Case Report

Metachronous nasopharyngeal carcinoma masquerading as a base of skull metastasis in a case of primary extraskeletal vulvar Ewing's sarcoma

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ABSTRACT

Ewing's sarcoma (ES) and primitive neuroectodermal tumor (PNET) resemble each other and commonly affect the skeletal system. Extraskeletal ES/PNET is a rare neoplasm. Here, we report a case of primary vulvar ES in an 18-year-old adolescent girl confirmed by histopathology and immunohistochemistry, who underwent surgery followed by adjuvant chemotherapy. Following 1 year of chemotherapy, she presented with multiple cranial nerve palsies (VI, IX, X, and XII). Contrast tomography of the base of the skull and nasopharynx showed a heterogeneous mass lesion involving the base of skull, sphenoid sinus, and left nasopharynx. Biopsy from the left nasopharyngeal mass revealed it to be well-differentiated squamous cell carcinoma, which was initially thought of metastasis to the base of the skull. In spite of its aggressive nature, a patient of primary sarcoma presenting with a second lesion should be adequately investigated before considering it as a metastatic lesion.

KEY WORDS: Ewing's Sarcoma; Extraskeletal; Metachronous; Nasopharyngeal Carcinoma; Vulva

INTRODUCTION

Ewing's sarcoma (ES) is a highly malignant childhood bone neoplasm. ES and primitive neuroectodermal tumor (PNET) comprise ES family of tumor (ESFT). It is characterized by *"t"* (11:22) (q24;q12) chromosomal translocation leading to a chimeric transcript EWS-FLI1 formation.[1] ESFT commonly affects diaphysis of the long bone. Extraskeletal ES (EES)/PNET, however, can have its origin anywhere in the body, including soft tissue, skin, and visceral organs,[2] but rarely from the female genital tract. Only a limited number of cases of EES have been reported arising from the vulva, vagina, cervix, uterine corpus, broad ligament, and ovary.[3]

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Double primary solid tumor in childhood is a rare entity, whereas second malignancy in childhood has been reported in survivors of leukemia and lymphoma.[4] Double primary tumor can be of synchronous or metachronous type. The synchronous cancer is defined as two or more malignancies identified simultaneously or within 6 months of initial diagnosis, whereas the metachronous cancer is defined as a second primary lesion detected after 6 months of diagnosis of first cancer.[5] Here, we report a case of metachronous nasopharyngeal carcinoma (NPC) presenting with multiple cranial nerve palsies in a case of primary EES of vulva in an adolescent girl.

CASE REPORT

An 18-year-old adolescent girl from a poor socioeconomic background presented with left labial swelling for 6 months. Clinically, it was a cystic mass of approximate size 1.5 cm × 1.5 cm. She underwent enucleation of the cyst and histopathological examination revealed a high grade small round blue cell tumor with features suggestive of EES

[Figure 1a]. Immunohistochemical (IHC) study was done for diagnostic confirmation, which showed strong membrane staining for CD-99 and friend leukemia integration-1 (FLI-1), whereas negative staining for CD-45/desmin/pancytokeratin [Figures 1b and c and 2a-c, respectively]. Positron emission tomography scan done for metastatic workup revealed no active lesion elsewhere. In view of high-grade and aggressive disease, she was given 9 cycles of adjuvant chemotherapy every 3 weekly with alternate cycle of injectable vincristine, adriamycin, and cyclophosphamide and ifosfamide and etoposide (VAC-IE) regimen. She was disease free during her 1st year follow-up. Following 1 year of completion of chemotherapy, she presented with blurring of vision, slurring of speech, and difficulty in swallowing.

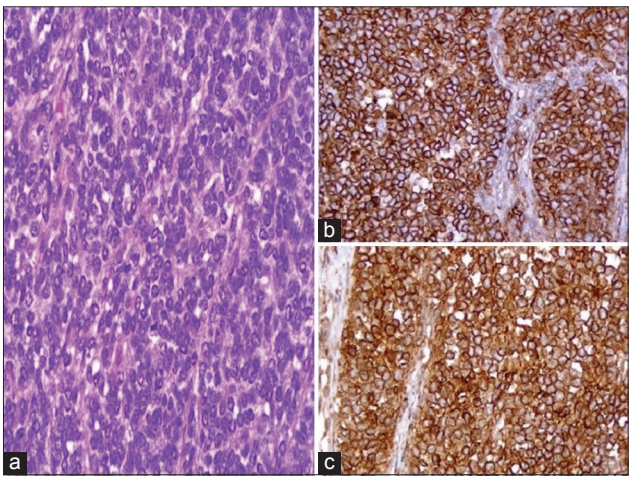

Figure 1: (a) Photomicrograph (H and E, ×400) showing monomorphic malignant small round blue cells with scanty cytoplasm arranged in sheets. (b) Photomicrograph immunohistochemical ([IHC], ×400) showing malignant cells with strong membrane staining for CD-99. (c) Photomicrograph (IHC, ×400) showing malignant cells with strong membrane and cytoplasmic staining for friend leukemia integration-1

