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Case Reports

An unusual finding of vulvar Ewing sarcoma – a case report and review of literature

M. Cantos[1], A. Agrawal[1], R. Chibbar[2], C. Theoret[3]

[1]Department of Obstetrics and Gynecology, [2]Department of Pathology and Laboratory Medicine, [3]Department of Radiology, University of Saskatchewan, Saskatoon, SK (Canada)

Summary

Superficial Ewing sarcoma/primitive neuroectodermal tumors (ES/PNET) are rare and have a relatively favourable prognosis compared to the osseous or deep soft tissue extraskeletal ES/PNET. ES/PNET arising in the female genital tract are exceptionally rare with only a few cases reported. The authors report an unusual case of a 52-year-old woman with vulvar Ewing sarcoma and compare the clinical course and pathological features with cutaneous ES/PNET. The patient received nine cycles of adjuvant chemotherapy after surgical excision of the tumor almost two years prior. In the most recent imaging, there is no evidence of local recurrence of disease or any distant metastasis. Because of the rarity of the case, the long term outcome and prognosis is unclear at this point. However, given the literature on cutaneous ES/PNET and that the patient's vulvar Ewing sarcoma is of the cutaneous subgroup of extraskeletal ES/PNET, it is likely that her disease prognosis will be more favourable than non-cutaneous extraskeletal ES/PNET. This case report and review of literature will help clinicians to inform patients of long term outcome of this rare tumor on initial presentation, and to help patients to make decisions regarding offered treatment and follow up.

Key words: Ewing sarcoma (ES); Extraskeletal peripheral neuroectodermal tumor (PNET); Cutaneous Ewing sarcoma; Vulvar Ewing sarcoma.

Introduction

Ewing sarcoma/primitive neuroectodermal tumors (ES/PNET) are a rare pediatric small round cell tumor that predominately affects bone and deep soft tissue [1]. An extremely rare subgroup of extraskeletal ES/PNET is the cutaneous ES/PNET form, with fewer than 100 cases reported in the literature [2-4]. Several cases of primary vulvar ES/PNET have also been described. Majority of cutaneous ES/PNET and vulvar ES are believed to have a better prognosis compared to osseous/extraosseous deep- seated soft tissue ES. Most of the vulvar ES found in the literature are single case reports or small case series [5-15]. There are no clear, concise guidelines or prognostic features to guide clinical decision making in vulvar ES. There are also no reports on comparison of clinical features and prognosis of vulva ES to cutaneous ES. Is vulvar ES another site of cutaneous ES and should be managed similarly or there are differences in clinicopathological features between these two entities? The purpose of this case report and literature review is to compare clinicopathological features of vulvar and cutaneous ES/PNET and to identify prognostic features to guide therapy and help patient and clinician discussion in treatment decision, prognosis, and long term follow up.

Case Report

A 52-year-old multiparous, obese (BMI: 57 kg/m^2), postmenopausal woman with several medical comorbidities presented with several months' history of an enlarging, painless, non-ulcerated, clitoral mass which, on examination, was found to be approximately 6-7 cm, firm, mobile, and sensitive to touch. Biopsy results were reported as ES/PNET. The patient was referred to Gynecologic Oncologist for further management. Staging CT and MRI revealed a large heterogeneous mass in the clitoris extending into the crura bilaterally and posteriorly. The bulbous portion of the lesion measured 3.5×5.0 cm in transverse and craniocaudal dimension. The lesion appeared to extend into the superior and anterior vaginal wall and up to the urethra. There were multiple, bilateral, enlarged inguinal lymph nodes, the largest measuring 5.0×1.8 cm on the right side and 3.8×2.0 cm on the left side (Figures 1a-b).

The patient underwent radical anterior vulvectomy. The clitoral mass measuring 6.0×4.8×3.5 cm (Figure 2) extended up to the pubic bone and into the bulbocavernosus muscle bilaterally as reported by MRI. Histology demonstrated cutaneous variant of extraskeletal ES/PNET with focal lymphovascular space invasion (Figure 3). Abnormally rearranged EWSR1 gene was noted on fluorescent in situ hybridization study (Figure 3). The deep and left bulbocavernous resected margins were focally positive. PET/CT post-vulvectomy reported possible residual tumor and bladder involvement.

