Manipal Alumni Science and Health Journal 2021; 6(2): 9

*CASE REPORT*

# An Unusual Case of Extraskeletal Ewing Sarcoma (EES) Post Therapeutic Radiation: A Case Report

Lee Ee Peng [1], Sekkapan A/L Thannimalai [2], Edmund Choong Yew Hoe [3], Raja Norazah Binti Raja Alam Shah [4]

*Corresponding Author Email: paigelee92@gmail.com*

***Key words: Extraskeletal Ewing Sarcoma, Breast, anterior abdominal wall***

**ABSTRACT**

Extraskeletal Ewing Sarcoma (EES) is a rare tumor under the umbrella of Ewing sarcoma family of tumors (EFT) and is increasingly being reported in literature. We present a case of EES of the upper anterior abdominal wall in a 46 years old lady, who previously had left breast invasive carcinoma which was treated with surgical resection accompanied with adjuvant radiotherapy 7 years ago (2013). Therapeutic radiotherapy in this case may had played a role in the genesis of the tumor.

## INTRODUCTION

EES together with primitive neuroectodermal tumor (PNET), Askin tumor and atypical ES forms the Ewing sarcoma family of tumors (EFT). In comparison to Ewing Sarcoma (ES) which are commonly seen in children and adolescent; EES is seen in older age group typically in the second to third decade of life; has a higher prevalence to the axial skeleton, paravertebral region and lower extremities as compared to the appendicular skeleton seen in ES [1]. Few cases of EES of the breast had been reported but not as a secondary tumor post radiation [2].

[1] Department of General Surgery, Hospital Sultanah Aminah, Johor Bahru, Malaysia.
[2] Department of General Surgery, Hospital University Kebangsaan Malaysia, Selangor, Malaysia
[3] Department of General Surgery, Hospital University Sains Malaysia, Kelantan, Malaysia.
[4] Department of Pathology, Hospital Sultanah Aminah, Johor Bahru, Malaysia

Imaging in EES are non-specific [3] and diagnosis can be made with histological and immunohistochemistry study which would reveal small round blue cells with positive stain of CD99 and FLI-1.

**Case**

A 46 years old female presented to the outpatient surgical clinic with a rapidly growing left hypochondriac region fungating mass for past 3 months. It measured around 8cm x 6cm, appeared cauliflower-like with no contact bleeding and was painless. Clinically was not fixed to underlying structures. (Figure 1)

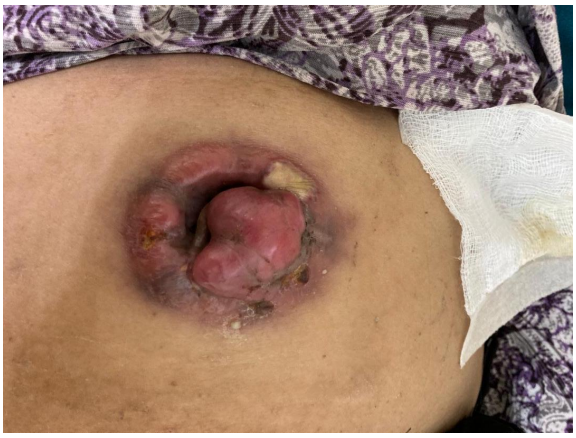

**Figure 1: Left hypochondriac region fungating mass measuring 8cm x 6cm.**

Patient's past medical history was significant for a stage 3 (T3N1M0) left breast invasive carcinoma, diagnosed 7 years ago. She received neoadjuvant chemotherapy comprising of 5-fluorouracil, epirubicin and cyclophosphamide for 6 cycles, subsequently underwent left mastectomy and axillary clearance with clear margins. Histopathology of the tumor revealed an infiltrating ductal carcinoma, Bloom and Richardson grade 3. Whereas hormonal status of the tumor was negative for estrogen receptor, progesterone receptors as well as C-erb-B2 oncoprotein. Hence, patient was subjected for radiotherapy to left chest wall with radiation dose of 45Gy/25 fractions. Since then, patient was on regular surveillance in our outpatient surgical clinic with no locoregional recurrence until present time.

