Case study

A RARE CASE OF SYNCHRONUS CARCINOMA BREAST WITH CHRONIC MYELOID LEUKEMIA

ABSTRACT: Chronic myeloid leukemia is an insidiously progressive condition and comparatively rare type of blood cell malignancy that begins in the bone marrow. Chronic myeloid leukemia typically affects adult population and is documented to be caused by chromosomal mutation that usually occurs spontaneously.

CML is more common in males than in females (male to female ratio of 1.4:1) and appears more commonly in the elderly with a median age at diagnosis of 65 years.[1] Exposure to ionising radiation is one of the risk factors, based on a 50 fold higher incidence of CML in Hiroshima and Nagasaki nuclear bombing survivors.[1] The rate of CML in these individuals seems to reach at its peak about 10 years after the exposure.[1]

Carcinoma breast on the other hand is one of the most common cause of death in middle aged women in western countries. There are numerous factors contributing as it's etiological factors such as age, gender, diet, endocrinal factors, previous radiation exposure, genetic factors, geographical factors.

We present a case report of a 44 old female who came to acharya vinoba bhave rural hospital , datta meghe institute of medical sciences and research with presenting complaint of lump in the left breast since 2 days and abdominal mass since 1 month. On investigations, patient was diagnosed with a rare case of chronic myeloid leukemia on the complete blood count and peripheral smear and the lump in the left breast also revealed carcinoma of the left breast.

KEYWORDS: chronic myeloid leukemia, carcinoma breast, peripheral smear

INTRODUCTION:

Synchronous presentation of carcinoma breast with chronic myeloid leukemia in the chronic phase as an incidental finding.

A number of case reports in literature show that leukemia such as chronic myeloid leukemia, acute lymphocytic leukemia, chronic myelomonocytic leukemia occurred after anthracycline-based therapy

of ca breast or synchronously with adenocarcinoma stomach/hairy cell leukemia but synchronus occurrence of chronic myeloid leukemia and ca breast has not been reported in the literature. [2] In general, a person with one malignancy is at an increased risk of developing another malignancy. Nineteen cases of second malignancies (ca prostate-4 cases, ca breast-1 case, adenocarcinoma stomach-1 case, lymphoma-1 case, ca ovary-2 cases, ca cervix 1 case, small cell lung cancer -1 case, ca rectum-1 case, basal cell cancer skin-1 case) in chronic myeloid leukemia patients have been reported but only 1 case of synchronous chronic myeloid leukemia with gastric adenocarcinoma. [3] Moertal et al reported 17 cases of chronic myeloid leukemia occurring in association with synchronous malignancies malignancies. In one study with age- and sex-matched controls, patients who were with median age of 40-60 years old when chronic myeloid leukemia was diagnosed. They had an approximately 10-fold higher frequency of other malignancies than did age-matched controls. Patients younger than 40 years did not have a synchronus malignancy. [4] Studies have shown that in chronic myeloid leukemia, mutation at the stem level. That is, in PH chromosome. It occurs around 6 years before the presentation of the disease, whereas carcinoma breast occurs many years prior to its presentation. [5] In summary, our case of synchronous presentation of carcinoma breast with chronic myeloid leukemia is a very rare presentation which has not been recorded in the literature.

CASE REPORT:

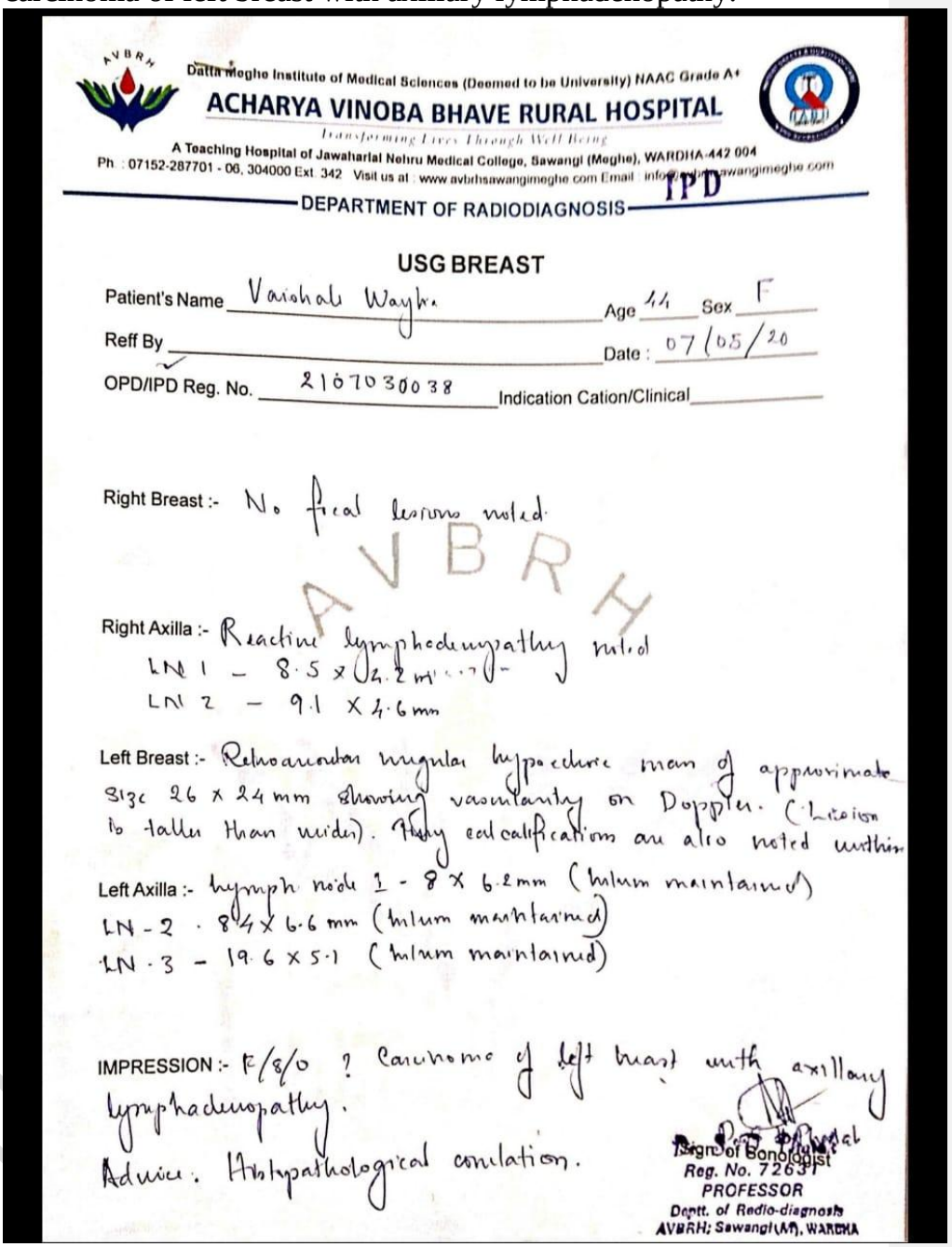
A 44 year old female presented in the out patient department with history of lump in the left breast which was insidious in onset, gradually progressive in nature and there were no aggravating or relieving factors associated with it. The patient also complaints of lump in the abdomen which was insidious in onset and gradually progressive in nature. On clinical examination there was splenomegaly of grade III as well as hepatomegaly of 8cm. On clinical examination the breasts were bilaterally asymmetrical with fullness in the upper outer quadrant of the left breast. There was retraction of nipple but no peau d orange observed. The lump was hard of size 4x5 cm in the upper outer quadrant of the left breast. Tenderness was present. The swelling was fixed to the chest wall.

Comment [SPP1]: Explain the terms with expansion of meaning

MANAGEMENT:

Patient’s peripheral smear was done and findings consistent with chronic myeloid leukemia in chronic phase were reported. USG breast was done for the patient and was reported as right breast :- no focal lesion noted, right axilla :- reactive lymphadenopathy noted LN 1 - 8.5 x 4.2 mm, LN 2 - 9.1 x 4.6 mm. Left breast :- retroareolar irregular hypochrine of approximate size 26 x 24 mm showing vascularity on doppler. The patient’s TBD was done i/v/o management of raised TLC and Tab Imatinib 400 mg OD and bone marrow study was advised. USG breast was s/o

carcinoma of left breast with axillary lymphadenopathy.



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DEPARTMENT OF RADIODIAGNOSIS — IPD

USG BREAST

Patient's Name Vaishali Waykar Age 44 Sex F

Reff By — Date : 07/05/20

OPD/IPD Reg. No. 210703038 Indication Cation/Clinical

Right Breast :- No focal lesions noted.

Right Axilla :- Reactive lymphadenopathy noted
LN 1 – 8.5 x 4.2 mm
LN 2 – 9.1 x 4.6 mm

Left Breast :- Retroareolar irregular hypoechoic mass of approximate size 26 x 24 mm showing vascularity on Doppler. (Lesion is taller than wider). Fatty calcifications are also noted within.