The patient was discussed in multidisciplinary tumor board (including pediatric oncology) and was treated with adjuvant multiagent chemotherapy VAC-M (day 1 outpatient doxorubicin,

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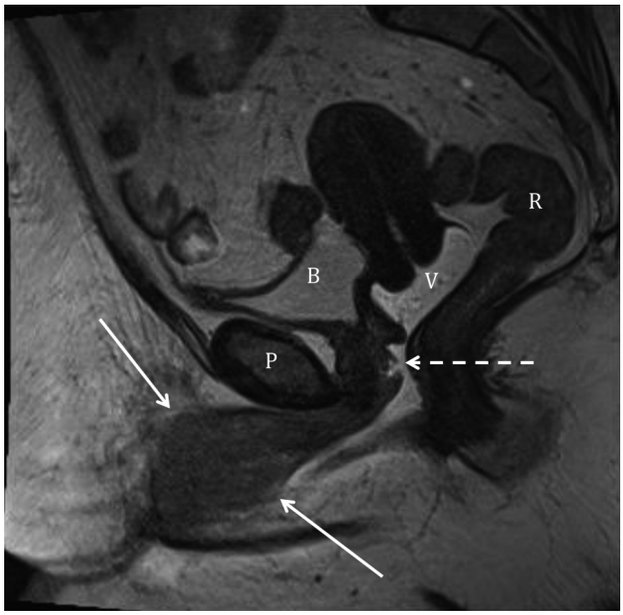


Figure 1a. — MRI (pre-op) sagittal T2-weighted image showing tumor expanding the clitoris extending along the anterior vaginal wall, surrounding the urethra extending to the base of urinary bladder. B: bladder, P: pubic bone, R: rectum, V: vagina distended with gel, solid arrows: mass expanding the clitoris, dashed arrow: extension along lower anterior vaginal wall.

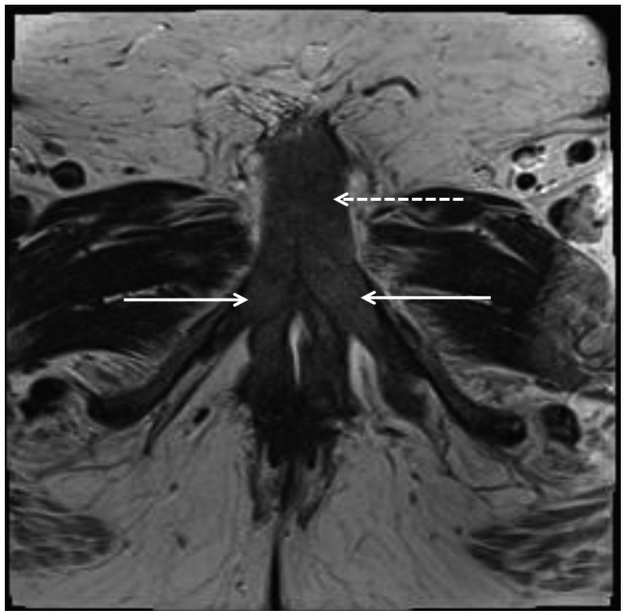


Figure 1b. — MRI (pre-op) axial T2-weighted image showing globally enlarged bilateral clitoral tissue, bulbous portion measuring 3.5×5.0 cm. Solid arrow: expanded right and left crus of clitoris, dashed arrow: expanded clitoris.

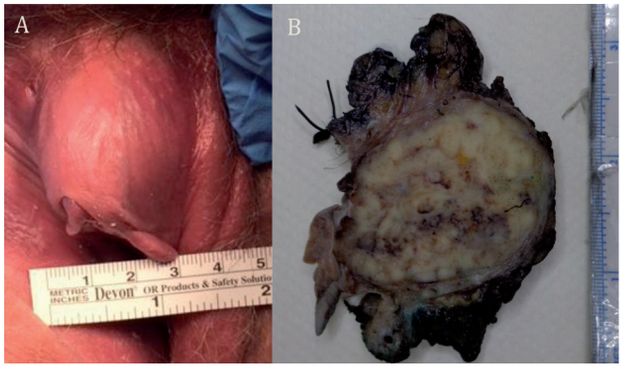
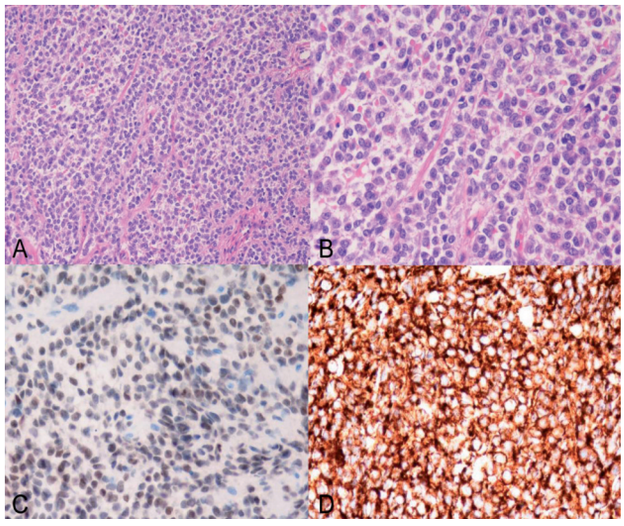


Figure 2. — a) Gross appearance of clitoral tumor prior to surgery. b) Full face cut surface of the tumor after formalin fixation demonstrating its closeness to vascular margin.