We proceeded with a wedge biopsy of the left hypochondriac mass which revealed features suggestive of an Ewing sarcoma (positive stains for CD99 and FLI-1). Contrasted Enhanced CT scan (Figure 2,3) showed a fungating homogenous mass with everted edges at left upper abdomen, measuring 5.4cm x 5.8cm x 6.3cm which does not appear to arise from the bone. It has a clear fat plane with adjacent rectus abdominis and transverse abdominis muscles. Bone scan was unremarkable.

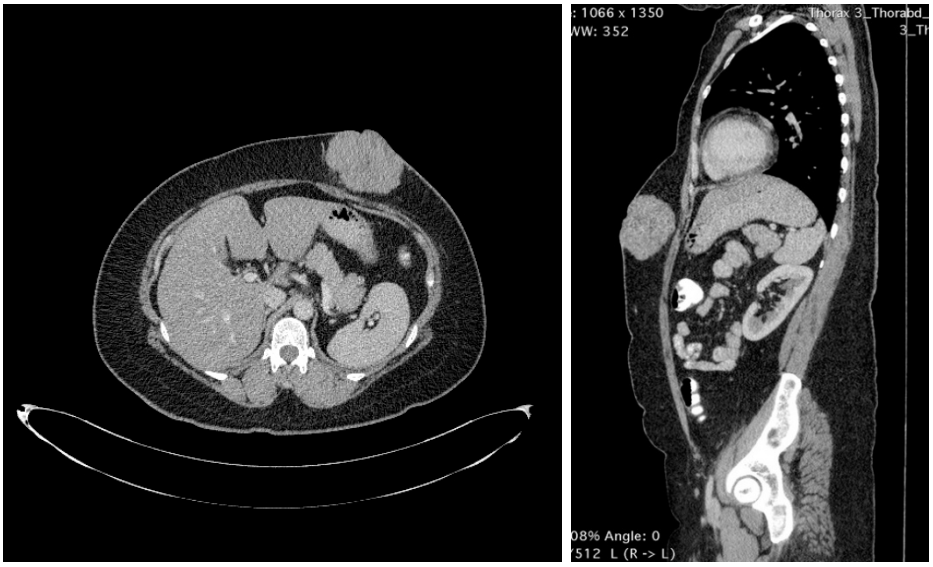


**Figure 2, 3: Left upper abdominal subcutaneous mass with suspicious features; does not breach the peritoneal cavity**

Patient was subsequently subjected for a wide local excision of the tumor (Figure 4).

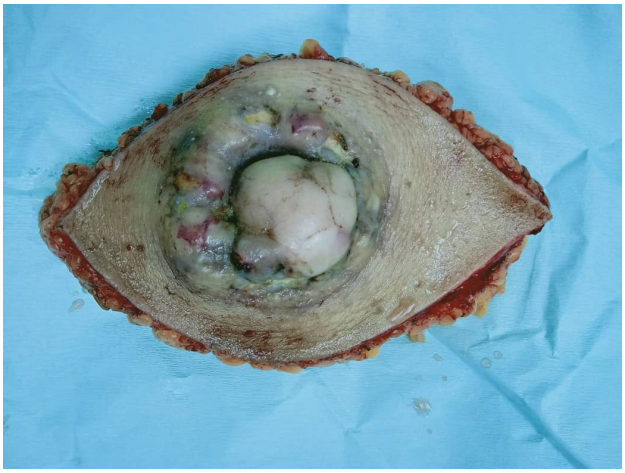

**Figure 4: Well circumscribe tumor of left hypochondriac region, measuring approximately 5cmx 6cm; irregular and firm in nature.**

A fairly circumscribed lobulated soft to firm cream tumor with areas of necrosis measuring 3.5x 7.5x 6.0cm was seen in gross cut section. Microscopically, the tumor is arranged in solid sheets with pseudorosettes divided by thin fibrous septa. Mitosis is brisk with necrosis seen (<50%). The tumor measures 3mm from closest radial margin and is seen in the deep margin. Immunohistochemistry showed tumor cells positive for CD 99, FL-1, CD 56, BCL-2,

CD117 and vimentin. (Figure 5a, 5b, 5c, 5d). The morphology and immunohistochemistry studies thus are confirmative for Extra-skeletal Ewing Sarcoma.