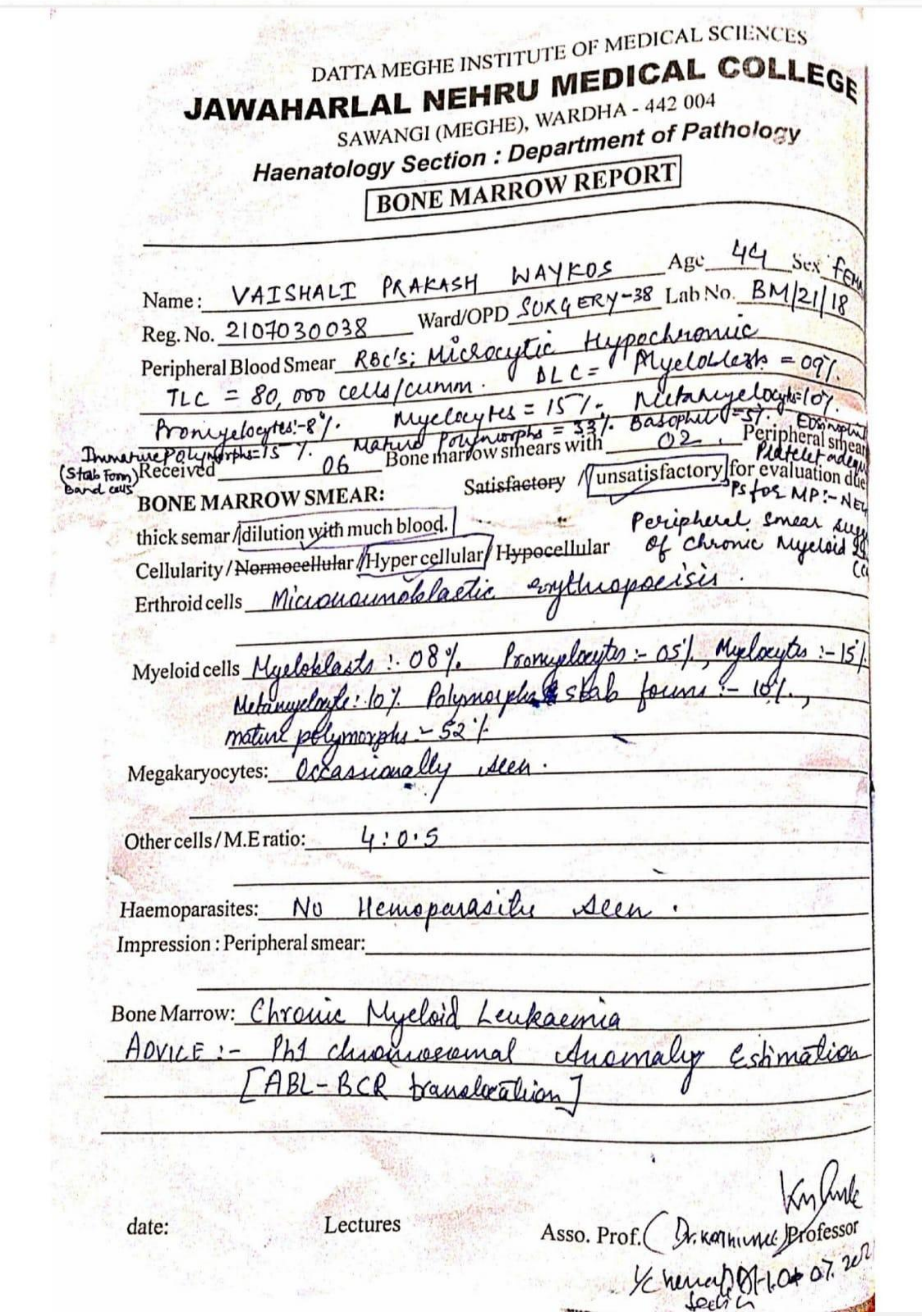
Left Axilla :- lymph node 1 - 8 x 6.2 mm (hilum maintained)
LN - 2 - 8.4 x 6.6 mm (hilum maintained)
LN - 3 - 19.6 x 5.1 (hilum maintained)

IMPRESSION :- F/8/O ? Carcinoma of left breast with axillary lymphadenopathy.

Advice : Histopathological correlation.

Signature of Sonologist
Reg. No. 72631
PROFESSOR
Deptt. of Radio-diagnosis
AVBRH; Sawangi(M), WARDHA

The bone marrow studies were suggestive of chronic myeloid leukemia



DATTA MEGHE INSTITUTE OF MEDICAL SCIENCES

JAWAHARLAL NEHRU MEDICAL COLLEGE

SAWANGI (MEGHE), WARDHA - 442 004

Haenatology Section : Department of Pathology

BONE MARROW REPORT

Name: VAISHALI PRAKASH WAYKOS Age 44 Sex Fem

Reg. No. 2107030038 Ward/OPD SURGERY-38 Lab No. BM/21/18

Peripheral Blood Smear RBC's: Microcytic Hypochromic

TLC = 80,000 cells/cumm. DLC = Myeloblasts = 09%. Metamyelocyte=10%.

