Indian Journal of Pathology and Oncology 2022;9(4):360–363

Content available at: https://www.ipinnovative.com/open-access-journals

Indian Journal of Pathology and Oncology

Journal homepage: www.ijpo.co.in

Case Report

Sarcomatoid carcinoma metastasis to bone marrow with unknown primary

Rekha Nirwan[1], Rateesh Sareen[1,*], G.N. Gupta[1]

[1] *Dept. of Pathology, Santokba Durlabhji Memorial Hospital (SDMH), Jaipur, Rajasthan, India*

ARTICLE INFO

Article history:
Received 28-10-2022
Accepted 15-11-2022
Available online 14-12-2022

Keywords:
Sarcomatoid carcinoma
Primary of unknown origin
Metastasis

ABSTRACT

Sarcomatoid carcinoma presenting as bone marrow metastasis with unknown primary is a rare entity. Usually patients present with widespread symptoms of extensive disease process. In the present case patient was evaluated for anemia and a subsequent bone marrow examination showed metastatic malignancy. All complimentary diagnostic tests were performed, Immunohistochemistry of bone marrow biopsy revealing presence of epithelia differentiation lineage markers with mesenchymal lineage markers also although routine biopsy showed only subtle mesenchymal component. The patient was referred to higher cancer centre and despite of elaborate laboratory work up including PET scan the primary origin of metastatic sarcomatoid carcinoma remained undetermined as patient unfortunately passed away within 10 days.

1. Introduction

Sarcomatoid carcinoma are rare malignant tumors arising in diverse organs including liver, salivary glands, uterus, ovary, skin and other organs.[1–4] They are characterized by mixture of epithelial and sarcomatous (mesenchymal) component. It was Virchow[5] in 1863 that noted the dual carcinoma and sarcoma component in the tumor and hypothesized origin- as either two lesions arising separately or admixed or may be one type giving origin to other. The advent of molecular techniques after 1970 gave sense that both the carcinoma and sarcoma component arise from same precursor cell.[6,7] The term carcinosarcoma and sarcomatoid carcinoma are used interchangeably, however carcinosarcoma is favored terminology where two distinct epithelia and mesenchymal areas are identified. The term sarcomatoid carcinoma is used where transition from epithelia to mesenchymal areas are seen in the tumor.

The present case is an uncommon malignancy that was diagnosed as metastasis in bone marrow and in spite of all work up- Immunohistochemistry (IHC), PET scan, the primary site could not be identified even after referral to higher oncology centre and the case was labeled as cancer of unknown primary (CUP), a carcinosarcoma presenting with bone marrow metastasis with unknown primary.

2. Case Report

A 61-year-old male was evaluated for complaints of dyspnoea, weakness, lethargy and slightly decreased appetite. The chest X-ray, abdominal CT scan did not reveal any abnormality. The laboratory investigations revealed- BUN- 32.6 mg/dl, Creatinine -0.59 mg /dl, Sodium 132 m mol/litre, potassium 2.96 m mol/liter, chloride 93.8 m mol/lit, glucose 161 mg/dl, SGOT- 43U/L, SGPT 25 U/L, total Bilirubin 0.65 mg/dl, Direct Bilirubin-0.26 mg/dl, Total protein-5.85 gm/dl, Albumin 2.20 gm/dl, globulin 3.65 gm/dl, A/G ratio 1.58, Alkaline Phoshatase 272 U/L, LDH-302 U/L, uric acid – 2.50 mg/dl, Serum calcium – 7.69 mg/dl, Serum Magnesium- 1.78 mg/dl, Serum AFP-1.18 ng/ml, Serum CEA <1.00 ng/ml, Serum beta HCG-0.97 Miu/ml, Serum Total PSA-0.69 ng/ml and Serum CA

* *Corresponding author*.
E-mail address: drrateeshsareen@yahoo.co.in (R. Sareen).