Figures 3a and 3b. — Histopathology demonstrates sheets of monotonous tumor cells with vesicular nuclei, amphophilic cytoplasm, and indistinct cell membranes. Figures 3c and 3d: Neoplastic cells are diffusely and strongly positive for Fli1(3c) and CD99 (3d) on immunohistochemistry.

vincristine, mesna, cyclophosphamide and day 14 inpatient over five days ifosfamide, mesna, and etoposide). She received a total nine cycles with many delays and interruptions due to chemotherapy-related febrile neutropenia, septicemia, and bone marrow suppression. She also received many blood transfusions. For the last four cycles, she only received day 1 (VAC-M) due to ifosfamide-induced encephalopathy.

The latest CT, MRI, and PET/CT imaging studies (Figures 4-6) done nine months after the last cycle of chemotherapy reported no evidence of residual/recurrent disease. The patient decided to be off further chemotherapy.

Materials and Methods

A literature review of PubMed using the key words: Ewing sarcoma, primitive neuroectodermal tumor, cutaneous, and vulvar were used to find articles consisting of mostly case series pointing to the rare nature of vulvar ES. The authors organized the findings of the different cases to compare and contrast cutaneous and vulvar ES in order to come up with treatment protocol and prognosis for the patient and others presenting with vulvar ES.

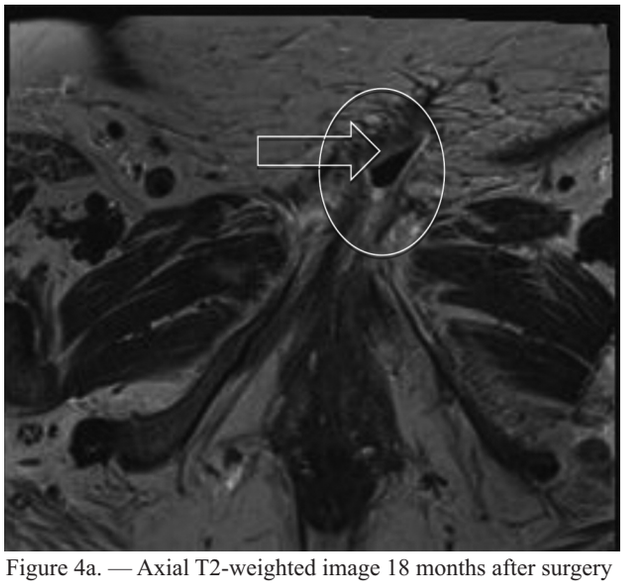


Figure 4a. — Axial T2-weighted image 18 months after surgery Circle: operative bed area, arrow: gas in operative bed.

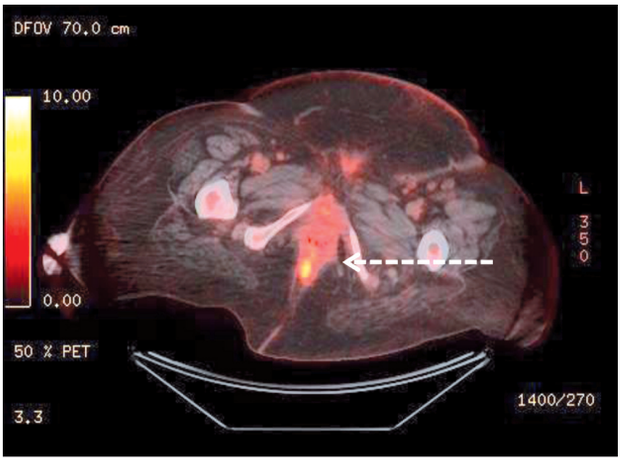


Figure 4b. — Axial PET/CT image 18 months after surgery. Dashed arrow: no FDG uptake in area of concern on MRI.

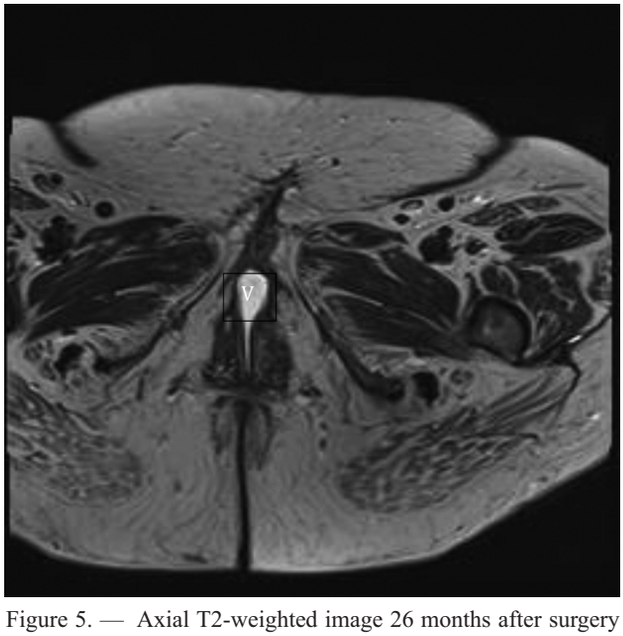


Figure 5. — Axial T2-weighted image 26 months after surgery showing continued healing in operative bed. V: gel in vaginal opening.

