Primary histiocytic sarcoma breast, a very rare case report

Nikita Jaiprakash Mulchandani[1], Bhavana Asit Mehta[2], Vipal Hasmukhbhai Parmar[1], Sandip Chandrakant Shah[3], Ankita Girish Murnal[4]

From [1]Consultant Histo-Pathologist, Department of Histopathology, Neuberg Supratech Reference Laboratories, [2]Head at Department of Histopathology, Neuberg Supratech Reference Laboratories and Professor at Sandip and Bhavini Research Institute, [3]Founder Director of Neuberg Supratech Reference Laboratories, [4]Research Associate, Department of Research, Sandip and Bhavini Research Institute, Ahmedabad, Gujarat, India

ABSTRACT

Histiocytic sarcoma (HS) is an uncommon, aggressively evolving histiocytic tumor showing macrophage differentiation. It is typically composed of non-cohesive large cells that show positive immunostaining for two or more histiocytic markers, are negative for T-cell, B-cell, myeloid cell, and follicular dendritic cell markers, and are also negative for CD1a and langerin. In this article, we present the case of a 49-year-old female who was diagnosed with mammary HS.

Key words: *Breast, Histiocytic, Primary, Sarcoma, Spindle cell tumor*

True histiocytic sarcomas (HSs) are rare, usually aggressive hematological neoplasms characterized by malignant proliferation of cells showing morphologic and immunophenotypic evidence of histiocytic differentiation [1]. HS can present as a solitary mass or disseminated disease, with most cases involving extranodal sites including the gastrointestinal tract, skin, superficial and deep soft tissue, lung, and nasal cavity [1-3]. Primary HS of the breast is uncommon. In this case report, we describe an out-of-the ordinary case of HS in a 49-year-old female who presented with a left breast lump.

CASE REPORT

A 49-year-old female presented with a breast lump of 6 months duration. A mammogram revealed a Breast Imaging-Reporting and Data Systems category 4 well-defined, ovoid, radio-dense lesion with lobulated margins in the upper inner quadrant of the left breast measuring 2.8 × 2 cm.

The biopsy was sent to us in multiple fragments. The bits were firm, from gray white to grey brown grossly. On microscopy, the hematoxylin-eosin-stained sections showed lesional tissue composed of sheets of loosely cohesive cells, largely histiocytic/epithelioid in appearance with abundant eosinophilic cytoplasm, moderately pleomorphic, indented/folded nuclei, and moderate eosinophilic cytoplasm showing occasional vacuolization (Fig. 1a). Numerous multinucleate giant cells and admixed lymphocytes were present. Foci of necrosis could be appreciated. Mitotic figures were in the range of 11–12/10 high power fields. Native breast ducts or lobules were not seen.

Based on this histomorphological picture at an unusual location, a handful of differentials were considered, including: giant cell tumor of soft tissue, HS, myeloid sarcoma, carcinoma with osteoclast-like stromal giant cells, Rosai-Dorfman disease (RDD), malignant melanoma, and cellular spindled histiocytic tumor complicating fat necrosis. Considering these differential diagnoses, immunohistochemistry (IHC) was performed. The details of these markers are given in Table 1.

On IHC, the tumor cells showed immunoreactivity to leukocyte common antigen (Fig. 2a), CD4, CD68 (Fig. 2b), and CD163 (Fig. 2c). Very focal CD1a positivity was noted. Ki-67 index (Fig. 2d) was in the range of 35–40%. The cells were negative for Pan-CK, CD21, CD23, S100, CD3, CD20, CD30, CD34, CD138, epithelial membrane antigen (EMA), PAX5, myeloperoxidase (MPO), anaplastic lymphoma kinase (ALK), and human melanoma black 45 (HMB45).

