ORIGINAL ARTICLE

Cranial computed tomographic findings in Nigerian women with metastatic breast cancer

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ABSTRACT

Introduction: Brain metastases (BM) occur in up to one-fifth of patients with metastatic breast cancer (MBC). Imaging plays a key role in diagnosis. The pattern and distribution of these changes are also crucial to their management. These patterns have not been fully studied in Nigerian women. **Materials and Methods:** Retrospective analysis of the findings on the cranial Computed Tomography (CT) scans performed in 59 breast cancer patients with suspected BM treated at the University Teaching Hospital in Ibadan, between 2005 and 2010. The imaging features were evaluated in relation to their clinical characteristics. **Results:** In the 59 patients studied (mean age 50.9 years ± 11.75 SD), headache (40.7%) and hemiparesis/hemiplegia (16.9%) were the commonest clinical presentation. Lytic skull lesions were seen in 15 patients (25.4%), most commonly in the parietal bones. Thirty-nine patients (66.1%), had parenchymal brain lesions, and only 8 (20.5%) of these were single lesions. Most of the lesions were isodense (19/39; 51.4%) the parietal lobe was the most common site with 50.8% (30/59) occurrence and the leptomeninges the least with 13.6% (8/59). Orbital or sellar region involvement occurred in only two patients. The size of the lesions, was <2 cm in 17 (28.8%), 2-5 cm in 14 (23.7%) and >5 cm in 5 patients. Sixteen (27.1%) patients were free of any lesion either in the skull or brain. Patient presenting with multiple brain lesions were more likely to have skull lesions though this was not statistically significant ($P = 0.584$). **Conclusion:** The brain continues to be a sanctuary site for breast cancer metastases and CT imaging remains an invaluable tool in the clinical evaluation and therapeutic management of Nigerian women with BM from MBC. It also appears that the demographic and imaging findings in these patients are similar to other racial groups.

Key words: Breast cancer, brain metastases, computed tomography, Ibadan

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INTRODUCTION

Breast cancer is the second most common solid tumor that forms brain metastases.[1] Altogether, up to 16% of patients with metastatic breast cancer will develop brain metastases (BM) during the course of the disease, although autopsy series reveal approximately twice as many cases (34%).[1,2] Expression or overexpression of S100A4 (p9Ka) or c-erbB2 in breast carcinoma are associated with increased metastatic potential.[3]

These patients are often in an advanced stage of the disease as it is rare to present with the manifestation of BM before the detection of the primary breast cancer.[4,5]

The metastatic deposit may involve the skull, the dura, or the brain parenchyma. Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) are useful tools in the evaluation of these patients. CT is best in determining the extent of bone destruction, either in bone metastases or in bone involvement resulting from metastases to the dura or brain while MRI is superior to CT in detecting leptomeningeal, dural and intraparenchymal lesions as small as 1 mm. The rate of haematogenous skull metastases, even though low in comparison to brain metastases, is higher in breast cancer than in many other tumors.[6]

Patients with brain or skull metastasis usually present late to the clinician as they usually remain asymptomatic for a long time. It has been estimated that they grow slowly allowing other complications of the underlying breast cancer to develop.[7] These and many other established imaging patterns of cranial breast metastasis are well

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known and documented in literature for several racial groups, but not as well in our patient population. We therefore seek to determine the nature and similarity of the pattern of CT imaging findings in Nigerian women with cranial breast metastasis.

MATERIALS AND METHODS

Cranial CT scans were performed on 59 patients with histologically confirmed breast cancer and with clinical features suggestive of intracranial metastasis over a five year period (2005 to 2010). CT scans were performed in the Department of Radiology of the University College Hospital Ibadan using a GE CT/e and Brightspeed CT scanners. Screening by brain imaging in asymptomatic patients is not performed routinely at our centre. The CT protocol included pre- and post- contrast axial slices of the brain obtained from the base of skull to the vertex. The demographic and clinical data as well as the CT findings were analysed using the Statistical Programme for the Social Sciences (SPSS) version 17 (SPSS Inc, IL, USA). Descriptive statistics were presented in sizes and proportions (percentages, means ± standard deviation,) Brain metastasis (present versus not present) was considered a binary response variable. The level of statistical significance was set at a $P \leq 0.05$

RESULTS

Fifty-nine patients were studied with ages ranging from 32 to 92 years with a mean of 50.9 ± 11.75 SD and the modal age group of 40-49 representing 32.2%.