Discussion

Patients with ES typically present with localized pain or swelling of a few weeks or months duration. [16] Even though fewer than 2% of patients have overt metastases at the time of initial diagnosis, ES is a systemic disease. Because of the high relapse rate (80-90%) in patients undergoing local therapy alone, it is inferred that most patients have subclinical metastatic disease at the time of initial diagnosis. [17] Multi-agent chemotherapy can successfully resolve these metastatic deposits and is usually administered prior to and following local treatment to control microscopic disease with the intention of long term remission and possible cure.

Poor prognostic factors in ES/PNET tumors of bone and deep soft tissue include lesions of the body trunk, patient age ≥ 15-years-old, tumor volume of ≥ 200 ml, presence of distant metastasis at the initial diagnosis, positive or close resection margin, a poor response to the first line adjuvant multi-agent chemotherapy, and recurrence within two years of completion of primary treatment. The most unfavorable prognostic factor is the presence of distant metastasis. Even with aggressive treatment, in patients with metastasis the long-term survival is 20% [7].

Unlike the deep soft tissue subgroup of ES/PNET, which has a poor prognosis, cutaneous ES seems to be associated with an indolent course and a comparatively favorable prognosis. The current ten-year survival rate of cutaneous ES was estimated to be 91% [18].

ES/PNET of the vulva is extremely rare. The present review shows that there have only been 24 cases reported so far in the English literature; the present case is the 25th case and only the third case in this age group (Table 1).

In comparing vulvar ES/PNET with cutaneous ES/PNET (Table 2), the authors have noted many similarities between the two subtypes. The incidence of both vulvar and cutaneous ES/PNET is rare with the median age of the case study participants being young at median age of 25 years for vulvar and 21 years for cutaneous ES. Tumor sizes are also similar with the median size of 5.6 cm for vulvar and 4 cm for cutaneous ES. Most of the studies reported an initial size of less than 5 cm (65% vulvar and 78.5% cutaneous). At the initial presentation, 44% of the patients had metastasis and the commonest site of metastasis was noted to be lung

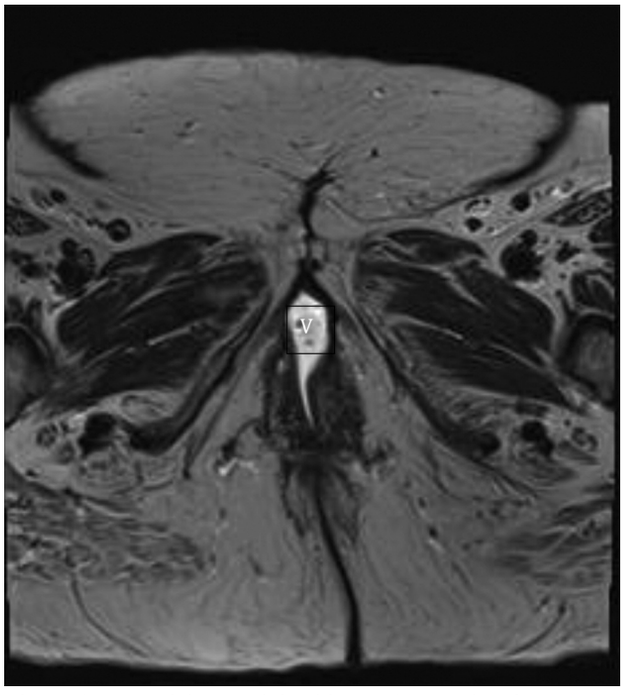


Figure 6a. — Axial T2-weighted image 30 months after surgery demonstrating further healing of the surgical site with no residual tumor seen. V: vaginal opening distended with gel.

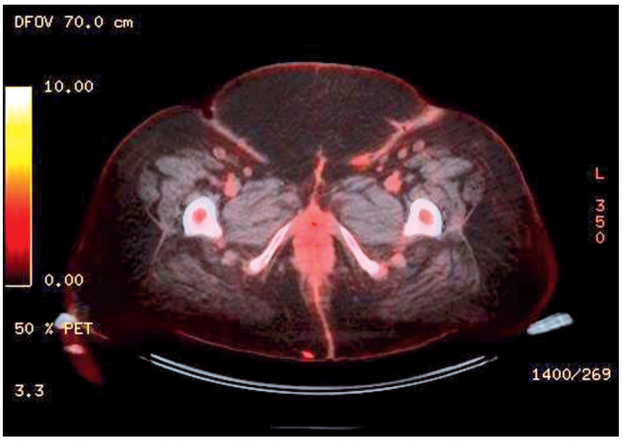


Figure 6b. — Axial PET/CT image 30 months after surgery showing no FDG uptake in area of concern on MRI in anterior vagina, suggesting MRI findings are not due to residual or recurrent disease.

