable.

Breasts: The breasts were symmetrical and the overlying skin was grossly normal. There was no area of ulceration or change in the skin. The nipples were not retracted. Cut sections of both breasts showed diffuse white fibrous tissue in areas and no obvious lymphadenopathy was noted.

Central Nervous System: The cranium was intact, no fracture in the skull. The meninges were unremarkable; there was no epidural, subdural or subarachnoid haemorrhage. The brain weighed 1400g. There were no contusions or softening, and there was narrowing of sulci and flattening of gyri. There was no significant uncal and tonsilar herniation. The cranial vessels had a normal anatomical distribution with no aneurismal dilatation and no significant atheroma. Serial coronal sections of the cerebral hemispheres at 1.0cm intervals revealed no old or recent pathological changes. The cerebellum and brain stem appeared unremarkable.

Histological Findings

Breast Tumour: Histologic sections of the breast tissue showed uniform small bland cells with round nuclei and inconspicuous nucleoli invading a fibrotic fibrocollagenous stroma and adipocytes in single files. There was poor attempt at tubule formation.

Lungs: Histological section of the lungs showed infiltration by malignant epithelial cells similar to ones seen in the breast. There were haemorrhages, congestion and edema in the alveolar interstitium, and some of the alveolar were filled with fibrinous material. Also seen were numerous mixed inflammatory cell infiltrates.

Nodular masses: Histological section showed infiltration of tissue by malignant cells similar to those seen in the breast.

Liver: Histologic section of the liver showed microvesicular steatosis in benign appearing hepatocytes and mature adipocytes within the parenchyma. No metastasis was seen.

Spleen: Histologic section of the spleen showed congestion and scattered within the parenchyma were mixed inflammatory cells.

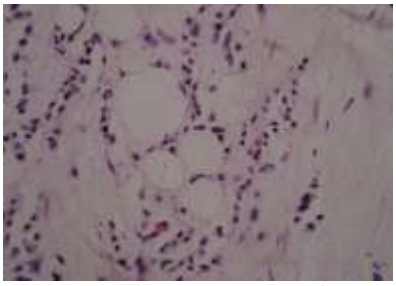
Kidney: Histologic section of the kidney showed normal appearing glomeruli but numerous dilated tubules lined by benign low cuboidal epithelium.

Brain

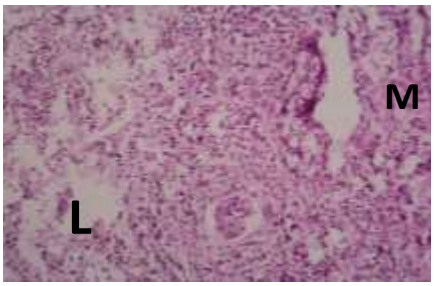
Histologic section of the brain showed moderate cerebral edema.

Final Diagnosis: Invasive lobular carcinoma of the breast, with widespread metastasis to the lungs, pleural and peritoneum.

Cause of Death: (a) Carcinomatosis (b) Invasive lobular carcinoma of the breast.



Micrograph 1: Section of breast showing uniform bland epithelial cells infiltrating adipose tissue in linear pattern (x400)



Micrograph 2: Infiltrating lobular carcinoma metastasis to the lungs (M) and lung alveoli (L) (x100)