Promyelocytes:-8%. Myelocytes = 15%. Basophil=5%. Eosinophil

Immature Polymorphs=15%. (Stab Form) Band cells. Matured Polymorphs = 33%.

Received 06 Bone marrow smears with 02. Peripheral smear

Satisfactory / unsatisfactory for evaluation due

Platelet adequate. PS for MP:- Neg.

BONE MARROW SMEAR:

thick semar / dilution with much blood.

Peripheral smear sugg. of Chronic Myeloid Leukaemia

Cellularity / Normocellular / Hyper cellular / Hypocellular

Erthroid cells Micronormoblastic erythropoeisis.

Myeloid cells Myeloblasts :- 08%. Promyelocytes :- 05%, Myelocytes :- 15%. Metamyelocyte: 10%. Polymorphs stab forms :- 10%., mature polymorphs - 52%

Megakaryocytes: Occasionally seen.

Other cells / M.E ratio: 4:0.5

Haemoparasites: No Hemoparasite seen.

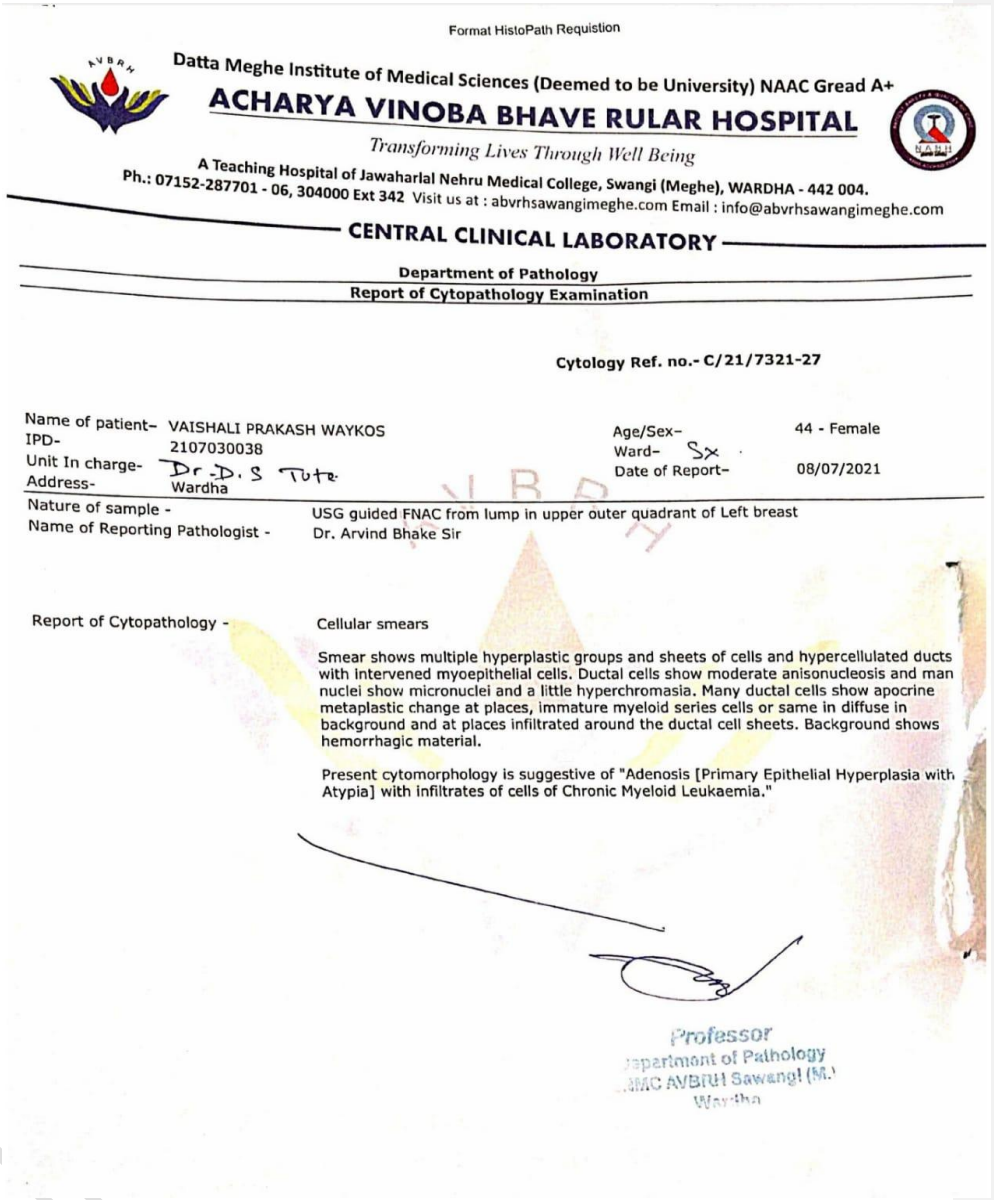
Impression : Peripheral smear:

Bone Marrow: Chronic Myeloid Leukaemia

ADVICE :- Ph1 chromosomal Anomaly estimation [ABL-BCR translocation]

date: Lectures Asso. Prof. (Dr. Karnimnee) Professor

Patients USG guided FNAC was done and was s/o Adenosis with infiltrates of cells of Chronic Myeloid Leukemia.



Format HistoPath Requistion

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CENTRAL CLINICAL LABORATORY

Department of Pathology

Report of Cytopathology Examination

Cytology Ref. no.- C/21/7321-27

Name of patient- VAISHALI PRAKASH WAYKOS
IPD- 2107030038
Unit In charge- Dr. D. S Tute
Address- Wardha

Age/Sex- 44 - Female
Ward- Sx
Date of Report- 08/07/2021

Nature of sample - USG guided FNAC from lump in upper outer quadrant of Left breast
Name of Reporting Pathologist - Dr. Arvind Bhake Sir

Report of Cytopathology - Cellular smears

Smear shows multiple hyperplastic groups and sheets of cells and hypercellulated ducts with intervened myoepithelial cells. Ductal cells show moderate anisonucleosis and man nuclei show micronuclei and a little hyperchromasia. Many ductal cells show apocrine metaplastic change at places, immature myeloid series cells or same in diffuse in background and at places infiltrated around the ductal cell sheets. Background shows hemorrhagic material.

Present cytomorphology is suggestive of "Adenosis [Primary Epithelial Hyperplasia with Atypia] with infiltrates of cells of Chronic Myeloid Leukaemia."

Professor
Department of Pathology
JMC AVBRH Sawangi (M.)
Wardha

Trucut biopsy was done from left breast lump which was s/o Invasive Ductal Carcinoma of breast.

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CENTRAL CLINICAL LABORATORY

Department of Pathology

HISTOPATHOLOGY REPORT

Lab. Ref. No.	:- B/21/6992	**Date of Report**	:- 13-Jul-2021
Patients Name	:- VAISHALI PRAKASH WAYKOS		
Age	:- 44	**Gender**	:- F
Hospital	:- AVBRH	**Ward**	:- WARD
Department	:- SURGERY/M.F.S/NUR		
Consultant I / C	:- DR.	**Hospital Regn. No.**	:- 2107030038
Nature of Material	:- TISSUE FROM LEFT BREAST LUMP.		

HISTOPATHOLOGY REPORT

Seen by Dr. :- Dr. KISHOR HIWALE

Received 4 containers unlabelled.

Container 1
Received very tiny, whitish black, thread like tissue pieces aggregating 0.5 x 0.2 x 0.1 cm.

Container 2
Received single, very tiny, thread like whitish brown tissue piece measuring 0.2 x 1 x 0.1 cm.

Container 3
Received single, thread like tissue piece measuring 0.3 x 0.1 x 0.1 cm.

Container 4
Received very tiny thread like tissue piece measuring 0.5 x 0.1 x 0.1 cm.

Sections from given tissue piece show histopathological features suggestive of Invasive Ductal Carcinoma of Breast.

Professor
Department of Pathology
JNMC AVBRH

Immunohistochemistry examination was done on the breast lump of left side which was s/o triple positive status.

Comment [SPP2]: Immunohistochemistry results with data to be presented

DATTA MEGHE INSTITUTE OF MEDICAL SCIENCES (DU)

Jawaharlal Nehru Medical College

Department of Pathology

Immunohistochemistry Report

IHC test advised by:
Patient: VAISHALI WAYKOS **Ward:** Surgery
Registration number :2107030038 **Unit In-charge :** Dr. DARSHANA **Age/Sex:**44/F
Histopathology Diagnosis : :- Invasive ductal carcinoma of breast