(50%) and groin lymphadenopathy (42%). Only one patient in each group had bony metastasis at the time of presentation. Both categories patients were treated initially with surgery including simple excision or radical surgery (94% for vulvar and 92% for cutaneous) and received adjuvant treatment. Only two patients did not undergo surgery and were treated with chemotherapy and chemo-radiation respectively [30, 31]. In terms of adjuvant therapy, about half of the patients in both categories received multi-agent chemotherapy, and 25% received both chemotherapy and local radiotherapy. The increased groin lymph node metastasis at the initial presentation with vulvar ES/PNET may have to do with the location and proximity to the groin lymph nodes (42%). Vulva having a very rich blood supply may have contributed in higher incidence of lung metastasis. Given the similarity of prognostic factors between vulvar and cutaneous ES/PNET - such as young age at presentation, initial tumor size ≤ 5cm – good response to multimodal treatment with low (15%) recurrence rate can be expected for both groups. Almost half (56%) of the patents were alive and free of disease at the time of reporting, and 36% of the patients died of disease, who had metastasis at the time of diagnosis or they developed metastasis within one year of diagnosis and treatment. The presence of positive margin (19%) after surgery does not seem to influence cutaneous vulvar subtype outcome, it appears that adjuvant chemotherapy played significant role in long term cure, and it could be inferred that vulvar ES/PNET has the same favorable prognosis as the cutaneous subtype.

Conclusion

As extraskeletal ES/PNET are rare and the vulvar and subcutaneous even more so rare, it is important to know that vulvar ES/PNET may behave as cutaneous ES/PNET and can be treated similarly with the expectation of better outcome. This information can be provided to the patients at the time of initial diagnosis with the assurance that despite being so rare, this cancer has possibility of long term remission with the advised treatment plan of initially radical surgery followed by adjuvant chemotherapy and in selected cases adjuvant radiotherapy leading to a possible cure. In addition, knowing that the vulvar ES/PNET is cutaneous subtype and there is chance of better overall outcome with only adjuvant chemotherapy, it may point to limiting use of adjuvant radiotherapy in all cases to decrease subsequent patient morbidity. This would increase patient compliance with the treatment plan and may result in higher rate of achieving successful treatment completion. The goal should be to tailor treatment to the individual to minimize treatment-related morbidity, while maintaining high remission rate and possible cure. Based on our case, it can be recommended that multi-agent chemotherapy regimen used for osseous ES is not necessary in all vulvar subtypes and these patients can be treated with less intensive chemotherapy regimen with expectation of favorable outcome. The present authors also conclude that radical surgery should be the initial treatment in all cases even when margin may not be negative, as in this review of 25 cases it does not seem to affect overall prognosis.

Table 1. — *Summary of cases of vulvar Ewing sarcoma.*

No.	Author / year	Age	Site	Size (cm)	Metastasis / site	Treatment	Follow up (months)
1	Rekhi *et al.* 2015	10	L Labia	12	Yes / pulmonary	WLE, CTX +ve margin	18 AFD
2	Tunitsky-Bitton *et al.* 2015	15	L LMi	4	No	WLE + ve margin CTX partial vulvectomy -ve, margin	10 AFD
3	Narayanan *et al.* 2014	17	Clitoral	3	Local and bony, lung 4 months after	WLE / CTX / RTX	DOD 22
4	Che *et al.* 2013	37	Left vulva two	5 and 3	Pulmonary after 1 month	WLE / CTX	12 AFD
5	Xiao *et al.* 2013	20	L LMa	-	Lung and bony	Biopsy	1 DOD
6	Xiao *et al.* 2013	36	R LMi	-	Lung after 8 months	RV / LND / CTX	15 DOD
7	Kelling *et al.* 2012	18	R LMa	1.7	pulmonary	WLE and RV / LND / CTX / RTX	3 AFD
8	Halil *et al.* 2011	14	L, Vulva	4.5	Pulmonary	WLE and RV / CTX / RTX	9 DOD
9	Dadhwal *et al.* 2010	20	LMa ext to pubis & urethra	20	Groin & mediastinal LN, plural & diaphragmatic nodules	RV	DOD
10	Boldorini *et al.* 2010	52	R LMa	4	No	WLE/ CTX / RTX	12 AFD
11	Centiner *et al.* 2009	23	L LMa	4	No	RV / pelvic groin LND CTX / RTX	84 AFD
12	Centiner *et al.* 2009	29	L LMa	1	No	RV / LND / CTX	51 AFD
13	Fong et al. 2008	17	L LMa	2.1	No	RV / CTX	48 AFD
14	McCluggage *et al.* 2007	40	R LMi	3	No	WLE / CTX / RV	12 AFD
15	McCluggage *et al.* 2007	20	R LMa	6.5	Pulmonary	CTX / RV	DOD
16	McCluggage *et al.* 2007	19	Vulva	4	No	CTX	NA
17	Moodley & Jordaan, 2005	26	R LMa	5	Pulmonary	CTX / RTX	DOD during treatment
18	Lazure *et al.* 2001	15	Labia Maj	20	No	RV / CTX	7 AFD
19	Takeshima *et al.* 2001	45	R LMa	3	Local recurrence	RV	36 AWD
20	Vang *et al.* 2000	28	R LMi	0.9	No	RV / CTX	18 AFD
21	Nirenberg *et al.* 1995	20	R LMa	12	Pulmonary	RV / CTX / RTX	10 DOD
22	Paredes *et al.* 1995	29	L LMa	5	Groin LN	RV RTX / CTX	8 AFD
23	Scherr *et al.* 1994	10	L LMa	6.5	Groin & femoral LN	RV	10 DOD
24	Habib *et al.* 1992	23	Labia Maj	1.5	Groin LN	NA	NA
25	Present case	52	Clitoral	6	No	RV/ CTX	23 AFD