DISCUSSION

Invasive lobular carcinoma accounts for 5%–15% of all reported cases of breast cancer. [10] On average, patients are 3 years older at diagnosis in comparison to invasive ductal carcinoma and are generally diagnosed at a more advanced stage of disease. Thus, tumors are often larger and show a greater degree of lymph node involvement at clinical presentation. The incidence of invasive lobular carcinoma has also increased over the past two decades, particularly in women over the age of 50 and is likely a result of diagnostic advances. It has also been correlated with the use of hormone replacement therapies, particularly those containing progesterone. [11] Several studies [12,13] have suggested that the use of combined hormonal replacement therapy is related to a higher relative risk of breast cancer. Since invasive lobular carcinoma is strongly ER-positive, it is unsurprising that prolonged and increased exposure to hormones represents a risk factor. Traditional hormone-related risk factors, including earlier menarche, later menopause, low parity, and late age at first birth, are all associated with increased incidence of invasive lobular carcinoma. [14] It has also been suggested that some lifestyle factors like alcohol consumption may play a role in invasive lobular carcinoma and invasive ductal carcinoma incidence. [12] A study [15] showed that consuming more than 30g of alcohol per day may enhance the breast cancer risk in premenopausal women and that an early start to drinking alcohol may increase the relative risk for breast cancer even beyond menopause. A great number of studies followed investigating the risk of alcohol intake and breast cancer. Invasive lobular carcinoma is more frequent in the Western world while its incidence is much lower in the Middle East, Africa and Asia, accounting for only around 5% of breast cancer cases in these regions. [11] This is likely due to genetic factors. Hereditary Invasive lobular carcinoma is rare but cases have been reported to occur as a secondary tumor in patients or families with hereditary diffuse gastric cancer syndrome who harbor a germ line mutation of the CDH1 gene. [16] The Cancer Genome Atlas study has also identified a number of ILC-enriched mutations including FOXA1, RUNX1, and TBX3. [17] FOXA1 expression is high in breast cancer and mutations are present in approximately 7% of all ILC cases. [18] FOXA1 is as a key transcription modulator of ER activity, therefore mutations can affect ER function as the loss of ER-binding blocks ER-mediated gene expression, altering the response of endocrine targeted therapies such as Tamoxifen. [14] In a study conducted by Desmedt et al. [19], aimed to characterize the genome of 630 ILC tumors, CDH1 mutations occurred in 65% of tumors. However, the phosphatidylinositol 3-kinase pathway showed three key genes with alterations: phosphatidylinositol-4,5-bisphosphate 3-kinase catalytic subunit alpha, phosphatase and tensin homolog and AKT1 mutations were present in 50% of cases. PIK3CA mutations were associated with low proliferation rates, as defined by Ki-67 and AKT1 tumors and were related to a short-term risk of relapse. Invasive lobular carcinoma is overwhelmingly characterized by HER2 negativity, displaying a low rate of ERBB2 amplification. However, ERBB2 mutations or amplifications have been found in up to 8% of ILCs. [20] These mutations are most associated with pleomorphic and solid histology and this is thought to account for the aggressive tumor phenotype.

CONCLUSION

The 54 year old woman who died of invasive lobular carcinoma of the breast was found to have diffuse bilateral fibrous breast tumour with widespread metastasis to the lungs, parietal, peritoneum and diaphragm. Histologic sections of the breast tissue showed uniform small bland cells with round nuclei and inconspicuous nucleoli invading a fibrotic fibrocollagenous stroma and adipocytes in single files. A thorough autopsy of deaths of women of

postmenopausal age was recommended in other to identify associated pathologies.

Declaration by Authors
Acknowledgement: None
Source of Funding: None
Conflict of Interest: The authors declare no conflict of interest.