METHODS + Testing Performed on Block Number(s): B/21/6992
Fixative: Formalin
Other (specify): _____
Estrogen Receptor
Primary Antibody SP1/ 6F11/ 1D5/ Other (specify): _____
Progesterone Receptor
Primary Antibody : 1E2/ 636 / 16 / SP2/ 1A6/ 1294/ 312 / Other (specify)_____
Cold Ischemia and Fixation Times:
Meet requirements as per guidelines
Do not meet requirements as per guidelines
Cannot be determined (explain):

	ER Scoring System	PR Scoring System
Proportion score	03	03
Intensity score	03	03
Total Allred score	06	06
Impression:	POSITIVE	POSITIVE

HER 2 :
SCORE : 3+

Impression:- POSITIVE

Ki67: >75%

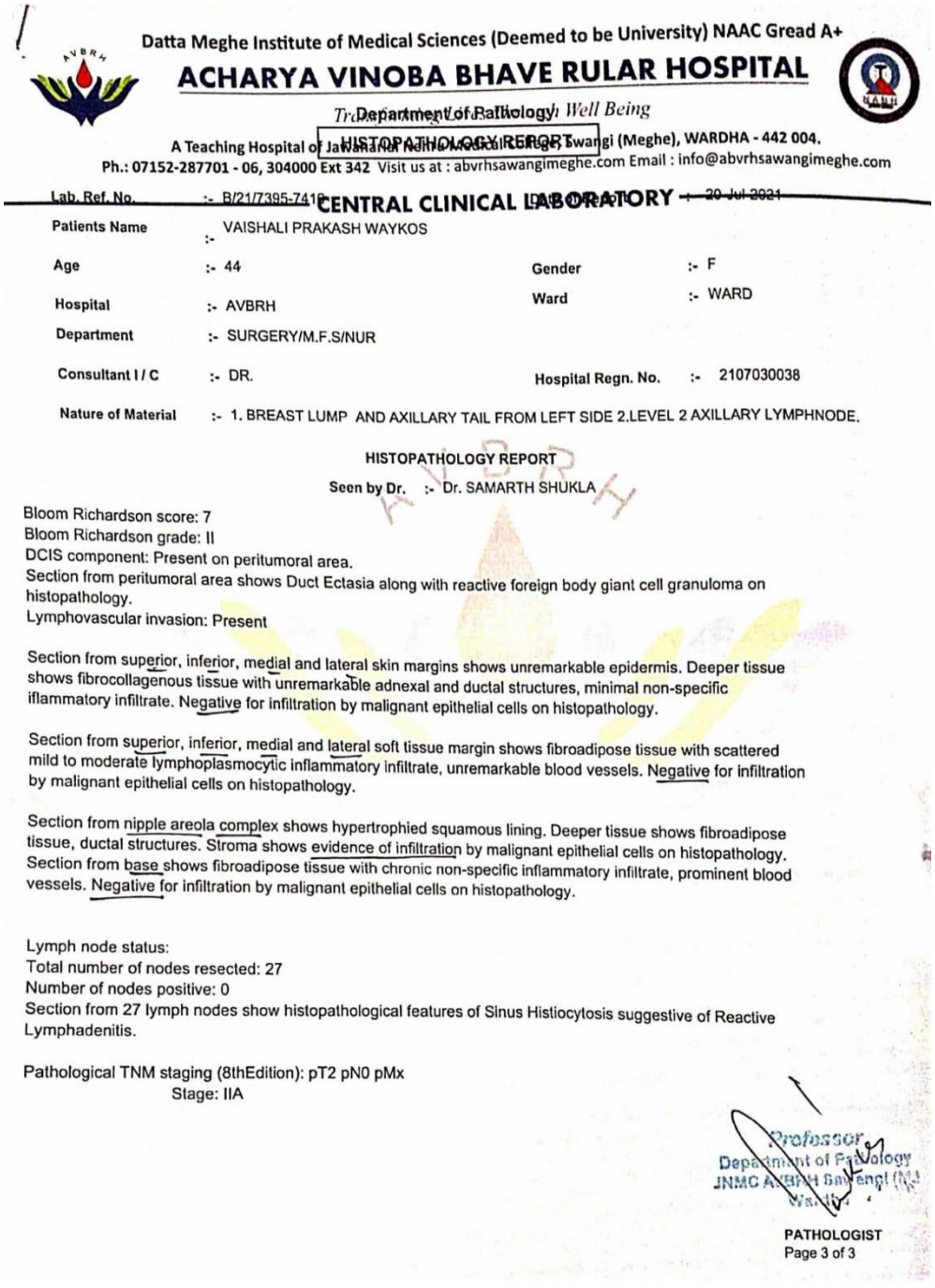
Final Immunohistochemistry impression-

Molecular subtype- **Luminal Type B**
Triple Positive Breast Carcinoma.