L: left; R: right; LMa: labia major; LMi: labia minor; GLND: groin lymph node dissection; Bx: biopsy; WLE: wide local excision; RV: radical vulvectomy; LN: lymph nodes; NA: not available; NS: not specified; RTX: radiotherapy; CTX: chemotherapy; DOD: died of disease; AFD: alive fee of disease, AWD: alive with disease.

References

[1] Grier H.E.: "The Ewing family of tumors. Ewing's sarcoma and primitive neuroectodermal tumors". *Pediatr. Clin. North Am*., 1997, *44,* 991.

[2] Boland J.M., Folpe A.L.: "Cutaneous neoplasms showing EWSR1 Rearrangement". *Adv. Anat. Pathol*., 2013, *20*, 75.

[3] Pradhan A., Grimer R.J., Spooner D., Peake D., Carter S.R., Tillman R.M., *et al.*: "Oncological outcomes of patients with Ewing's sarcoma: is there a difference between skeletal and extra-skeletal Ewing's sarcoma?" *J. Bone Joint Surg. Br*., 2011, *93,* 531.

[4] Applebaum M.A., Worch J., Matthay K.K., Goldsby R., Neuhaus J., West D.C., DuBois S.G.: "Clinical features and outcomes in patients with extraskeletal Ewing sarcoma". *Cancer*, 2011, *117,* 3027.

[5] Rekhi B., Chinnaswamy G., Vora T., Shah S., Rangarajan V.: "Primary Ewing sarcoma of vulva, confirmed with molecular cytogenetic analysis: A rare case report with diagnostic and treatment implications". *Indian J. Pathol. Microbiol*., 2015, *58,* 341.

[6] Tunitsky-Bitton E., Uy-Kroh M.J., Michener C., Tarr M.E.: "Primary Ewing Sarcoma Presenting as a Vulvar Mass in an Adolescent: Case Report and Review of Literature". *J. Pediatr. Adolesc. Gynecol*., 2015, *28,* e179.

[7] Matsuda M., Ichimura T., Kasai M., Murakami M., Hoshi M., Kawamua N., Sumi T.: "Primitive neuroectodermal tumor originating in the vulva: A case report". *Oncol. Lett*., 2014, *8,*187.

[8] Che S.M., Cao P.L., Chen H.W., Liu Z., Meng D.: "Primary Ewing's sarcoma of vulva: a case report and a review of the literature". *J. Obstet. Gynaecol. Res*., 2013, *39,* 746.

[9] Anastasiades E.N., El Abiad S.A., Chouairy C.J.: "Ewing sarcoma/primitive neuroectodermal tumor (PNET) of the vulva. Case report and review of the literature". *J. Med. Liban*., 2012, *60,* 113.

[10] Kelling K., Noack F., Altgassen C., Kujath P., Bohlmann M.K., Hoellen F.: "Primary metastasized extraskeletal Ewing sarcoma of the vulva: report of a case and review of the literature". *Arch. Gynecol. Obstet*., 2012, *285,* 785.

[11] Halil S., Kucuk M., Arvas M., Aydin O., Calay Z.Z.: "Peripheral primitive neuroectodermal tumor (PNT) of the vulva: a case report". *Eur. J. Gynaecol. Oncol*., 2011, *32,* 117.

[12] Dadhwal V., Bahadur A., Cupta R., Bansal S., Mittai S.: "Peripheral neuroectodermal tumor of the vulva: a case report". *J. Low. Genit. Tract Dis*., 2010, *14,* 59.

[13] Cetiner H., Kir G., Gelmann E.P., Ozdemirli M.: "Primary vulvar Ewing sarcoma/primitive neuroectodermal tumor: a report of 2 cases and review of the literature". *Int. J. Gynecol. Cancer*, 2009, *19,* 1131.

[14] Fong Y.E., Lopez-Terrada D., Zhai Q.J.: "Primary Ewing sarcoma/peripheral primitive neuroectodermal tumor of the vulva". *Hum. Pathol*., 2008, *39,* 1535.