REFERENCES

1. Li CI, Anderson BO, Daling JR, Moe RE. Trends in incidence rates of invasive lobular and ductal breast carcinoma. JAMA. 2003; 289(22): 1421–1424.
2. Eheman CR, Shaw KM, Ryerson AB, Miller JW, Ajani UA, White MC. The changing incidence of in situ and invasive ductal and lobular breast carcinomas: United States, 1999–2004. Cancer Epidemiol Biomarkers Prev. 2009; 18(15): 1763–1769.
3. Rossouw JE, Anderson GL, Prentice RL, LaCroix AZ, Kooperberg C, Stefanick ML. Risks and benefits of estrogen plus progestin in healthy postmenopausal women: principal results from the Women's Health Initiative randomized controlled trial. JAMA. 2002; 288(17): 321–33.
4. Li CI, Uribe DJ, Daling JR. Clinical characteristics of different histologic types of breast cancer. Br J Cancer. 2005; 93(21): 1046–1052.
5. Li CI, Daling JR. Changes in breast cancer incidence rates in the United States by histologic subtype and race/ethnicity, 1995 to 2004. Cancer Epidemiol Biomarkers Prev. 2007; 16(20): 2773–2780.
6. Laure D, Patrick RB. Invasive lobular carcinoma. Breast Cancer Res. 2015; 13(1):17-37.
7. Weigelt B, Horlings HM, Kreike B, Hayes MM, Hauptmann M, Wessels LF. Refinement of breast cancer classification by molecular classification of histological special types. J Pathol. 2008; 216(12): 141–150.
8. Loo LWM, Grove DI, Williams EM, Neal CL, Cousens LA, Shubert EL. Array comparative genomic hybridization analysis of genomic alterations in breast cancer subtypes. Cancer Res. 2004; 64(27): 8541–8549.
9. Guilford P, Hopkins J, Harraway J, McLeod M, McLeod N, Harawira P. E-cadherin germline mutations in familial gastric cancer. Nature. 2018; 16(7): 392-402.
10. Li CI, Malone KE, Daling JR. Differences in breast cancer hormone receptor status and histology by race and ethnicity among women 50 years of age and older. Cancer Epidemiol Biomarkers Prev. 2002; 11: 601–607.
11. Daling JR, Malone KE, Doody DR, Voigt LF, Bernstein L, Coates RJ. Relation of regimens of combined hormone replacement therapy to lobular, ductal, and other histological types of breast carcinoma. Cancer. 2002; 95(12): 2455–2464.
12. Colditz GA, Hankinson SE, Hunter DJ, Willett WC, Manson JE, Stampfer MJ. The use of estrogens and progestins and the risk of breast cancer in postmenopausal women. N Engl J Med. 2015; 332(24): 1589–1593.
13. Fournier A, Berrino F, Clavel-Chapelon F. Unequal risks for breast cancer associated with different hormone replacement therapies: results from the E3N cohort study. Breast Cancer Res Treat. 2008; 107: 103–111.
14. Luveta J, Parks RM, Heery DM, Cheung KL. Invasive Lobular Breast Cancer as a Distinct Disease: Implications for Therapeutic Strategy. Oncol Ther. 2019; 1–11.
15. Van't Veer P, Kok FJ, Hermus RJ, Sturmans F. Alcohol dose, frequency and age at first exposure in relation to the risk of breast cancer. Int J Epidemiol. 2019; 18(3): 511–517.
16. Pharoah PD, Guilford P, Caldas C. The International Gastric Cancer Linkage Consortium. Incidence of Gastric Cancer and Breast Cancer in CDH1 (E-Cadherin) Mutation Carriers from Hereditary Diffuse Gastric Cancer Families. Gastroenterol. 2001; 121(18): 1348–1353.
17. Sledge GW, Chagpar A, Perou C. Collective Wisdom: Lobular Carcinoma of the Breast. Am Soc Clin Oncol. 2016; 35(1): 18–21.
18. Ciriello G, Gatza ML, Beck AH, Wilkerson MD, Rhie SK, Pastore A. Comprehensive molecular portraits of invasive lobular breast cancer. Cell. 2015; 163(2): 506–519.
19. Desmedt C, Zoppoli G, Gundem G, Pruneri G, Larsimont D, Fornili M. Genomic Characterization of Primary Invasive

Lobular Breast Cancer. J Clin Oncol. 2016; 34(16): 1872–81.

20. Christgen M, Bartels S, Radner M, Raap M, Rieger L, Christgen H. ERBB2 mutation frequency in lobular breast cancer with pleomorphic histology or high-risk characteristics by molecular expression profiling. Genes Chromosomes Cancer. 2019; 58(3): 175–185.

How to cite this article: Offiah, A.U., Amadi, A.N., Azuamah, Y.C. et.al. Autopsy pathology of invasive lobular carcinoma of the breast: a case report. *International Journal of Research and Review*. 2023; 10(2): 260-265. DOI: *https://doi.org/10.52403/ijrr.20230232*

******