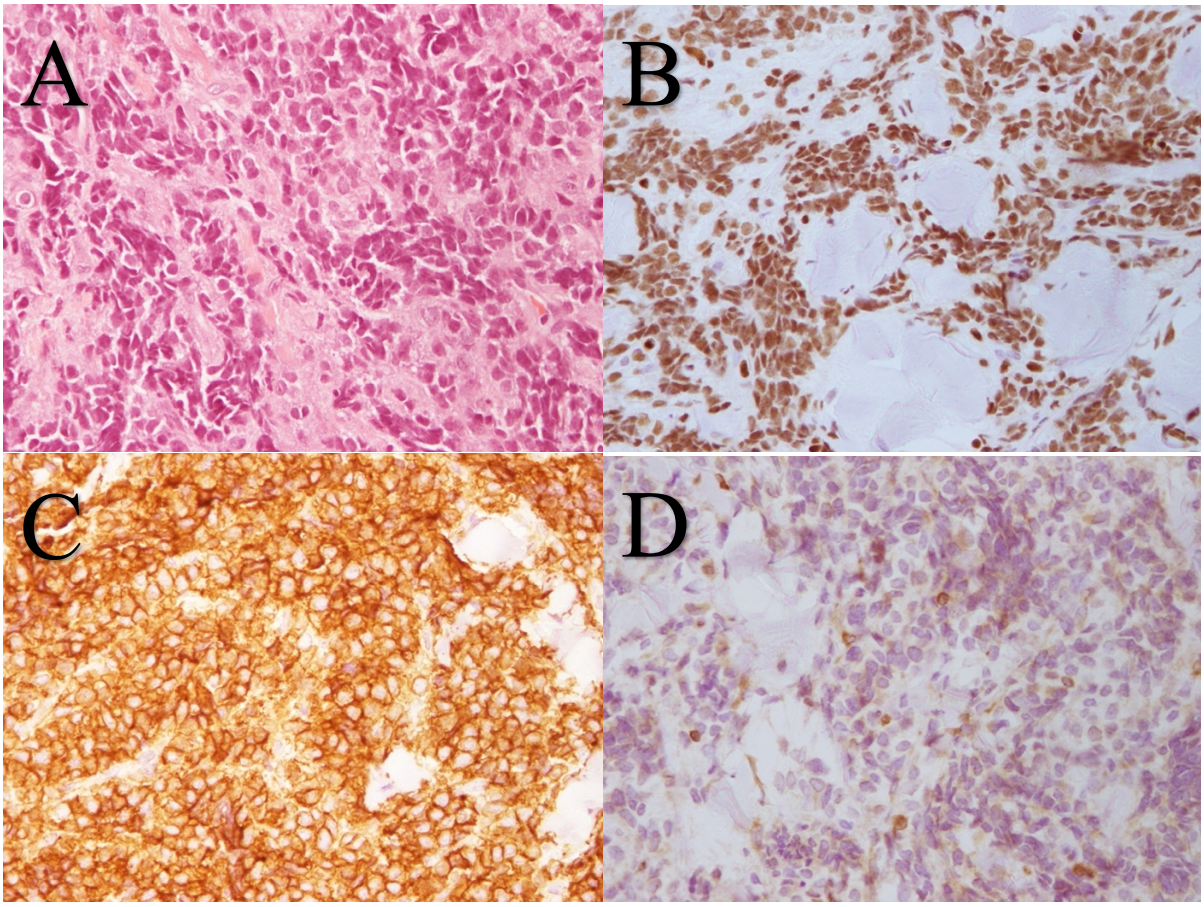


**Figure 5(A) Hematoxylin and Eosin staining (magnification x40) showing tumour cells arranged in pseudorosettes; (B) Immunohistochemical staining for FL-1 (magnification x40), patchy; (C) Immunohistochemical staining for CD99 (magnification x40), tumor cells positive (membranous, diffuse); (D) Immunohistochemical staining for BCL-2 (magnification x40), patchy, weak.**

In view of involved margin, patient was planned for 14 cycles of chemotherapy. A CT scan was repeated prior to commencement of chemotherapy which showed no residual tumor (Figure 6).

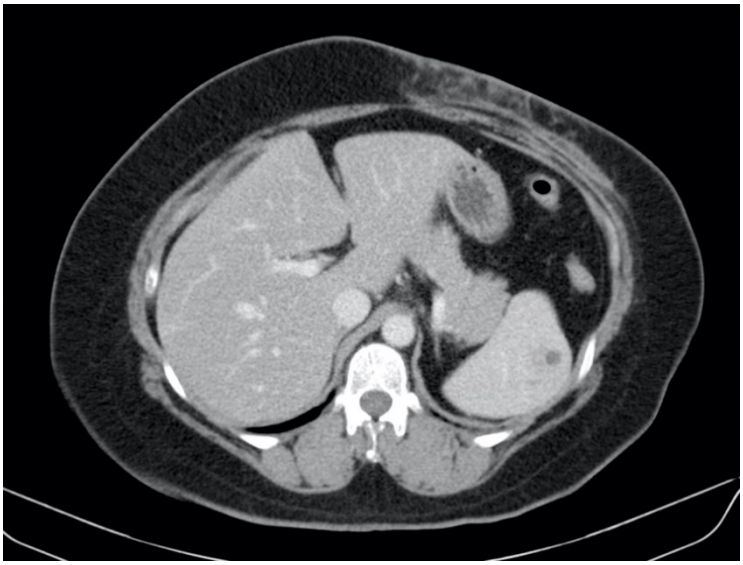

**Figure 6: CT abdomen post wide local excision of tumor; prior to commencement of radiotherapy**

## DISCUSSION

As treatment for invasive breast carcinoma with breast conserving surgery supplemented with adjuvant radiotherapy and chemotherapy become more popular, the incidence of secondary tumor post radiotherapy is increasing [4]. Specifically, more cases of soft tissue sarcoma are reported in breast cancer survivor patients who had received radiotherapy prior and was related to radiation dose [5,6].

The above patient had received therapeutic radiotherapy for invasive breast carcinoma 7 years ago. In accordance to Cahan et al [7] and later modified by Arlen et al [8], the definition of radiation induced sarcoma (RIS) includes sarcoma that arises within the field of radiation; has a different histology with previous tumor that was treated with radiation and lastly patient should have been treated with radiation at least 3 years prior to development of sarcoma. Additionally, the commonest RIS in breast cancer includes angiosarcoma and rarely osteosarcoma. To the best of the author's knowledge, there are no case reports of EES post therapeutic radiation. Hence, in view of location of the tumor at the upper anterior abdominal wall which was in near proximity of previous irradiation field, radiation may have played a significant role in manifestation of this patient's secondary tumor.

As previously mentioned, EES is a rare tumor. Location of these tumors have been reported in various organs including jejunum, pancreas, and even as a synchronous tumor with gallbladder carcinoma [9,10,11]. Diagnosis of EES can only be made by immunohistological studies and confirmatory diagnosis is via molecular study which would show a translocation of chromosome 11 and 12, t(11:12), as imaging for EES is nonspecific. Due to unavailability of molecular study in our center, our patient's diagnosis was confirmed via immunohistological studies.

