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CASE REPORT

Case Report: Intramammary lymph node metastasis of an unknown primary, probably occult breast, undifferentiated carcinoma [version 1; peer review: 2 approved, 1 approved with reservations]

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Abstract

Little is known about the clinical importance of intramammary lymph node metastasis of breast cancer, even though it is not rare. In the present paper, the authors present an unusual, rare case of an intramammary lymph node metastasis of an unknown primary, probably occult breast cancer, and its management. The patient was submitted to various staging exams and surgical procedures and a definitive diagnosis was not established. From a multidisciplinary context, it was assumed that the patient had a breast triple negative primary with axillary involvement. This decision lead to adjuvant chemo and radiotherapy. Challenging cases like the one described here, should always be managed within the multidisciplinary team context and recorded in the institution's database.

Keywords

Breast cancer, occult breast cancer, intramammary lymph node metastasis, multidisciplinary approach

Open Peer Review

Approval Status

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2. **Ramesh Omranipour**, Tehran University of Medical Sciences, Tehran, Iran

3. **Kenji Gonda** , Nihon University School of Medicine, Tokyo, Japan

Any reports and responses or comments on the article can be found at the end of the article.

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Background

Intramammary lymph node metastasis is an unknown in everyday clinical practice and very little is known about its importance.

Case presentation

A woman, 33 years old, from Goa (India) presented to our consultation for a palpable mass on the upper external quadrant of the right breast. The patient had no personal relevant history. Menarche had occurred at 15 years with regular menses of 4/26 days, GPO, without anticonceptual pills use, and no drug or alcohol abuse. The patient's family history showed that the mother passed away at 40 years old with metastatic (brain) breast cancer and her maternal uncle was deceased at the age of 45 from esophageal cancer.

Investigations

The patient had already undergone ultrasound and bilateral breast mammography that reported the 'presence of nodular multiloculated formation at the upper external quadrant of the right breast with 3 cm of diameter, probably corresponding to inflammatory/infectious lymph node' (Figure 1).

On clinical observation, voluminous breast with grade III ptosis and a palpable solid mass was observed. It was an irregular mass of approximately 4 cm on the upper external right breast quadrant, not adherent to the skin or to the pectoralis muscle. The patient was submitted to an ultrasound guided fine-needle aspiration biopsy (FNAB) that reported 'fragments of lymph node with poorly differentiated neoplastic infiltration. Presence of epithelioid neoplastic cells positive for AE1/E3 and negative for CK20, CEA, vimentin, protein S100, P63, CD56, TTF-1, GCDFFP-15, estrogen receptors. Conclusion: lymph node metastasis of poorly differentiated carcinoma of unknown primary origin'.

The patient underwent a magnetic resonance imaging scan in which there was detected an additional 17mm lesion (BI-RADS-5) adjacent posterior to the lymph nodal mass previously detected,

which was submitted to an ultrasound second look and FNAB (Figure 2). In this biopsy, no neoplastic tissue was identified, and the results reported 'mammary gland fragments with inflammatory process, no isolated epithelial cells identified after IHC with CK8/18'.

Consequently, the decision of the multidisciplinary team was to perform complementary studies (upper gastroscopy, otorhinolaryngological consultation, dermatology consultation, thoracic-abdominal-pelvic tomography, and full analytics with tumor markers). All the complementary studies were negative. Therefore, the multidisciplinary team decided that 'the patient to be proposed for lumpectomy with axillary lymphadenectomy' with a PET-TC scan positive only for the mass to the upper external quadrant of the right breast. The patient was submitted to lumpectomy on oncoplastic pattern, followed by axillary dissection level II, and was discharged without any complication on the third post-operative day.

The anatomopathology report of the surgical specimen stated that the 'lumpectomy specimen constituted of skin, adipose tissue and mammary tissue where there exists a nodule, well delimited, white, with posterior margin of 1mm, consisting of a lymph node agglomerate with poorly differentiated metastasis with CK7 positive and rare CD56 positive cells, focally positive for EMA' (Figure 3). In addition, the 'lymphadenectomy specimen [had] 15 reactive, free of metastasis, lymph nodes'.

A second pathology review of the lumpectomy specimen (external to our institution), indicated that the excised nodule consists of five lymph nodes as an agglomerate with histology of an undifferentiated metastasis, of a probable triple negative of mammary origin primary tumor. Therefore, the multidisciplinary team decided to propose the patient for total mastectomy, which was performed and the anatomopathological report showed neither abnormalities, nor the presence of neoplastic tissue in the remaining breast.

Figure 1. Ultrasonography of nodular formation at the upper external quadrant of the right breast.

Figure 2. Ultrasound second look and fine-needle aspirate biopsy of the second lesion.

Figure 3. Metastatic lymph node agglomerate.

Treatment

In an adjuvant setting, the patient was administered with the TAC chemotherapy protocol (docetaxel 75 mg/m², doxorubicin 50mg/m² and cyclophosphamide 500mg/m², every 21 days, accompanied with pegfilgrastim) and successfully completed 6 cycles. The patient later received standard thoracic and lymphatic chain radiotherapy (50 Gy in 25 fractions over 5 weeks and boost to the tumor bed).

BRCA 1 and 2 genetics were negative.

Outcome and follow-up

The patient is currently in remission and had an uneventful follow-up at the Medical Oncology and Senology Department at our institution. According to our protocol, the patient undergoes clinical observation every three months accompanied by laboratory full set analysis (tumour markers included) and an annual breast imaging

Discussion

Very little is known about the clinical importance of intramammary lymph node metastasis of breast cancer, even if they are not a rare site for metastasis. However, it is believed that metastasis to intramammary lymph nodes is an independent factor of poor prognosis for breast cancer patients^{1,2}.

