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Original Research Paper

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MEDULLOBLASTOMA METASTASIZING TO BREAST: CASE REPORT AND REVIEW OF LITERATURE

Chhavi Gupta	MD, Department of Pathology, BALCO Medical Centre, Sector 36, Naya Raipur, Chhattisgarh, India, 493661.
Sandeep Ojha*	MD, Department of Pathology, BALCO Medical Centre, Sector 36, Naya Raipur, Chhattisgarh, India, 493661. *Corresponding Author
Deba Dulal Biswal	MD, DNB, Department of Medical Oncology, BALCO Medical Centre, Sector 36, Naya Raipur, Chhattisgarh, India, 493661.
Shishir Agrawal	DNB, Department of Radiology, BALCO Medical Centre, Sector 36, Naya Raipur, Chhattisgarh, India, 493661.

ABSTRACT

Introduction: Extra-mammary tumor metastasis to breast is very rare, and much rarer is the central nervous system as primary, with only few case reports documenting metastasis from medulloblastoma. We document another case of breast metastasis from medulloblastoma, which is only seventh case so far.

Case report: A 26-year-old female with a history of recurrent cerebellar medulloblastoma (managed at other hospital), came to our hospital with history of weight loss and respiratory symptoms, 4 months after her last hospital visit. On investigations, she was found to have bilateral breast nodules and widespread metastatic lesions in body. Biopsy of breast nodule revealed a malignant small round cell tumor which on immunohistochemistry was positive for Synaptophysin and negative for Gross Cystic Disease Fluid Protein 15 (GCDFP-15), thus confirming metastasis of medulloblastoma. A palliative chemotherapy was started, however, patient succumbed to her illness within a month.

Conclusion: Increased awareness of such rare sites as primary when dealing with breast lump with a suspicion of metastasis, can help arriving at correct diagnosis, which is crucial to avoid unnecessary surgical procedures in these patients. The diagnosis is conclusively made on histopathological examination.

KEYWORDS : Medulloblastoma, Metastasis to breast, Extra-mammary, Central Nervous System tumor, Histopathology

INTRODUCTION

Metastasis to breast from extra-mammary primary, although a well-known entity, is rare in itself. The common primaries include hematological malignancies, carcinomas from various sites and melanoma.[1-3] Metastasis of primary CNS malignancies to breast have very rarely been reported in literature, and that being of medulloblastoma. There are 6 such cases so far to the best of our knowledge.[4-9] We hereby report another case of medulloblastoma in an adult female with metastasis to breast in addition to other sites. It is crucial to arrive at correct diagnosis so that patient can be prevented from undergoing unnecessary procedures.