Treatment of EES generally includes surgical resection with clear margins, followed by chemotherapy. Few studies concluded that radiotherapy may not improve overall survival despite patient receiving an R1 resection [12]. However, there are still no standard guidelines for treatment of EES and the above patient was not subjected for radiotherapy. During time of writing, patient is receiving her 2$^{nd}$ cycle of chemotherapy.

## CONCLUSION

In conclusion, with the increasing trend of treatment with neoadjuvant and adjuvant radiotherapy in breast cancer, there is an increasing incidence of radiation induced secondary tumors. It is imperative for clinicians to be aware of the effects of radiation and the need for long term follow up and early detection of radiation effects.

## REFERENCES

1. Applebaum MA, Worch J, Matthay KK, et al. Clinical features and outcomes in patients with extraskeletal Ewing sarcoma. Cancer. 2011;117(13):3027-3032. doi:10.1002/cncr.25840
2. Chuthapisith, S., Prasert, W., Warnnissorn, M., Pradniwat, K., Srimuninnimit, V., & Angsusinha, T. (2012). Ewing's sarcoma and primitive neuroectodermal tumour (ES/PNET) presenting as a breast mass. Oncology Letters, 4, 67-70. https://doi.org/10.3892/ol.2012.69
3. O'Keeffe F, Lorigan JG, Wallace S. Radiological features of extraskeletal Ewing sarcoma. Br J Radiol. 1990 Jun;63(750):456-60. doi: 10.1259/0007-1285-63-750-456. PMID: 2379070.
4. Dracham, Chinna Babu et al. "Radiation induced secondary malignancies: a review article." Radiation oncology journal vol. 36,2 (2018): 85-94. doi:10.3857/roj.2018.00290
5. Rubino, Carole et al. "Radiation dose and risk of soft tissue and bone sarcoma after breast cancer treatment." Breast cancer research and treatment vol. 89,3 (2005): 277-88. doi:10.1007/s10549-004-2472-8
6. Rubino C, de Vathaire F, Shamsaldin A, Labbe M, Le MG. Radiation dose, chemotherapy, hormonal treatment and risk of second cancer after breast cancer treatment. Br J Cancer. 2003 Sep 1;89(5):840-6. doi: 10.1038/sj.bjc.6601138. PMID: 12942115; PMCID: PMC2394476.

7. Cahan, W. G., Woodard, H. Q., and et al. Sarcoma arising in irradiated bone; report of 11 cases. Cancer, 1: 3-29, 1948.
8. Arlen, M., Higinbotham, N. L., Huvos, A. G., Marcove, R. C., Miller, T., and Shah, I. C. Radiation-induced sarcoma of bone. Cancer, 28: 1087-1099, 1971.
9. Cantu, Colby et al. “Extraskeletal Ewing Sarcoma of the Jejunum: A Case Report.” The Permanente journal vol. 23 (2019): 18-255. doi:10.7812/TPP/18-255
10. Saif, Muhammad W, and Kristin Kaley. “Extraosseous Ewing's Sarcoma of the Pancreas: An Uncommon but Treatable Disease.” Cureus vol. 9,11 e1882. 26 Nov. 2017, doi:10.7759/cureus.1882
11. Plis A, Zygulska A, Püsküllüoğlu M, et al. Synchronous extraskeletal Ewing's sarcoma/PNET and gallbladder carcinoma: a case report and literature review. *Contemp Oncol (Pozn)*. 2016;20(6):496-500. doi:10.5114/wo.2016.65612
12. Augustine M. Saiz, Alicia A. Gingrich, Robert J. Canter, Amanda R. Kirane, Arta M. Monjazeb, R. Lor Randall, Steven W. Thorpe, "Role of Radiation Therapy in Adult Extraskeletal Ewing’s Sarcoma Patients Treated with Chemotherapy and Surgery", Sarcoma, vol. 2019, Article ID 5413527, 6 pages, 2019.