https://doi.org/10.18231/j.ijpo.2022.087

19-9 was <2.00 U/ml. The Prothrombin time was 23.4 seconds, APTT – 30.5 and INR – 1.68. An automated complete blood count (CBC) demonstrated Hemoglobin- 60 g/L (reference range 130-170 g/L), white blood cell count 11.2 x 10 3 /L (reference range 4-10 x 10 3 /L) Platelet count 494 x 10 9/L (reference range 150-450 x 10 6/L), Hematocrit 21.6% (reference range-36%-46%), differential count –Neutrophils- 82%, Lymphocytes-13%, Monocytes-4% and Eosinophils-1%. The ANA test was negative, Sputum for AFB did not show acid fast bacillus, and Malaria rapid antigen test and Widal were also negative. The routine urine examination did not show any abnormality. Bone marrow aspiration and biopsy was done. Bone marrow aspiration findings revealed cellular marrow with normoblastic erythroid hyperplasia, normal grnulopoiesis and thrombopoesis. The bone marrow biopsy showed diffuse replacement of bone marrow by sheets of spindle cells with pleomorphic hyperchromatic nuclei having large nucleoli with abundant eosinophilic cytoplasm (Figures 1, 2 and 3) Brisk mitotic activity was noted. A diagnosis of poorly differentiated malignant epithelial neoplasm was made and IHC advised. Immunohistochemistry revealed – Positivity for EMA and PAX -8 Vimentin, MPO, CD 68 (Focally), CK (Focal and patchy). CD 45, HMB 45, CD 34, P63, CD56, CD15, CD117, PAX5, CK-7, CK-20, TTF-I, GATA3, SF1, MELAN A, CD10, Inhibin and NKX3.1 were negative. The PET scan showed diffuse increased FDG uptake in bone marrow – likely to be metabolically active disease. FDG uptake in right adrenal was increased with preaortic lymph nodes and liver lesions as suspicious for mitotic pathology (Figures 4, 5 and 6). A possibility of primary from adrenal was suggested. However, the IHC did not confirm adrenal primary and hence a diagnosis of Sarcomatoid carcinoma of unknown primary was made.

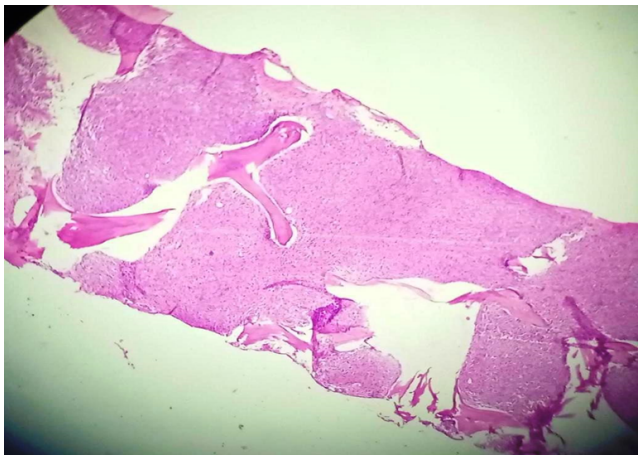

Fig. 1: H & E section bone marrow biopsy (10 x)

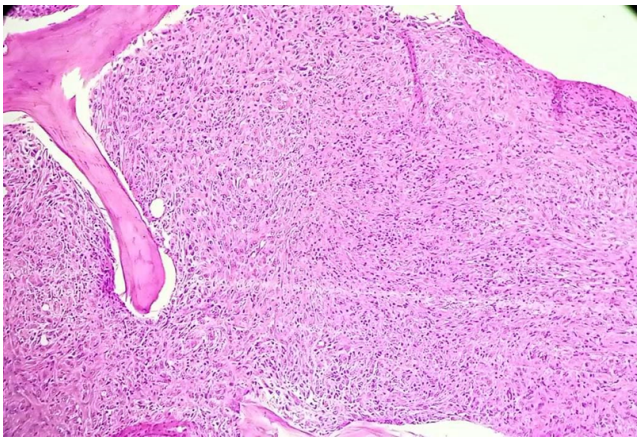

Fig. 2: H & E section bone marrow biopsy (100 x)