CASE REPORT

A 26 years old female patient, with a known diagnosis of Medulloblastoma, came to our hospital with respiratory symptoms and history of weight loss. Patient was not on any medications. A detailed history was elicited, which revealed irregular hospital visits with poor follow up. Patient was diagnosed to have cerebellar medulloblastoma in November 2013, at the age of 20 years 8 months. She underwent craniotomy with gross total excision of the tumor which was reported as desmoplastic medulloblastoma on histopathological and immunohistochemical examination. Tumor cells were positive for GFAP and S100 protein, weakly positive for Synaptophysin. MIC2 was negative in the tumor cells, and Ki67 was approximately 30%. Post-operative radiotherapy was advised, but patient defaulted. Computed Tomography (CT) scan of the brain after 3 weeks suggested complete resolution of the tumor, and there was no abnormality on USG abdomen and pelvis. There was cerebellar recurrence in March 2016 for which a repeat surgery with gross total excision was done 2 weeks later, and post-operative local radiation therapy was given for a month. In August 2017, patient became symptomatic and was found to have bone marrow metastasis, confirmed by Immunohistochemistry. Six cycles of chemotherapy with Carboplatin and Etoposide were given. In November 2018 patient presented again with multiple skin nodules for 6 months which were confirmed on biopsy to be metastasis. Following this, patient defaulted again and presented at our Hospital in March 2019 with breathing difficulty and recent history of multiple pleural fluid taps. She was re-evaluated. CT scan of brain revealed post-operative changes in the cerebellum with mild communicating hydrocephalus with periventricular cerebrospinal fluid (CSF) ooze. CT scan of thorax and abdomen revealed multiple nodular, heterogeneously enhancing lesions in upper half and peri-areolar region of left breast region, largest measuring 4.2 x 3.4 x 2 cm. Another heterogeneously enhancing nodular lesion was seen in lower central region of right breast measuring 2.8 x 1.4 x 2.1 cm. Additionally, there was left side pleural effusion, multiple pleural-based mass lesions, and nodal, skeletal and pancreatic metastases. Magnetic resonance imaging (MRI) brain and whole spine was suggested, but was not done due to financial constraints. Core biopsy of the breast lump showed a malignant tumor with round cell morphology with peri-ductal and peri-lobular infiltration (Figure 1 a-b). By immunohistochemistry (IHC), tumor cells displayed weak immuno-staining for Synaptophysin, while were negative for GCDFP-15 (Figure 1 c-d). A final impression of metastasis of medulloblastoma was made. In view of relapsed and progressive disease, palliative care including palliative chemotherapy was started, however patient died within a month.

DISCUSSION

Metastasis to breast from extra-mammary primaries account for approximately 2% of all breast malignancies,[1,2] however the incidence may be higher on post mortem.[10] The common primaries in adults include hematological malignancies, melanoma and carcinomas from lung, ovary, prostate, kidney and stomach, and carcinoid tumors, while in children rhabdomyosarcoma and lymphoma are the most common.[1-3] Some of the largest series highlighting tumor metastases to breast did not document CNS as the primary, except for the few case reports of medulloblastoma as the primary tumor.[4-9]

The non-hematological metastases usually develop in fifth-sixth decade,[3] however, in line of expectations, the patients with medulloblastoma metastasis (including the present case) were younger, with age at the time of breast metastasis ranging from 12 to 35 years (Table 1). One of these patients was a male child. Medulloblastoma has propensity to spread along the craniospinal axis through CSF pathways. Distant extracranial metastasis of medulloblastoma occurs in approximately 7.1% of the patients. The most common sites of metastasis are bones and lymph nodes in both adults and children, followed by lungs in adults and liver in children.[11,12]

It is critical to diagnose metastases as the management is different between primary and secondary tumors of breast, and also depends upon the primary tumor. The metastases usually present as a single or multiple well-defined masses. In majority of the patients with breast metastasis, primary tumor is known and diagnosis can be accurately made by radiology and morphologic appearance of the tumor by fine needle aspiration cytology or biopsy. Histopathological features which suggest metastasis include well circumscribed mass, peri-ductal and peri-lobular infiltration of the tumor cells, and absence of in situ component.[2,3,13] Similar histological findings were noted in our case. Interestingly, in the case reported by Brydon and Carey,[5] medulloblastoma involved pre-existing fibroadenoma of the breast. In some cases, IHC is required, especially when the primary is unknown and morphology does not support primary breast tumor diagnosis. In the present already diagnosed case of medulloblastoma, tumor morphology of small round cells suggested a diagnosis of medulloblastoma metastasis, which was confirmed by IHC which showed Synaptophysin expression similar to the primary tumor. Absence of expression of GCDFP-15 by tumor cells supported the diagnosis.

Standard treatment of medulloblastoma includes surgery and irradiation of the craniospinal axis. It is a chemo-sensitive tumor and adjuvant chemotherapy is given to high risk patients, in recurrent cases, and in children to reduce the radiation dose. In adults, role of adjuvant chemotherapy is not very clear, however, there are several reports demonstrating prolonged remission in recurrent cases by the use of salvage chemotherapy.[14]

Most of the patients with secondaries in breast already have widespread disease, and thus finding of the metastasis in breast is a sign of poor prognosis.[3] In small number of cases discussed here, 3 cases including ours already had metastases elsewhere in the body, before developing breast secondary. Follow up data was available in 5 patients, all of which died of the disease with maximum follow up period of 6 years 2 months reported by Ternier et al.[9] Two of the patients were lost to follow up, whereas, it was not mentioned in case report by Baliga et al[6] (Table 1).