Table 2. — *Comparison of vulvar versus cutaneous ES/PNET.*

	Vulvar (from Table 1)	**Cutaneous (40)**
Incidence	Rare	Rare
No. of cases	25	56
Age (years)	Median age = 25.4 (10-52)	Median age = 21.5 (1.5-82)
Sex	Female: 100%	Female: 66% Male: 34%
Location	LMa: 16/25 = 64% LMi: 3/25 = 12% Vulva NS: 4/25 = 16% Clitoral: 2/25 = 8%	Trunk: 39% Lower extremities: 28.5% Upper extremities: 20% Head & neck: 12.5%
Size (cm)	Median = 5.59 (1-20)	Median = 4 (1-13)
Side	L: 10/25 = 40% R: 9/25 = 36% NS: 4/25 = 16% Central: 2/25 = 8%	Not reported
Metastasis at diagnosis	Total: 11/25 = 44% Lung: 6/12 = 50% LNDS: 4/12 = 42% Bone & lung: 1/12 = 8%	2/56 = 3.5% (1 bone, 1 other)
CD99 +ve	19/25 reported = 76%	51/51 = 100%
Treatment (Sx / CTX / RTX)	Bx only: 1/25 =5 % WLE: 8/25 = 32% Repeat Sx: 3/25 = 12% RV: 13/25 = 52% RV + LND: 5/25 = 20% CTX: 1/25 = 5% CTX + RTX: 1/25 = 5% Adj CTX: 10/25 = 40% Adj CTX + RTX: 7/25 = 25% No Adj: 3/25 = 12%	Bx only: 19/56 = 34% Initial surgery 37/56 = 66% - Radical: 18/37 = 49% - Marginal: 15/37 = 41% - Intralesional: 3/37 = 8% CTX - 55/56 = 98% - Adj CTX 36/55 = 65% - Neo-Adj 19/55 = 35% RTX: 27/56 = 48%
	Median = 16 (1-84)	Median = 72 (12-180)

L: left; R: right; NS: not specified; LMa: labia major; LMi: labia minor; NA: not available; NS: not specified; Adj: adjuvant; WLE: wide local excision; RV: radical vulvectomy; Sx: surgery; LN: lymph nodes; RTX: radiotherapy; CTX: chemotherapy; LND: lymphadenectomy; Bx: biopsy.

[15] Rud N.P., Reiman HM, Pritchard D.J., Frassica F.J., Smithson W.A.: Extraosseous Ewing's sarcoma. A study of 42 cases". *Cancer*, 1989, *64,* 1548.

[16] Mary M., Tomayko C., Reynolds P.: "Determination of subcutaneous tumor size in athymic (nude) mice". *Cancer Chemother. Pharmacol.,* 1989, *24,* 148.

[17] Widhe B., Widhe T.: "Initial symptoms and clinical features in osteosarcoma and Ewing sarcoma". *J. Bone Joint Surg. Am*., 2000, *82,* 667.

[18] Delaplace M., Lhommet C., de Pinieux G.: "Primary cutaneous Ewing sarcoma: a systematic review focused on treatment and outcome". *Br. J. Dermatol*., 2011, *166*, 721.

[19] Mankin H.J.: "Ewing sarcoma". *Curr. Opinion Ortho.*. 2000, *11*, 479.

[20] Craft A., Cotterill S., Malcolm A., Spooner D., Grimer R., Souhami R., et al.: "Ifosfamide-containing chemotherapy in Ewing's sarcoma: The Second United Kingdom Children's Cancer Study Group and the Medical Research Council Ewing's Tumor Study". *J. Clin. Oncol*., 1998, *16,* 3628.

[21] Paulussen M., Ahrens S., Dunst J., Winkelmann W., Exner G.U., Kotz R., *et al.*: "Localized Ewing tumor of bone: final results of the cooperative Ewing's Sarcoma Study CESS 86". *J. Clin. Oncol*., 2001, *19,* 1818.

[22] Nesbit M.E. Jr., Gehan E.A., Burgert E.O. Jr., Vietti T.J., Cangir A., Tefft M., *et al.*: "Multimodal therapy for the management of primary, nonmetastatic Ewing's sarcoma of bone: a long-term follow-up of the First Intergroup study". *J. Clin. Oncol*., 1990, *8,* 1664.

[23] Obata H., Ueda T., Kawai A., Ishii T., Ozaki T., Abe S., et al.: "Japanese Musculoskeletal Oncology Group. Clinical outcome of patients with Ewing sarcoma family of tumors of bone in Japan: the Japanese Musculoskeletal Oncology Group cooperative study". *Cancer*, 2007, *109,* 767.

[24] Donaldson S.S., Torrey M., Link M.P., Glicksman A., Gilula L., Laurie F., *et al.*: "A multidisciplinary study investigating radiotherapy in Ewing's sarcoma: end results of POG #8346. Pediatric Oncology Group". *Int. J. Radiat. Oncol. Biol. Phys*., 1998, *42,* 125.