Table 1 shows the distribution of their major clinical presentations and indications for CT. Headache (40.7%) and hemiparesis/hemiplegia (16.9%) were the commonest clinical presentation.

The CT findings showed skull lesions in 15 (25.4%) patients. Of these, six (40.0%) were in multiple locations or generalized. All the demonstrated skull lesions were lytic in nature and the parietal bone was the most common location.

Only six patients (6/15) with skull lesions showed evidence of associated soft tissue swelling which occurred most commonly in the right parietal region in four patients (66%).

Brain lesions were seen in thirty-nine patients (66.1%), only eight of these patients (20.5%) had single lesions, the remaining 31 patients (79.5%) had multiple lesions in various locations of the brain [Figure 1].

Most of the lesions as shown in Table 2 were isodense (19/39; 51.4%). This indicates that without contrast medium most of these lesions may have been missed or unidentified.

Table 1: Clinical indication for brain imaging for suspected metastatic breast cancer in this study

Clinical symptoms (*n*=59)	*N*	%
Headache	24	40.7
Hemiparesis/ hemiplegia	10	16.9
Seizures	9	15.3
Visual impairment	7	11.9
CN deficit	3	5.1
LOC	5	8.5
Scalp swelling	1	1.7
Total	59	100.0

CN – Cranial nerve; LOC – Loss of consciousness

Table 2: Predominant CT attenuation pattern in each patient with brain parenchymal lesion in this study

Pre-contrast density	*N*	%
Isodense	19	48.7
Hyperdense	9	23.1
Hypodense	8	20.5
Mixed	3	7.7
Total	39	100.0

CT – Computed tomography

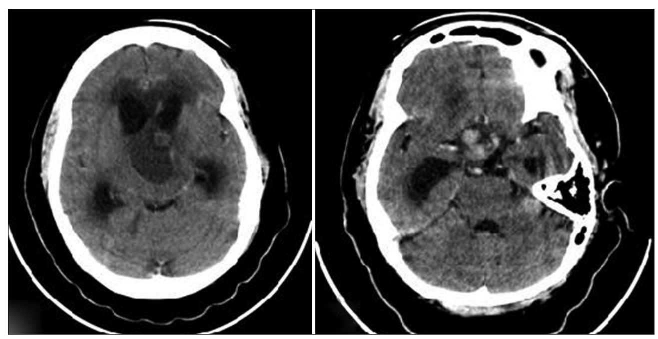

Figure 1: Pre-contrast- and post-contrast-enhanced CT of patient with breast cancer. Huge mixed density metastatic mass in the suprasellar region with resultant hydrocephalus

Figure 2 shows the distribution of the enhancement pattern seen in these patients.

The distribution of intracranial breast metastases by location is seen in Figure 3 where the parietal lobe represents the commonest site accounting for (30/59) 50.8% and the leptomeninges the least with (8/59) 13.6% of patients.

The intracranial brain lesions exhibited mass effect in 51.3% (20/39) of patients with (12/20) 60% showing significant midline shift. The pattern among patients with edema was mostly local perilesional vasogenic type (19/30; 63.3%). Dural sinus infiltration was described in half of the patients with leptomeningeal involvement.

There was orbital involvement in only two patients. Similarly metastatic deposits to the sellar region [Figure 1] were also recorded in 2 patients.

The size of the largest intracranial lesion in each patient was less than 2 centimeters (cm) in seventeen patients (28.8%), and greater than 5 cm in only [Figure 4], the remaining lesions ranged between 2 and 5 cm in 14 patients (23.7%).

Sixteen (27.1%) of the 59 patients showed no detectable lesion on CT either in the skull or brain.

Of the 15 patients with skull lesions, only 4 (26.7%) showed no associated evidence of a corresponding intracranial brain lesion. Patients presenting with multiple brain lesions were more likely to have skull lesions [Figure 5] though this was not statistically significant ($P = 0.584$).

Patients older than 50 years did not have any statistically significant difference in the pattern of intracranial metastases, skull lesions or size of lesions compared with those younger than 50 years.

DISCUSSION

Brain metastases are a significant cause of morbidity and mortality in patients with breast cancer and are found to occur in about 25% of all cancer patients.[8] The incidence of BM in our environment is thought to be increasing but this may only be due to the increased use of available brain imaging facilities.