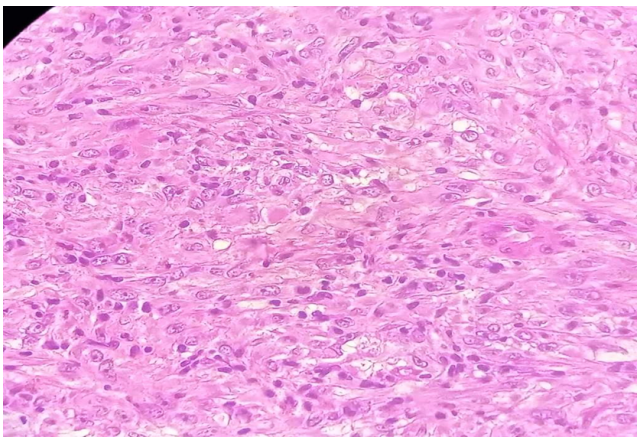

Fig. 3: H & E section bone marrow biopsy (400 x)

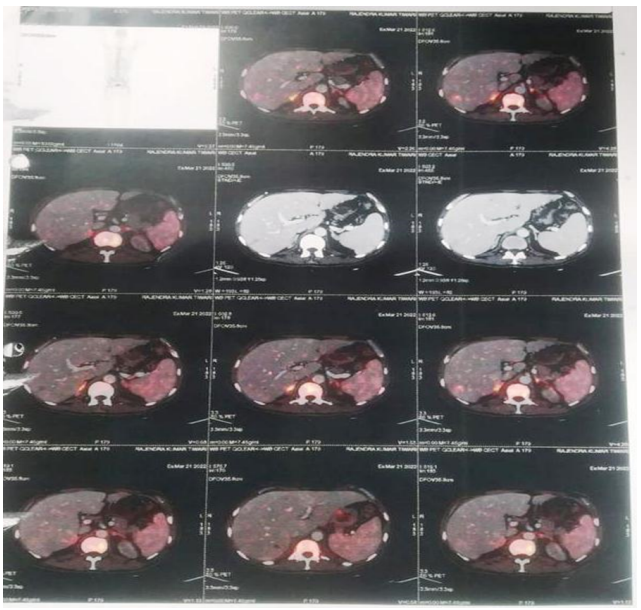

Fig. 4: PET scan

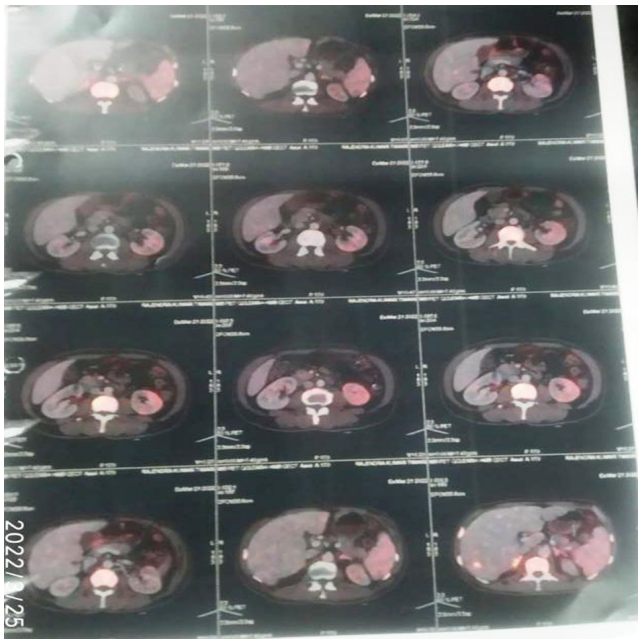

Fig. 5: PET scan

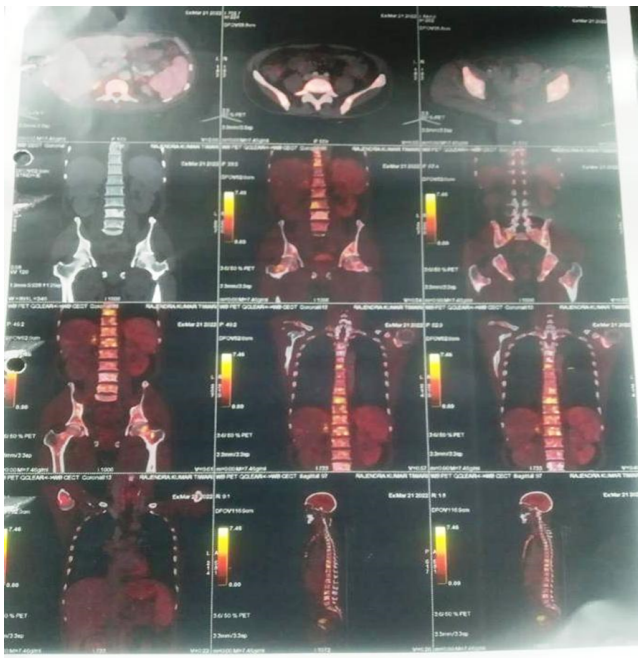

Fig. 6: PET scan

3. Discussion

The present case was diagnosed as carcinosarcoma based on morphology and IHC in bone marrow. The primary site could not be found although an elaborate work up was done. Considering it as primary carcinosarcoma of bone marrow which is exceedingly rare entity, the present case will be the first reported case. Carcinosarcoma from lung, breast, skin, CBD, liver and uterus- adenexae have been reported in literature but none as primary in bone marrow. Carcinosarcoma of unknown primary is of rare occurrence, these unusual tumors are most commonly gynecologic in origin where they are referred as Mullerian tumors (MMT's).[8] They are named as metaplastic carcinoma in breast[9] and sarcomatoid carcinoma in lung.[10]

There are various hypotheses that have been put forward to explain the origin of carcinosarcoma – the collision tumor hypothesis, the composition hypothesis, combination hypothesis and the conversion / divergence hypothesis.[11,12] According to the collision theory carcinosarcoma arises due to collision of two independent tumors resulting in single neoplasm. The composition hypothesis believed that the mesencymal componenet arises due to pseudosarcomatous reaction to epithelia malignancy. The combination theory suggested that both components arise from a pluripotent stem cell. The conversion/ divergence hypothesis put forward metaplastic sarcomatoid transformation of epithelia component. The recent IHC and molecular