[25] Nilbert M., Saeter G., Elomaa I., Monge O.R., Wiebe T., Alvegård T.A.: "Ewing's sarcoma treatment in Scandinavia 1984-1990 – ten-year results of the Scandinavian Sarcoma Group Protocol SSGIV". *Acta Oncol*., 1998, *37,* 375.

[26] Raney R.B., Asmar L., Newton W.A. Jr., Bagwell C., Breneman J.C., Crist W., et al.: "Ewing's sarcoma of soft tissues in childhood: a report from the Intergroup Rhabdomyosarcoma Study, 1972 to 1991". *J. Clin. Oncol*., 1997, *15,* 574.

[27] Ferrari S., Mercuri M., Rosito P., Mancini A., Barbieri E., Longhi A., *et al.*: "Ifosfamide and actinomycin-D, added in the induction phase to vincristine, cyclophosphamide and doxorubicin, improve histologic response and prognosis in patients with non-metastatic Ewing's sarcoma of the extremity". *J. Chemother*., 1998, *10,* 484.

[28] Kinsella T.J., Miser J.S., Waller B., Venzon D., Glatstein E., Weaver-McClure L., Horowitz M.E.: "Long-term follow-up of Ewing's sarcoma of bone treated with combined modality therapy". *Int. J. Radiat. Oncol. Biol. Phys*., 1991, *20,* 389.

[29] Rodríguez-Galindo C., Liu T., Krasin M.J., Wu J., Billups C.A., Daw N.C., *et al.*: "Analysis of prognostic factors in Ewing sarcoma family of tumors: review of St. Jude Children's Research Hospital studies". *Cancer*, 2007, *110,* 375.

[30] McCluggage W.G., Sumathi V.P., Nucci M.R., Hirsch M., Dal Cin P., Wells M., et al.: :Ewing family of tumors involving the vulva and vagina: report of a series of four cases". *J. Clin. Pathol*., 2007, *60*, 674.

[31] Moodley M., Jordaan A.: "Ewing's sarcoma of the vulva: a case report". *Int. J. Gynecol. Cancer*, 2005, *15*, 1177.

[32] Vang R., Taubenberger J.H., Mannion C.M.: "Primary vulvar and vaginal extraosseus Ewing's sarcoma/peripheral neuroectodermal tumor: diagnostic confirmation with CD99 immunostaining and reverse transcriptase-polymerase chain reaction". *Int. J. Gynecol. Pathol*., 2000, *19,* 103.

[33] Nirenberg A., Ostor A.G., Slavin J.: "Primary vulvar sarcomas". *Int. J. Gynecol. Pathol*., 1995, *14*, 55.

[34] Lazure Y., Alsama I.A., Meuric S.: "Primary uterine and vulvar Ewing's sarcoma/peripheral neuroectodermal tumors in children: two unusual locations". *Ann. Pathol*., 2001, *21,* 263.

[35] Habib K., Finet J.F., Plantier F.: "Rare lesion of the vulva". *Arch. Anat. Cytol. Pathol*., 1992, *40*, 158.

[36] Paredes E., Duarte A., Couceiro A.: "A peripheral neuroectodermal tumor of the vulva". *Acta Med. Port*., 1995, *8*, 161.

[37] Takeshima N., Tabata T., Nishida H.: "Peripheral primitive neuroectodermal tumor of the vulva: report of a case with imprint cytology". *Acta Cytol*., 2001, *45*, 1049.

[38] Scherr G.R., d'Ablaing G. 3rd, Ouzounian J.G.: "Peripheral primitive neuroectodermal tumor of the vulva". *Gynecol. Oncol*., 1994, *54*, 254.

[39] Boldorini R., Riboni F., Cristina S.: "Primary vulvar Ewing's sarcoma/primitive neuroectodermal tumor in a post-menopausal woman: a case report". *Pathol. Res. Pract*., 2010, *206*, 476.

[40] Di Giannatale A., Frezza A.M., Le Deley M.C., Marec-Berard P., Benson C., Blay J.Y., *et al.*: "Primary Cutaneous and Subcutaneous Ewing Sarcoma". *Pediatr. Blood Cancer*, 2015, *62*, 1555.

[41] Xiao C., Zhao J., Guo P., Wang D., Zhao D., Ren T., Yang J., Shen K., Lang J., Xiang Y., Cui Q.: "Clinical Analysis of Primary Primitive Neuroectodermal Tumors in the Female Genital Tract". *Int. J. Gynecol. Cancer*, 2014, *24*, 404.

[42] Narayanana G., Rajana V., Puthusseria J., Kattoorb J., Somana L.V.: "Primitive Neuroectodermal Tumor of the Vulva in an Adolescent Girl". *World J. Oncol*., 2014, *5*, 220.

Corresponding Author:
M. CANTOS, M.D.
103 Hospital Drive
Saskatoon SK, S7N 0W8 (Canada)
e-mail: mae.cantos@usask.ca