Once brain metastasis occurs, the outcome for breast cancer patients is generally poor. Although radiotherapy or surgery has been used to improve the survival and quality of life of patients with brain metastases, the outcome has not been generally satisfactory.[9] The 1-year survival rate of breast cancer patients with BM is 20%[10] which is somewhat better than other types of cancer owing to the relatively indolent nature of the disease. The median time of diagnosis of breast cancer to the occurrence of BM is usually 2-3 years[11], however in our study we did not estimate the length of time before presentation for imaging as this data was not assessable at the time of writing. What is evident is that all patients were in an advanced stage of the disease at the time of imaging. BM

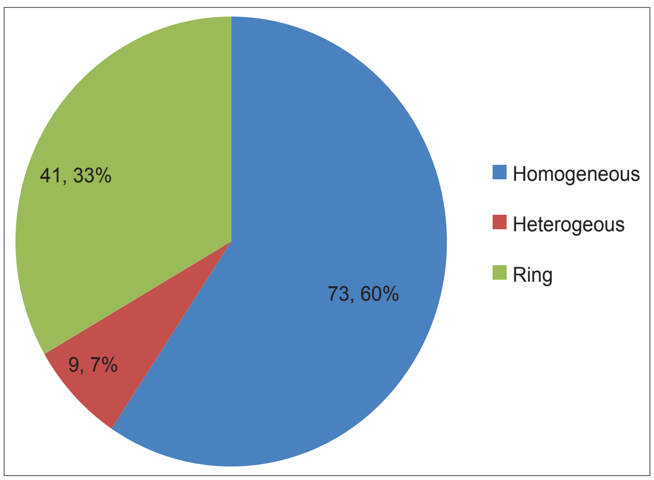

Figure 2: Distribution of contrast enhancement pattern of parenchymal brain lesions

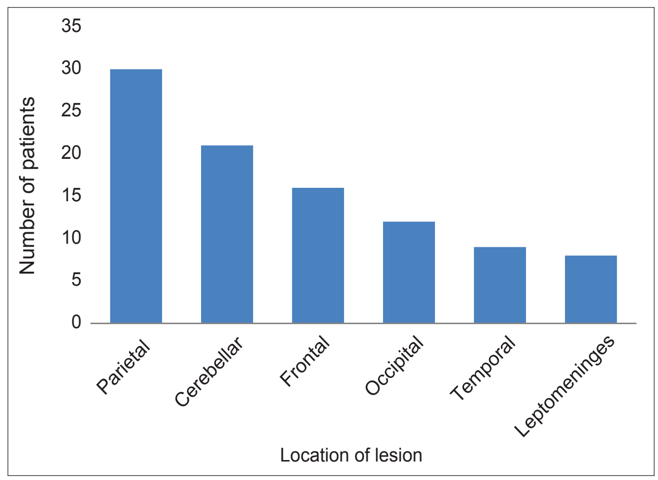

Figure 3: Distribution of intracranial breast metastases by location*some patients had lesions in multiple sites

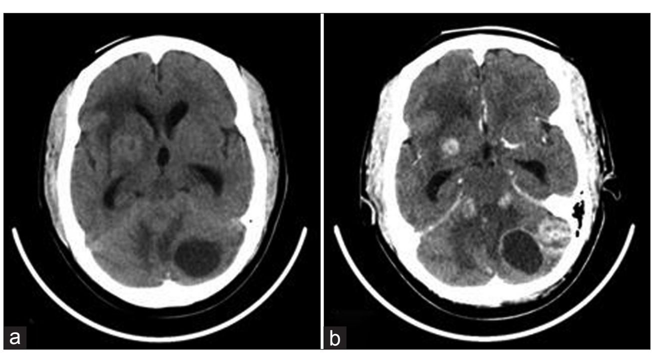

Figure 4: (a) Pre- and (b) post- contrast images of a patient with metastases multiple sites and showing varying patterns of enhancement. Homogenous in the right deep parietal lobe and ring and heterogeneous pattern in the posterior fossa with perilesional edema

