CASE REPORT

Primary Vaginal Ewing's sarcoma: A Rare Case Report

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Introduction

Extra skeletal Ewing's sarcoma (EES) is an uncommon, rapidly growing, and round-cell malignancy of uncharacterized mesenchymal cell origin. The extra skeletal forms usually occur in the soft tissue of lower extremities, paravertebral tissues, chest wall, and retro peritoneum. Extra

osseous ES are uncommon, with occasional reports of tumors affecting the genitourinary tract. Only few cases of primary vaginal Ewing's sarcoma have been previously reported in the literature (only 22 cases).

Ewing sarcoma (ES) and Primitive Neuroectodermal Tumor (PNET) family of tumors were classified differently in the past. But now due to their common molecular and clinical features they are considered as single tumor category known as Ewing family of tumors (EFTs) [1]. More than 90 % of these tumors contain Ewing Sarcoma RNA-binding protein 1 (EWSR1)-FLI1 fusion protein due to t (11; 22) (q24; q12) chromosomal translocation.

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Case Report

Thirty-year-old female patient presented with chief complaints of irregular vaginal bleeding and feeling of lump in the left lateral wall of the vagina since 1 month. Her obstetric and family history was unremarkable. On physical

examination she had normal height, weight, and body surface area according to her age. Her vitals were normal and Eastern Co Operative Oncology group (ECOG) performance score was one.

Clinical examination of vagina revealed hard, lobulated mass lesion arising in the left lateral vaginal wall extending to labia majora. Uterus, cervix, and all the vaginal fornices were free from mass. On digital rectal examination, rectal mucosa and bilateral parametria were free. Computed Tomography scan of abdomen and pelvis (A + P) in axial view shows well-defined lobulated soft tissue density lesion noted involving lower part of vagina and extending into labia majora on left side. Other organs including uterus, ovary, and peritoneal cavity were normal (Fig. 1).

Punch biopsy from mass revealed small round-cell infiltration with high mitotic rate. Nuclei were hyper chromatic and cytoplasm was scanty (Fig. 2). Immunohistochemistry (IHC) showed positivity toward vimentin, CD99 (Fig. 3) and negativity for BCL2 and leukocyte common antigen (Fig. 4). Final diagnosis of ES of vagina was made from morphological and IHC findings. Her metastatic disease work up like CT thorax and bone marrow aspiration and biopsy did not reveal any abnormality.

Patient was managed with combination chemotherapy with High-Risk (HR) protocol (vincristine 2 mg/m^2 , doxorubicin 75 mg/m^2 , cyclophosphamide $1,200 \text{ mg/m}^2$, and mesna alternating every 3 weeks combined with ifosfamide $1,800 \text{ mg/m}^2$ and etoposide 100 mg/m^2). After 12 weeks of combination chemotherapy, there was a partial response of the tumor by response evaluation criteria in solid tumors (RECIST) criteria. As per the protocol after 12 weeks of chemotherapy patient received total 55 Gy of radiotherapy at 180 cGy per fraction, once a day for 5 days in a week. Chemotherapy was given for 17 cycles and was

Fig. 1 Axial view of CT scan of pelvis shows well-defined lobulated soft tissue density lesion in lower part of vagina and extending into labia majora on *left side*

Fig. 2 Histopathological examination revealed vaginal infiltration by small round-cell tumor. Cells which have high mitotic rate with nuclei are hyper chromatic and cytoplasm is scanty

Fig. 3 IHC image showing positivity for CD99

Fig. 4 IHC image showing negativity for leukocyte common antigen (LCA)

uneventful. Patient is under regular surveillance for any recurrence or progression of the disease at local site or metastasis.

Table 1 Literatures review of possible all the 22 cases of Vaginal Ewing Sarcoma till date [7, 8]

No.	Place (year)	Author	Age (years)	T size (cm)	Treatment
1	Paris (1992)	Habib et al.	23	–	–
2	Los Angeles, USA (1994)	Scherr et al. (2nd case in English literature)	10	6.5	–
3	Gaia, Europe (1995)	Paredes et al.	29	5	CT and RT
4	Melbourne, Australia (1995)	Nirenberg et al.(CD99 –ve)	20	12	CT and RT
5	Hawaii, USA (2000)	Farley et al.	35	4	CT and RT
6	Vang et al (2000)	Vang et al. (2 cases)	35	3	Surgery + CT + RT
			28	0.9	
7	Tokyo, Japan (2001)	Takeshima et al.	45	3	–
8	France, Europe (2001)	Lazure et al.	15	20	CT
9	Croatia, Europe (2002)	Petkovic et al.	45	9	CT and RT
10	Mexico (2003)	Gaono-Luviano et al.	34	4	Surgery + CT + RT
11	Beijing, China (2004)	Liao et al.	30	5	Surgery + CT
12	Durban, South Africa (2005)	Moodley et al.	26	5	–
13	Northan Ireland, UK (2007)	McCluggage et al. (4 cases)	19	4	CT
			20	6.5	–
			30	3	–
			40	8	CT
14	Doha, Qatar (2009)	Al-Tamimi et al.	47	–	–
15	Taiwan (2009)	Yip et al.	27	6	Surgery + RT
16	Mumbai, India (2010)	Rekhi et al.	17	10	CT and RT
17	Shenyang, China (2012)	Pang et al.	54	4	RT
18	Pondicherry, India (2014)	Das et al.	50	7	CT and RT