CONCLUSION

Extra-mammary tumor metastasis to breast is rare and that from CNS is much rarer. A pathologist should be aware of such rare possibilities and diagnose correctly, so as to avoid unnecessary procedures in these patients. A previous history and imaging help in diagnosis which is conclusively made on biopsy.

Conflict of interest: I do not believe that there is a conflict of interest that could potentially be construed to affect the material contained in the manuscript that is being submitted to the Journal.

Table 1: Literature review for metastasis of medulloblastoma to breast (including the present case).

Author name, year	Gender/ Age of patient at first diagnosis of medulloblastoma	Time interval between first diagnosis of medulloblastoma and breast metastasis	Diagnosed on	Initial treatment of medulloblastoma	Other extracranial metastasis during the course of illness	Follow up duration after first diagnosis (dead or alive)	Autopsy findings (if performed)
Brutschin,[4] 1973	F/18 years	2 years 3 months	Excision biopsy	Surgery + RT	Bones, lung	2 years 7 months, dead	ND
Brydon,[5] 1991	F/17 years	1 year 3 months	Excision biopsy	Surgery + RT + CT	NK	1 year 4 months, dead	Cerebellar recurrence, leptomeningeal deposits, bones
Baliga,[6] 1994	F/34 years	1 year 4 months	FNAC, followed by trucut biopsy	Surgery + RT	Pleural effusion, bones	NK	NK
Kapila,[7] 1996	M/9 years	3 years	FNAC	Surgery + RT + CT	None	5 years 2 months, then lost to f/u	
Lamovec,[8] 2001	F/31 years	2 years	FNAC, followed by excision biopsy	Surgery + RT	Ovary, peritoneum	4 years, 9 months, dead	ND
Ternier,[9] 2010	F/24 years	5 years	Core biopsy	Surgery + RT	Bones, bone marrow, abdomen, retroperitoneal lymph nodes	6 years 2 months, dead	NK
Present case	F/20 years	5 years 4 months	Core biopsy	Surgery	Bone marrow, skin, pleura, lymph nodes, bones, pancreas	5 years 5 months, dead	ND

FNAC: Fine needle aspiration cytology, RT: Radiation therapy, CT: Chemotherapy, NK: Not known, ND: Not done, f/u: follow-up

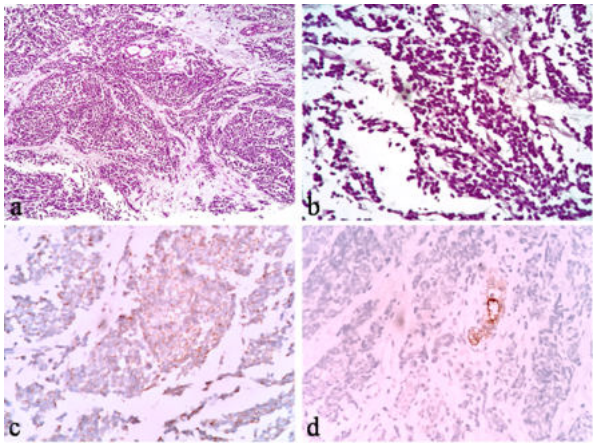

Figure 1 legend

Medulloblastoma tumor cells with typical small round blue cell morphology, with peri-ductal spread (a). **a**) H&E 100x, **b**) H&E 400x, **c**) Immunoexpression of Synaptophysin by tumor cells, IHC 400x, **d**) GCDFP-15 negativity in tumor cells (positive expression in benign duct is noted), IHC 400x.

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