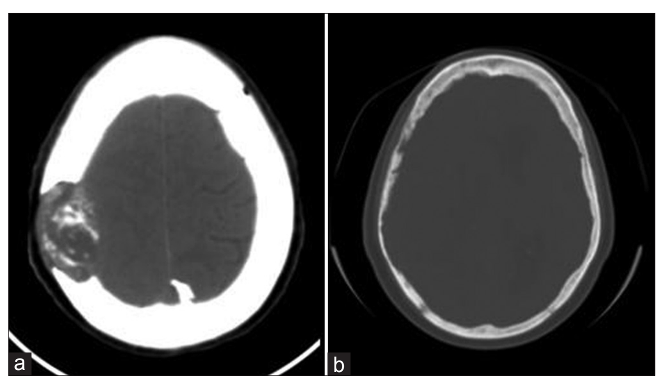

Figure 5: CT bone window of a patients with breast cancer. (a) Multiple irregular and lytic lesions in the calvarium (b) single bony destruction with dural metastatic involvement

can appear at any time in the course of breast cancer; most often they are metachronous, but may occur synchronously or even rarely prior to diagnosis of the primary tumour.[4]

The presenting features of brain metastasis are usually related to the involved brain area.[1] Most patients presents with headache or focal neurological deficits. Common focal symptoms include, gait disturbances, visual field defects and aphasia.

Symptoms usually evolve over a few weeks. However, hemorrhage into the metastases can result in a more dramatic presentation. The propensity to bleed is relatively less common in breast cancer compared to tumors like malignant melanoma, thyroid cancer, renal cell cancer and choriocarcinoma.[6]

The major presenting feature in our series was headache, which is consistent with other reports as this is usually a first indication of a neurological problem in this group of patients.[4,12,13] Leptomeningeal metastases is recognized as a common feature among breast cancer patients as shown in this report and may present with non-localizing symptoms such as headache, nuchal rigidity and seizures.[5,13]

An important, and potentially fatal, initial symptom is the subacute or acute rise of intracranial pressure due to blockage of cerebrospinal fluid (CSF) flow by otherwise asymptomatic metastases along the CSF pathway leading to obstructive hydrocephalus [Figure 1].

As in other standard care centers, we do not perform routine brain screening in asymptomatic patients, as there are no convincing data to support the benefit related to early diagnosis and treatment of brain metastases.[7]

A CT or MRI usually establishes the diagnosis of brain metastases. MRI is regarded as the gold standard due to its high soft tissue resolution. However MRI is unavailable to most patients in our environment and CT is acceptable to be adequate to exclude BM in most patients. Nevertheless it is known to miss small lesions or tumors located in the posterior fossa. It is also likely that the group of patients in our series in whom no lesions were found may have turned out with detectable lesions if examined with MRI which is undoubtedly a superior test for evaluation of metastatic brain disease. A high-quality, contrast-enhanced MR scan should therefore be obtained in such patients where the location, number and distribution of lesions are necessary to define or direct treatment protocol or when simply looking for evidence of leptomeningeal disease.[6,14]

Brain metastases from breast are usually enhancing isodense lesions surrounded by edema, which extends into the white matter. Unlike primary brain tumors, they rarely involve the corpus callosum or cross the midline.[6] Since the radiographic appearance of BM is nonspecific, and may mimic other processes, such as infection, we interpreted all scans within the context of the clinical picture of the individual patient, particularly since cancer patients are vulnerable to opportunistic CNS infections or may develop second primaries, which can include primary brain tumors.[14]

The pattern and distribution of BM has been variously studied with the view to understand the disease more clearly and to aid in prognostic analysis and direct follow up.[11,12]

Macki *et al*.[15] found two major patterns of spread of metastatic breast carcinoma which are: Patients with estrogen receptor1/progesterone receptor 1(ER+/PR+) tumors tend to develop osseous but not brain metastases. Patients with ER-/PR– tumors tend to develop brain but not osseous metastases. They concluded that appreciation of these distributions will aid the radiologist in the detection of metastatic lesions, and may serve to allow structured follow-up imaging and knowledge of these patterns of metastases will also help the clinician to estimate the likelihood of metastases to various organ systems, which may potentially allow targeted prophylactic therapy of these patients. In our study, even though a retrospective one which did not consider the breast cancer sub-type, it is evident that, brain lesions were more commonly encountered as compared to osseous lesions. It would be interesting to further investigate to see if the findings of Macki *et al*.[15] could also be replicated in our environment. We hope to make this the focus of future studies in our center.