In a Pubmed search between 1900 and 2016, there is only one paper concerning metastatic intramammary lymph nodes as the primary presenting sign of occult breast cancer, which describes

two cases³. The cases presented by Kouskos *et al*³ have some histological differences from the present one (for example, estrogen receptor positivity, axillary lymph node involvement, and late presentation of the primary breast tumour), and also the late appearance of the primary breast tumour. In our case and up until now, we have never detected a primary breast tumor. Similarly to our case, the other cases required an extensive complementary study of the patient.

Our decision to treat the patient as a triple negative breast cancer patient with axillary metastatic involvement was based on the histopathological suspicion of a breast-like primary site and the patient's strong family history (1st degree familial with breast cancer at <40 years old age).

In conclusion, intramammary lymph node metastasis requires a challenging workup and there is an urgent need to clarify its importance. Breast cancer patients should always undergo treatment in a multidisciplinary context. Being an extremely rare event, the one described here, good medical practice imposes a broad discussion among the various specialities that only can be achieved in the multidisciplinary setting. Decisions about treatment strategies to be offered are vast and should be patient centred.

Take home messages

Intramammary lymph node metastasis requires challenging workup

There is urgent need to clarify its importance

Breast Cancer patients should always undergo treatment in multidisciplinary context

Consent

Written informed consent from the patient has been obtained for the publication of this manuscript.

Author contributions

ZS is the attending surgeon; CS, IG and TT performed the case and literature review; FA is the attending medical oncologist; LM is the responsible pathologist.

Competing interests

No competing interests were disclosed.

Grant information

The author(s) declared that no grants were involved in supporting this work.

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Reviewer Report 30 June 2017

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Kenji Gonda

Division of Breast and Endocrine Surgery, Department of Surgery, Nihon University School of Medicine, Tokyo, Japan

The authors described that Intramammary lymph node metastasis of an unknown primary, probably occult breast, undifferentiated carcinoma. These findings in this manuscript are interesting, and this manuscript is worthy of indexing. There are some problems should be resolved before publishing.

1. What is the TNM classification for staging of this breast cancer patient?
2. Do you think that this ectopic breast tissue may be accessory breast cancer?
3. You should reveal breast pathological diagnosis of the lumpectomy specimen, for example, papillo-tubular carcinoma or scirrhous carcinoma with mammary gland.
4. What is the result of the human epidermal growth factor receptor 2 (HER-2/neu) and Ki-67 marker?
5. You should refer to an article of Egan, because intramammary lymph node metastases in the breast were reported for the first time in the world by Egan and McSweeney in 1983¹.
6. Are additional ancillary studies, including immunostainings, beneficial to evaluate site of origin (in case of this tumor is CD10 focally positive)?
7. What are the second line therapy options for this rare pathology, when this patient will have recurrence of breast cancer?
8. What is the role of family history and its impact on therapy?

References

1. Egan RL, McSweeney MB: Intramammary lymph nodes. *Cancer*. 1983; **51** (10): 1838-42 [PubMed Abstract](#)

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

No

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Reviewer Report 30 May 2017

<https://doi.org/10.5256/f1000research.11933.r21962>

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Ramesh Omranipour

Division of Surgical Oncology, Cancer Institute, Tehran University of Medical Sciences, Tehran, Iran

It is better to added the images of MRI and PET scan of the patient.

The discussion is too brief, although this presentation for intramammary lymph node is rare but there are many reports in the literature about the clinical importance and prognostic value of involved intramammary lymph node.

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Partly

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Partly

Is the case presented with sufficient detail to be useful for other practitioners?

Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Surgical oncologist

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 07 Jun 2017

Zacharoula Sidiropoulou, Hospital São Francisco Xavier-CHLO, Lisbon, Portugal

Dear Colleague,

First of all thank you for your comments.

As a reply:

"Better to added the images of MRI and PET scan of the patient"

- Unfortunately we are not in possession of this imaging

"Discussion is too brief, although this presentation for intramammary lymph node is rare but there are many reports in the literature about the clinical importance and prognostic value of involved intramammary lymph node."

- Hereby our intention was just to report this specific unusual case, our first submission was more extended but afterwards we decided to limit to the presentation and not to proceed to a literature review of intramammary lymph node involvement in known,diagnosed breast cancer

We hope our answer meet your kind and helpful comments

Once more thank you for the review and we wait your feedback.

Competing Interests: No competing interests were disclosed.

Reviewer Report 24 April 2017

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Sergi Vidal-Sicart

Nuclear Medicine Department, Hospital Clinic Barcelona, Barcelona, Spain

Immaculada Alonso

Gynaecology and Obstetrics Department, Hospital Clinic Barcelona, Barcelona, Spain

It is a well-written paper concerning an infrequent case of intramammary metastases without a known primary tumor.

The case description is adequate and nicely presented. We only have to add some minor requirements to the authors.

- It could be adequate to add the MR and PET images demonstrating their findings.
- Did the authors consider that carboplatin could be added to the treatment. It seems that this agent offers good results in TN breast cancer.
- Finally, do you consider to expand the genetic study, even with a negative BCRA, due to a possibility to express other gens like PALB2?

Is the background of the case's history and progression described in sufficient detail?

Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?

Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?

Yes

Is the case presented with sufficient detail to be useful for other practitioners?

Partly

Competing Interests: No competing interests were disclosed.

We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

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