The absence of CD3, CD20, CD30, CD138, PAX5, and ALK (B- and T-cell-related markers) immunostaining in the cells of interest ruled out the possibility of a host of non-Hodgkin lymphomas, including anaplastic large cell lymphoma. CD34 and MPO-negative immunostains ruled out the possibility of myeloid sarcoma. Negative CD21, CD23, and S100 with focal CD1a immunostaining ruled out the possibility of tumors derived from Langerhans cells and interdigitating and follicular dendritic cell sarcomas. Negative Pan-CK and S100 immunstaining ruled

Access this article online

Received - 02 February 2024
Initial Review - 16 March 2024
Accepted - 12 April 2024

DOI: 10.32677/ejms.v9i2.4468

Quick Response code

Correspondence to: Mrs. Ankita Girish Murnal, Neuberg Supratech, Ground Floor, Kedar Building, Opp. Krupa Petrol Pump Parimal Garden, Ahmedabad, Gujarat 380006, India. E-mail: contact@sbri.org.in

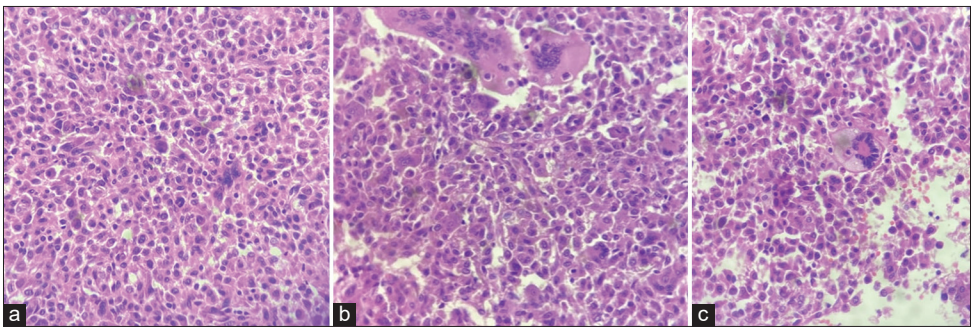

Figure 1: (a) Neoplasm composed of sheets of histiocytoid cells with (b) occasional multinucleate giant cells and few (c) touton-type giant cells

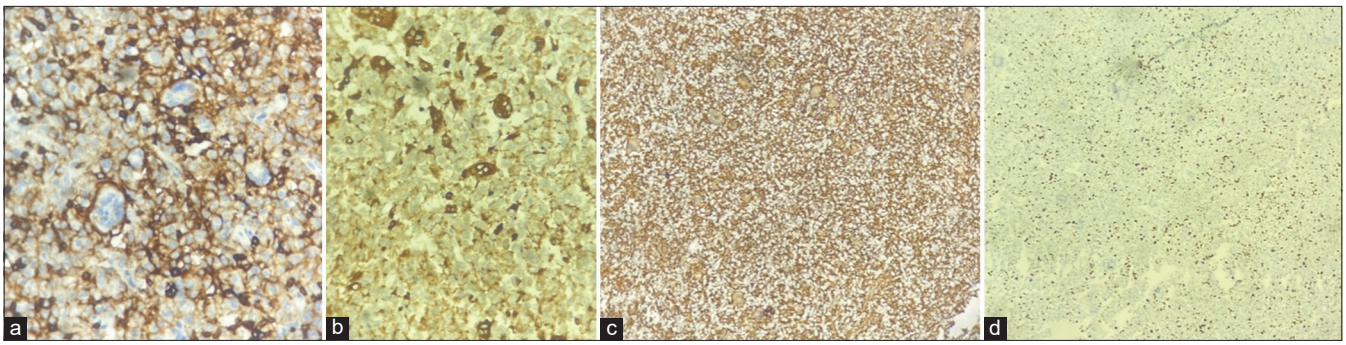

Figure 2: (a) The neoplastic cells express CD45, (b) CD68 and (c) CD163, (d) The Ki67 index is approximately 35–40%

Table 1: Source and details of immunohistochemistry markers used

Name	Clone	Source	Dilution
LCA	2B11+PD7/26	Monoclonal mouse anti human CD45	RTU
CD3	F-7.2.38	Dako	RTU
CD20	L26	Dako	RTU
CD4	4B12	Dako	RTU
CD68	KP1	Dako/BioSB	RTU
CD163	EP324	PathnSitu	RTU
CD21	1F8	Dako	RTU
CD23	DAK-CD23	Dako	RTU
CD1a	O10	Thermo Fisher	RTU
S100	Polyclonal	Dako	RTU
CD34	QBEND10	Dako	RTU
CD138	MI15	Dako/PathnSitu	RTU
EMA	E29	Dako	RTU
Pan-CK	AE1/AE3	Dako	RTU
PAX5	DAK-PAX-5	Dako	RTU
MPO	Polyclonal	Dako	RTU
ALK-CD246	ALK 1	Dako	RTU
HMB45	HMB-45	Dako	RTU