Metastases are usually spherical or quasispherical and are well demarcated from the adjacent brain tissue. Their location is generally related to the proportion of blood flow. Thus, about 80-85% of metastases are located in the cerebral hemispheres in the grey-white matter junctions in watershed areas between anterior, middle and posterior cerebral arteries, 10-15% in the cerebellum, and 3-5% in the brainstem.[16]

In our study, over three quarters of lesions were in the cerebral hemispheres, with only a fifth in the cerebellum [Figure 6] while no brainstem lesions were

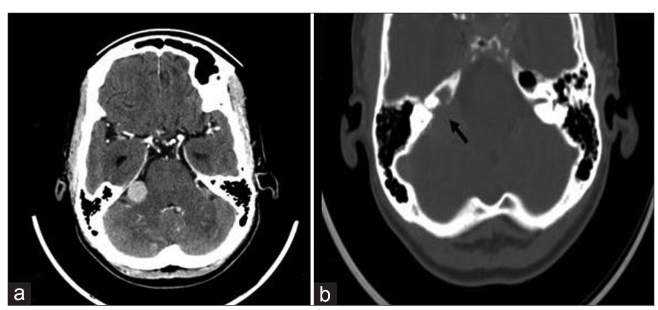

Figure 6: CECT in a 56 year-old woman presenting with recurrent headache and hemiparesis. (a) Axial image showing a homogeneously enhancing right cerebellopontine metastasis. (b) Bone window image showing bony destruction (arrow) of the adjacent petrous apex

reported. Greater than half of the lesions were isodense. This indicates that without contrast medium most of these lesions may have been missed or unidentified.

Notably, about a third of BM may escape detection during Life.[9] Sixteen (27.1%) of our patients were found to be free of any detectable lesion either in the skull or brain, this may turn out to fall under this category.

Factors that have been well-known to negatively influence survival include multiple metastases, infratentorial location, and leptomeningeal spread.

Metastatic spread or seeding of tumour to the leptomeninges is a recognised feature in patients with breast carcinoma.

Imaging plays a key role in the diagnosis and management of leptomeningeal metastatic disease because it often provides the first clue to the presence of the disease.[17]

We demonstrated leptomeningeal changes in over a tenth of the patients but the sensitivity for this detection would most definitely have been greater with MRI which has a recognised greater sensitivity.[17]

CT era data suggest that BM from solid tumors tend to be single or solitary in fifty percent of patients at diagnosis. However, more recent studies based on MRI suggest that less than one third of patients have a solitary or single brain metastasis at the time of diagnosis of brain metastasis. The findings in our cohort are in closer agreement with the latter and more contemporary data than the former.

By definition, 'solitary' brain metastasis is distinguished from 'singular' brain metastasis. The term 'solitary' indicates the absence of extracranial metastatic disease, while the term 'singular' merely indicates the presence of one cerebral metastasis with additional metastases in other organ systems.[18]

In view of our limitations to access the full clinical data of all patients in this series, we adopted the definition of single metastasis as appropriate.

Where MRI is unavailable, CT has been shown to be adequate in excluding BM in most patients, but it is known to miss small lesions or tumors located in the posterior fossa or next to bone in a frontotemporal location.

This might explain the relatively low frequency of posterior fossa lesions detected in our series.

Definitive therapy for BM is intended to restore neurologic function, improve quality of life, and extend survival. Therapeutic modalities that may be used in management of these patients include surgical resection, stereotactic radiosurgery (SRS), whole brain radiation therapy (WBRT), and more recently chemotherapeutic agents with some degree of central nervous system activity. These therapeutic modalities may be used singly or in combination.[7] Imaging frequently plays a substantial role in determining the choice of treatment. The imaging method of choice for BM is MRI. Although in our setting due to its unavailability and high cost, CT continues to play this role with demonstrable good results. It is clear that CT cannot unequivocally differentiate metastases from other lesions; certain features in the appropriate clinical scenario however suggest metastatic disease.

Several factors have been identified in previous studies to be associated with a higher risk of brain metastases.[19-21] Most of these factors are immunological/genetic and usually are related to the specific cancer subtype.

In future, we hope to look into any possible correlations between molecular subtypes of breast cancer and imaging features in Nigeria women.

CONCLUSION

The brain continues to be a sanctuary site for breast cancer and CT imaging remains an invaluable tool in the evaluation and therapeutic management of Nigerian women with BM from MBC. However the demographic and imaging findings appear similar to other racial groups.

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