Discussion

EFTs have two different spectra; undifferentiated ES at the one end of spectrum and features of neuroectodermal differentiation by PNET at the other end of spectrum [2, 3]. Extra osseous ES is common and mainly affects soft tissues of the chest wall (Askin tumor), paravertebral regions, retroperitoneal regions, skin, visceral organs, head, and neck.

Ewing Sarcoma RNA-binding protein 1(EWSR1)-FLI1 fusion protein is present in more than 90 % of EFTs cases and the remaining cases have variant translocations involving the EWSR1 gene on chromosome region 22q12, such as t(21;22) (q22;q12), t(7;22) (p22;q12), or t(2;22) (q33;q12) resulting in different fusion proteins, EWSR1-ERG, EWSR1-ETV1 or EWSR1-FEV, respectively [4, 5]. Above fusion protein of EFTs is detected by fluorescence in situ hybridization (FISH) and reverse transcriptase polymerase chain reaction (RT-PCR).

Though morphologically ES is characterized by small round cells, three reported cases have appreciable amount of cytoplasm [6]. Classical IHC findings of EFTs at any sites are positive for vimentin, CD99, and FLI-1. Though AE may be focally positive sometimes. Tumor shows negativity toward leukocyte common antigen, BCL2, and desmin. CD99 is highly sensitive marker for diagnosing EFTs. It is not very specific as also positive in various tumors like rhabdomyosarcoma, small cell carcinoma,

Merkel cell carcinoma, mesenchymal chondrosarcoma, synovial sarcoma, lymphoblastic lymphoma, and leukemia.

Table 1 shows review of literature of all the 22 cases worldwide reported till date [7, 8]. There are eight cases from Europe, seven cases from Asia, three cases from North America, one case from South Africa, one case from Australia. First case of vaginal ES was reported by Habib et al. from Paris in 1992. In India, only two cases reported till now. Age range between 10 and 54 years with median age is 30 years. T size is variable between 0.9 and 20 cm with average size around 6.2 cm. Most common occurring site is in right labium. All the cases are CD99 positive except one described by Nirenberg et al. from Australia.

There are no standard treatment guidelines available due to rarity of its occurrence. Though multimodality approaches like surgery, radiotherapy, and chemotherapy are mentioned in literature. In metastatic settings where the intent of treatment is mainly palliative, combined chemotherapy is preferred. VAC alternate with I + E is given in lines of ES occurring at any site [8].

Conclusion

ES of vagina is very rare but should be suspected in any undifferentiated carcinoma involving vagina. CD99 is the

key factor to pursue the diagnosis. Definite guidelines are not present till now but can be treated with multimodality approach in curative setting. Combined chemotherapy should be the mainstay of treatment in metastatic disease.

Compliance with ethical requirements and Conflict of interest None.

References

1. Dagher R, Pham TA, Sorbara L, et al. Molecular confirmation of Ewing sarcoma. *J Pediatr Hematol Oncol*. 2001;23:221–4.
2. Dehner LP. Primitive neuroectodermal tumor and Ewing's sarcoma. *Am J Surg Pathol*. 1993;17:1–13.
3. Liao X, Xin X, Lü X. Primary Ewing's sarcoma-primitive neuroectodermal tumor of the vagina. *Gynecol Oncol*. 2004;92:684–8.
4. De Alava E, Pardo J. Ewing tumor: tumor biology and clinical applications. *Int J Surg Pathol*. 2001;9:7–17.
5. Folpe AL, Goldblum JR, Rubin BP, et al. Morphologic and immunophenotypic diversity in Ewing family tumors: a study of 66 genetically confirmed cases. *Am J Surg Pathol*. 2005;29:1025–33.
6. McCluggage WG, Sumathi VP, Nucci MR, et al. Ewing family of tumors involving the vulva and vagina: report of a series of four cases. *J Clin Pathol*. 2007;60:674–80.
7. Yip CM, Hsu SS, Chang NJ, et al. Primary vaginal extra osseous Ewing sarcoma/primitive neuroectodermal tumor with cranial metastasis. *J Chin Med Assoc*. 2009;72(6):332–5.
8. Rekhi B, Qureshi S, Basak R et al. Primary vaginal Ewing's sarcoma or primitive neuroectodermal tumor in a 17-year-old woman: a case report. *J Med Case Rep*. 2010;4:88.