ALK: Anaplastic lymphoma kinase, CD: Cluster of differentiation, CK: Cytokeratin, EMA: Epithelial membrane antigen, HMB: Human melanoma black, LCA: Leukocyte common antigen, MPO: Myeloperoxidase, RTU: Ready to use

out the possibility of carcinoma and RDD, respectively. Negative HMB45 with S100 eliminated the possibility of malignant melanoma.

The possibility of a cellular spindled histiocytic tumor complicating fat necrosis was dismissed in view of the clinico-radiological picture, lack of fat necrosis, increased mitotic count, and elevated Ki67 proliferation index. Due to the absence of hemorrhage, aneurysmal bone cyst-like areas, reactive fibrosis, and metaplastic bone formation, the closest differential of a giant cell tumor of soft tissue was disregarded, and a final impression of HS was rendered.

DISCUSSION

HS is an uncommon histiocytic neoplasm among a heterogenous group of histiocytic and dendritic cell tumors. It poses a diagnostic

challenge for both pathologists and clinicians. The diagnosis of HS relies on a combination of morphological and immunophenotypic findings. These tumors are driven by certain recently uncovered molecular mechanisms, the identification of which has thereby improved the diagnostic adequacy [4].

HS, although common in adults, can present at any age from infancy to old age and shows a male pre-dominance [1,4]. Its occurrence at extranodal sites is often with other metachronous malignancies like mediastinal germ cell tumors, malignant lymphomas, and leukemias like follicular lymphomas and chronic lymphocytic lymphoma/small lymphocytic leukemia [5,6]. An intrasinusoidal presentation in lymph nodes, liver, and spleen is also known [4]. Similar to this study, Bang *et al*. have reported a case of primary breast HS in a 75-year-old female [7]. Nangal *et al*. and Trevisan *et al*. have also reported HS in the axillary soft tissue and in the subcutis of breast skin, respectively [8,9].

HS has a relatively diverse morphologic appearance [4]. Morphologically, the neoplastic cells are spindled to pleomorphic with abundant cytoplasm, which proliferates in diffuse, poorly cohesive sheets. The nuclei could be monotonous, with nuclear pleomorphism ranging from mild to severe. Mitotic activity is variable. Admixed plasma cells, reactive small lymphocytes, neutrophils, eosinophils, and plasma cells are seen [1,4]. Multinucleated giant cells with emperipolesis (Fig. 1b), Touton-type giant cells (Fig. 1c), and xanthomatous cells as seen in our case are also noted [1,4,10].

HS on IHC shows characteristics of mature tissue histiocytes and macrophages. For its diagnosis, the expression of one or more histiocytic markers which include CD68, CD163, CD4, CD11c, C14, and lysozyme, is crucial. Immunoreactivity for S100 is seen in 50% of cases. This, in combination with negativity for B- and T-cell markers, other markers of histiocytic and dendritic cell neoplasms (CD21, CD23, CD35, CD1a, langerin), myeloid sarcoma markers (CD13, CD33, MPO), Pan-CK, EMA, and melanocytic markers (HMB45), is sufficient for the diagnosis of HS [1,11].

We worked up our case in a similar fashion. What was peculiar about IHC in our case was the expression of CD1a. However, due to negative S100 immunostaining, the possibility of Langerhans cell histiocytosis was ruled out. Facchetti *et al*. mention cases with double histiocytic and Langerhans cell components in cases classified as Langerhans cell tumors and HS [4]. The diagnosis of these cases required double immunostaining which was not available in our setting, posing a limitation. The line distinguishing various histiocytic and dendritic cell tumors may be blurred in some cases. In such situations, the final diagnosis relies on identifying the main cell component.