genetic studies have supported the concept of epithelial – mesenchymal transition (EMT) as the favoured notion for understanding the origin of these biphasic tumors where the two components are genomically related to one another supported by the presence of identical mutations of p53 and Kras in both components.

CUP itself is a heterogeneous group of cancers for which in spite of detailed evaluation the anatomical site of origin remains unidentified.[13,14] The pathogenesis of CUP is poorly understood and they have early dissemination with short symptom history (< 3 months).[15] The diagnosis is always challenging and prognosis is poor. The criteria for CUP include biopsy proven malignancy and even after detailed physical examination, blood tests, chest radiograph, computed tomography (CT) and ancillary tests the primary anatomic site remains unknown.[16] The role of CT scan in CUP is not clearly defined and has its own limitations but scan prevents it from being considered as standard of care.

The present case had a very aggressive clinical evolution culminating in patient demise which is in agreement with literature studies on these types of tumors.[16–21] The role of IHC in the diagnosis of sarcomatoid carcinoma also uses organ specific markers to determine organ of primary tumor origin however the present case they were unable to ascertain primary site.[20,22]

The rare occurrence, difficulty in diagnosis, absence of typical clinical and morphological features to diagnosis

mandates requirement of molecular studies affording quick timely diagnosis and improved treatment options as the current therapy strategies are inadequate.[16,18,19]

4. Conflict of Interest

None.

5. Source of Funding

None.