DR. KISHOR HIWALE
PROFESSOR
DEPT. OF PATHOLOGY
Professor
Department of Pathology
JNMC AVBRH Sawangi (M.S.)
Wardha

Patient was taken for left sided MRM with axillary lymph node dissection.

Histopathological examination was done on the MRM specimen which was s/o pt2 pn0 pmx (stage IIa).



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HISTOPATHOLOGY REPORT

CENTRAL CLINICAL LABORATORY

Lab. Ref. No. :- B/21/7395-741 Date :- 20-Jul-2021

Patients Name :- VAISHALI PRAKASH WAYKOS

Age :- 44 Gender :- F

Hospital :- AVBRH Ward :- WARD

Department :- SURGERY/M.F.S/NUR

Consultant I / C :- DR. Hospital Regn. No. :- 2107030038

Nature of Material :- 1. BREAST LUMP AND AXILLARY TAIL FROM LEFT SIDE 2.LEVEL 2 AXILLARY LYMPHNODE.

HISTOPATHOLOGY REPORT

Seen by Dr. :- Dr. SAMARTH SHUKLA

Bloom Richardson score: 7
Bloom Richardson grade: II
DCIS component: Present on peritumoral area.
Section from peritumoral area shows Duct Ectasia along with reactive foreign body giant cell granuloma on histopathology.
Lymphovascular invasion: Present

Section from superior, inferior, medial and lateral skin margins shows unremarkable epidermis. Deeper tissue shows fibrocollagenous tissue with unremarkable adnexal and ductal structures, minimal non-specific iflammatory infiltrate. Negative for infiltration by malignant epithelial cells on histopathology.

Section from superior, inferior, medial and lateral soft tissue margin shows fibroadipose tissue with scattered mild to moderate lymphoplasmocytic inflammatory infiltrate, unremarkable blood vessels. Negative for infiltration by malignant epithelial cells on histopathology.

Section from nipple areola complex shows hypertrophied squamous lining. Deeper tissue shows fibroadipose tissue, ductal structures. Stroma shows evidence of infiltration by malignant epithelial cells on histopathology.
Section from base shows fibroadipose tissue with chronic non-specific inflammatory infiltrate, prominent blood vessels. Negative for infiltration by malignant epithelial cells on histopathology.

Lymph node status:
Total number of nodes resected: 27
Number of nodes positive: 0
Section from 27 lymph nodes show histopathological features of Sinus Histiocytosis suggestive of Reactive Lymphadenitis.

Pathological TNM staging (8thEdition): pT2 pN0 pMx
Stage: IIA

Professor
Department of Pathology
JNMC AVBRH Sawangi (M)
Wardha

PATHOLOGIST

Page 3 of 3

Review TBD was done and Tab Imatinib 400mg od lifelong and Tab Tamoxifen 20mg od for 10 years was advised. The patient was then discharged with an advise to follow up on a later date.

DISCUSSION:

Carcinoma of the breast is a frequently encountered malignancy particularly in the post menopausal females and reproductive age group females. Various studies have been performed on the association of carcinoma breast with synchronous malignancies. There have been reported cases having various synchronous malignancies such as carcinoma stomach, carcinoma ovary, carcinoma cervix, carcinoma lung etc. Many theories have been advanced to describe this increased risk, including the impairment of the immune system, genetic susceptibility, age. They may also have heightened responses to the various carcinogens. Therapy related myelodysplastic syndromes are also noted in some cases where there was detection of such a malignancy after the treatment or during the treatment of carcinoma breast. There was no evidence of synchronous presentation of chronic myeloid leukemia and carcinoma breast. The management of dual tumours is challenging. The decisions that have to be made include sequence of treatment, chemotherapy regimen and management of complications. These patients are also prone to infections as there is immune dysfunction and lower rates of survival or even response.

Comment [SPP3]: Please quote the relevant reference with research study

CONCLUSION:

Chronic myeloid leukemia is an insidiously progressive condition and comparatively rare type of blood cell malignancy that begins in the bone marrow. The rate of CML in these individuals seems to reach at its peak about 10 years after the exposure. Carcinoma breast on the other hand is one of the most common cause of death in middle aged women in western countries. There are numerous factors contributing as it's etiological factors. The case report emphasises on the synchronous presentation of the carcinoma breast and chronic myeloid leukemia. We also wanted to propagate the notion that a larger prospective, randomised study is warranted to establish the association between and needful approach of management in synchronous presentation of carcinoma breast and chronic myeloid leukemia.