Patients with clinically localized disease and small primary tumors are shown to have favorable outcomes [1,12]. Recent studies have demonstrated therapeutically useful molecular alterations in the RAS-RAF-ERK pathway, more commonly involving the *BRAF* gene [13-15]. Histiocytic tumors with *BRAFV600E* mutations can be targeted with Vemurafenib.

CONCLUSION

Primary HS of the breast is extremely rare. A strong index of suspicion on histomorphology combined with a robust IHC workup is the key to clinching a diagnosis in these cases. Although treatment options range from surgery to radiotherapy and chemotherapy in these cases, the future appears to be changing with the recent identification of the RAS-RAF-ERK pathway in the tumorigenesis of histiocytic neoplasms and the recognition of druggable molecular alterations [14].

REFERENCES

1. Swerdlow SH, Campo E, Harris NL, *et al*. Histiocytic sarcoma. In: WHO Classification of Tumours of Haematopoietic and Lymphoid Tissues. Revised 4th ed. Lyon: International Agency for Research on Cancer; 2017. p. 468-70.
2. Hung YP, Qian X. Histiocytic sarcoma. Arch Pathol Lab Med 2019;144:650-4.
3. Bellalah A, Korbi I, Hammouda SB, *et al*. Small bowel and lung histiocytic sarcoma revealed by acute peritonitis: A case report with review of literature. Ann Med Surg (Lond) 2021;68:102638.
4. Facchetti F, Pileri SA, Lorenzi L, *et al*. Histiocytic and dendritic cell neoplasms: What have we learnt by studying 67 cases. Virchows Arch 2017;471:467-89.
5. Feldman AL, Arber DA, Pittaluga S, *et al*. Clonally related follicular lymphomas and histiocytic/dendritic cell sarcomas: Evidence for transdifferentiation of the follicular lymphoma clone. Blood 2008;111:5433-9.
6. Shiozawa E, Yamochi-Onizuka T, Takimoto M, *et al*. The GCB subtype of diffuse large B-cell lymphoma is less frequent in Asian countries. Leuk Res 2007;31:1579-83.
7. Bang S, Kim Y, Chung MS, *et al*. Primary histiocytic sarcoma presenting as a breast mass: A case report. J Breast Cancer 2019;22:491-6.
8. Nangal JK, Kapoor A, Narayan S, *et al*. A case of CD68 negative histiocytic sarcoma of axilla masquerading as metastatic breast cancer. J Surg Case Rep 2014;2014:rju071.
9. Trevisan F, Xavier CA, Pinto CA, *et al*. Case report of cutaneous histiocytic sarcoma: Diagnostic and therapeutic dilemmas. An Bras Dermatol 2013;88:807-10.
10. Jaffe ES, Arber DA, Campo E, *et al*. Hematopathology. 2nd ed. Philadelphia, PA: Elsevier; 2017.
11. Takahashi E, Nakamura S. Histiocytic sarcoma: An updated literature review based on the 2008 WHO classification. J Clin Exp Hematop 2013; 53:1-8.
12. Pileri SA, Grogan TM, Harris NL, *et al*. Tumours of histiocytes and accessory dendritic cells: An immunohistochemical approach to classification from the International Lymphoma Study Group based on 61 cases. Histopathology 2002;41:1-29.
13. Emile JF, Abla O, Fraitag S, *et al*. Revised classification of histiocytoses and neoplasms of the macrophage-dendritic cell lineages. Blood 2016;127:2672-81.
14. Emile JF, Diamond EL, Hélias-Rodzewicz Z, *et al*. Recurrent RAS and PIK3CA mutations in Erdheim-Chester disease. Blood 2014;124:3016-9.
15. Diamond EL, Durham BH, Haroche J, *et al*. Diverse and targetable kinase alterations drive histiocytic neoplasms. Cancer Discov 2016;6:154-65.

Funding: Nil; Conflicts of Interest: None Stated.

How to cite this article: Mulchandani NJ, Mehta BA, Parmar VH, *et al*. Primary histiocytic sarcoma breast, a very rare case report. Eastern J Med Sci. 2024;9(2):16-18.