References

1. Yoon GS, Choi DL. Sarcomatoid carcinoma of common bile duct: a case report. *Hepatogastroenterology*. 2004;51(55):106–9.
2. Leng Q, Xiang XI, Tang Y, Yang Y, l Qiu. Primary hepatic sarcomatoid carcinoma: a case report. *Exp Ther Med*. 2015;10(3):1145–8.
3. Lee JW, Kim MW, Choi NK, Cho IJ, Hong R. Double primary hepatic cancer (sarcomatoid carcinoma and hepatocellular carcinoma): a case report. *Mol Clin Oncol*. 2014;2(6):949–52.
4. Dong A, Dong H, Jing W, Zuo C. FDG PET/CT in sarcomatoid carcinoma of the gallbladder with chondroid differentiation. *Clin Nucl Med*. 2016;41(8):638–40.
5. Virchow R. Die Krankhaften Geschwülste. Berlin, Germany: Springer; 1863.
6. Zhao S, Bellone S, Lopez S, Thakral D, Schwab C, English DP, et al. Mutational landscape of uterine and ovarian carcinosarcomas implicates histone genes in epithelial-mesenchymal transition. *Proc Natl Acad Sci U S A*. 2016;113(43):12238–43.
7. Wada H, Enomoto T, Fujita M, Yoshino K, Nakashima R, Kurachi H, et al. Molecular evidence that most but not all carcinosarcomas of the uterus are combination tumors. *Cancer Res*. 1997;57(23):5379–85.
8. Kurman RJ, Carcangiu ML, Herrington CS, Young RH. WHO Classification of Tumours of Female Reproductive Organs. 4th ed. Geneva, Switzerland: World Health Organization; 2014.
9. Lakhani SR, Ellis IQ, Schnitt SJ, Tan PH, Vijver MJV. WHO Classification of Tumours of the Breast, Fourth Edition. Geneva, Switzerland: World Health Organization; 2012.
10. Travis WD, Brambilla E, Nicholson AG, Yatabe Y, Austin JHM, Beasley MB, et al. The 2015 World Health Organization Classification of Lung Tumors: Impact of genetic, clinical and radiologic advances since the 2004 classification. *J Thorac Oncol*. 2015;10(9):1243–60.
11. Zidar N, Gale N. Carcinosarcoma and spindle cell carcinoma–monoclonal neoplasms undergoing epithelial-mesenchymal transition. *Virchows Arch*. 2015;466(3):357–8.
12. Loh TL, Tomlinson J, Chin R, Eslick GD. Cutaneous carcinosarcoma with metastasis to the parotid gland. *Case Rep Otolaryngol*. 2014;2014:173235.
13. Varadhachary GR, Raber MN. Carcinoma of unknown primary site. *N Engl J Med*. 2014;371(8):757–65.
14. Pavlidis N, Pentheroudakis G. Cancer of unknown primary site. *Lancet*. 2012;379(9824):1428–35.
15. Kamposioras K, Pentheroudakis G, Pavlidis N. Exploring the biology of cancer of unknown primary: Breakthroughs and drawbacks. *Eur J Clin Invest*. 2013;43:491–500.
16. Bugat R, Bataillard A, Lesimple T, Voigt JJ, Culine S, Lortholary A, et al. Summary of the standards, options and recommendations for the management of patients with carcinoma of unknown primary site. *Br J Cancer*. 2002;89(1):59–66.
17. Huey R, Makawita S, Xiao L, Matamoros A, Estrella J, Overman MJ, et al. Sarcomatoid carcinoma presenting as cancers of unknown primary: a clinicopathological portrait. *BMC Cancer*. 2019;19(1):965.
18. Selves J, Long-Mira E, Mathieu M, Rochaix P, Ilié M. Carcinomas of unknown primary site. The role of the pathologist in 2018: introduction. *Ann Pathol*. 2018;38(3):164–97.
19. Kandalaft P, Gown A. Practical Applications in Immunohistochemistry - Carcinomas of Unknown Primary Site. *Arch Pathol Lab Med*. 2016;140(6):508–23.
20. Arshad HS, Dudekula RA, Niazi M, Malik S, Khaja M. A Rare Case of Sarcomatoid Carcinoma of the Lung with Spine Metastasis, Including a Literature Review. *Am J Case Rep*. 2017;18:760–5.
21. Huang SY, Shen SJ, Li XY. Pulmonary sarcomatoid carcinoma: a clinicopathologic study and prognostic analysis of 51 cases. *World J Surg Oncol*. 2013;11:252.
22. Abreu M, Kozlowski B, Cordeiro P, Sousa A, Nascimento M, Zamboni M. Sarcoma pleomórfico do pulmão- Caso Clínico. *Port J Pulmonol*. 2008;14(4):535–9.

Author biography

Rekha Nirwan, Consultant

Rateesh Sareen, Consultant https://orcid.org/0000-0003-2163-2819

G.N. Gupta, HOD

Cite this article: Nirwan R, Sareen R, Gupta GN. Sarcomatoid carcinoma metastasis to bone marrow with unknown primary. *Indian J Pathol Oncol* 2022;9(4):360-363.