SUMMARY :

In this case there was synchronous presence of carcinoma breast and chronic myelogenous leukemia. There are some studies in the literature which mention the synchronous presence of chronic myeloid leukemia

and other secondary malignancies but there is no proper documentation in the literature about synchronous presence of these two malignancies. The management of two malignancies are difficult but there should be a proper decision and plan of sequence of treatment, chemotherapy regimen, management of complications.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

References

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5. devita vt jr, hellman s, rosenberg sa. cancer principle and practice of oncology. 7 th ed. philadelphia: lippincott williams and wilkins; 2005. p. 1430.

Comment [SPP4]: References in capital letters and proper formatting to be done

Comment [SPP5]: Capitals of Names to be carried out

Comment [SPP6]: Capitals to be carried out

Data and materials availability

All data associated with this study are present in the paper

Contribution Details:

Enter the role of contributors in the first column and the names of the contributors in columns 2, 3, and so on.

Role (Concepts, Design, Definition of intellectual content, investigation, manuscript writing, etc.)	Contributor 1	Contributor 2	Contributor 3	Contributor 4	Contributor 5	Contributor 6	Contributor 7
Data acquisition, interpretation of data, manuscript writing, and editing	Dr. Varun Kulkarni						
concept and design, critical review, final approval of the version published		Dr. Anurag Bhattacharjee					
Guarantee, Critical review, final approval of the version			Dr. Harshal Ramteke				

to be published							
Critical reviewer				Dr. Abhishek Gupta	Dr Shubham Durge	Dr. Meenakshi Yeola (Pate)	Dr Sharang Kulkarni

Patient Declaration of consent statement: Written and oral informed consent was obtained from thepatient in this study

Reporting guidelines: The article adheres to the CARE reporting guidelines for case reports

Fill the CARE checklist given below:

Reporting guidelines for Case Report: CARE (2016)

Topic	Item	Checklist item description	Yes/ No
Title	**1**	The words "case report" should be in the title along with the area of focus	**yes**
Abstract	**2a**	Structured abstract with the headings: Rationale, Patient concerns, Diagnosis, Interventions, Outcomes, Lessons If unstructured abstract, all the details as per the above heading to be present	**Yes**
	2b	Abstract structure outlines in the Information to Authors and contains all the information mentioned in 2a.	**Yes**
Introduction			
	3a	One or two paragraphs summarizing why this case is unique	**Yes**
	3b	Statement to be cited adequately	**Yes**
Case report			
Patient Information	**4a**	De-identified demographic information and other patient-specific information	**yes**
	4b	Main concerns and symptoms of the patient	**yes**
	4c	Medical, family, and psychosocial history including relevant genetic information (also see timeline)	**Yes**
	4d	Relevant past interventions and their outcomes	**Yes**

Clinical Findings	**5**	Describe the relevant physical examination (PE) and other significant clinical findings	**Yes**
Diagnostic Assessment	**6a**	Diagnostic methods (such as laboratory testing, imaging, surveys)	**Yes**
	6b	Diagnostic challenges (such as access, financial, or cultural)	**Yes**
	6c	Diagnostic reasoning, including other diagnoses, was considered.	**Yes**
	6d	Prognostic characteristics (such as staging in oncology) where applicable	**Yes**
Therapeutic Intervention	**7a**	Types of intervention (such as pharmacologic, surgical, preventive, self-care)	**Yes**
	7b	Administration of intervention (such as dosage, strength, duration)	**Yes**
	7c	Changes in the intervention (with rationale)	**Yes**
Follow-up and Outcomes	**8a**	Clinician and patient-assessed outcomes (when appropriate)	**Yes**
	8b	Necessary follow-up diagnostic and other test results	**Yes**
	8c	Intervention adherence and tolerability (How was this assessed?)	**Yes**
	8d	Adverse and unanticipated events	**No**
	8e	Follow-up duration and the last known status of the patient	**No**
Discussion	**9a**	Discussion of the strengths and limitations in your approach to this case	**Yes**
	9b	Discussion of the relevant medical literature.	**Yes**
	9c	The rationale for conclusions (including assessment of possible causes)	**Yes**
	9d	The primary “take-away” lessons of this case report	**yes**
	9e	Citations adequate, preferably from recent literature	**Yes**
-Informed Consent	**10a**	Mention the patient (family/ legal representative) informed consent for publication of the case details. For minors (children), the consent statement should mention if "parental/ legal guardian consent" was obtained.	**yes**
	10b	Mention if the patient consent has been waived/ exempted by the IRB and mention the appropriate details (including the exempt number)	
Figures	**11**	Figures (full face) to be sufficiently obscured Confidential data like the patient's name, date of birth, and personal identification should not be displayed in the images, including radiographs.	**yes**