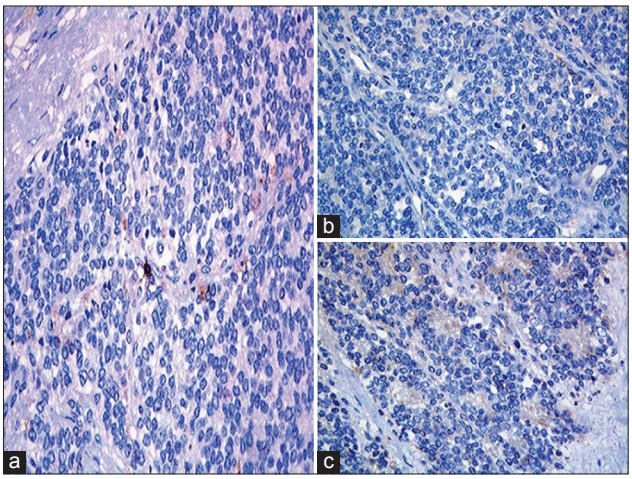

Figure 2: (a) Photomicrograph immunohistochemical ([IHC] ×400) showing malignant cells with negative staining for CD-45. (b) Photomicrograph (IHC ×400) showing malignant cells with negative staining for desmin. (c) Photomicrograph (IHC, ×400) showing malignant cells with negative staining for pancytokeratin

On examination, she had restricted lateral mobility of left eyeball, deviation of the tongue to the left side, left-sided tongue atrophy, and loss of gag reflex. Direct laryngoscopy revealed restricted mobility of the left vocal cord. Contrast-enhanced computed tomography (CECT) of the base of skull and nasopharynx showed contrast-enhancing heterogeneous mass lesion involving the left nasopharynx, sphenoid sinus, and base of skull [Figure 3], without any significant cervical lymphadenopathy. Biopsy from the nasopharyngeal mass showed well-differentiated squamous cell carcinoma [Figure 4]. She was started with external beam radiotherapy (EBRT) to the nasopharynx (planned dose of 70Gy/35#) by Telecobalt-60 unit.

DISCUSSION

EES is a rare, rapidly growing, aggressive soft tissue tumor having a wide range of occurrence from infancy to old age. It can affect practically any location, with most common

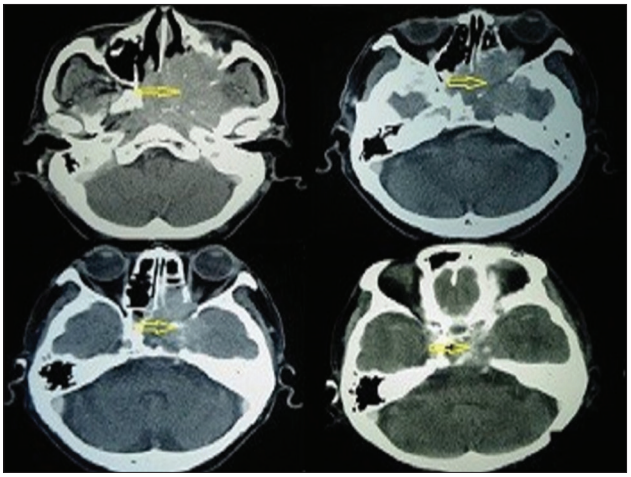

Figure 3: Contrast-enhanced computed tomography of nasopharynx showing enhancing heterogeneous mass lesion (yellow arrowed) involving left nasopharynx, sphenoid sinus, and base of the skull

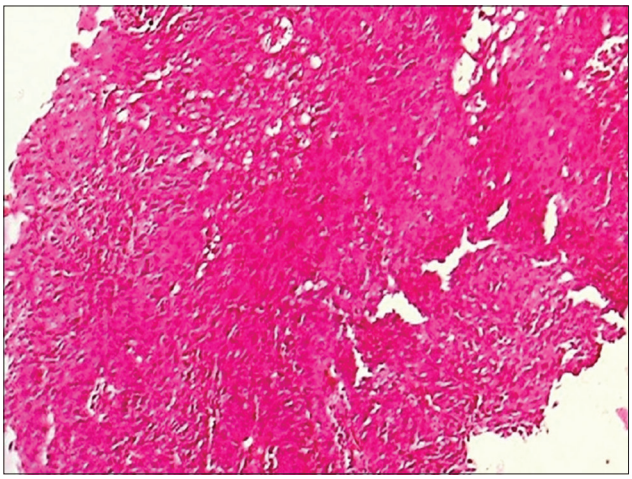

Figure 4: Photomicrograph (H and E, ×200) showing pleomorphic malignant squamous cells with hyperchromatic nuclei arranged in sheets

sites being paravertebral, intercostals regions followed by extremities, breast, etc. PNETs as primary genitourinary system have been reported rarely in the kidney, bladder, and prostate.[6,7] EES of the vulva is a rare malignancy, with a limited number of cases which have been reported so far. They are most commonly seen in young women of reproductive age with a median age of 20 years. The patient usually presents with a painless vulvar swelling[8] as was also seen in our case. The diagnosis of ES/PNET is based on histopathology, immunohistochemistry, cytogenetic, and molecular analysis. On histopathological examination, ES is seen as small round blue cells with scanty cytoplasm and high mitotic index. The IHC study of CD-99 (a cell membrane glycoprotein) and intranuclear FLI-1 (a DNA-binding transcription factor) is important to diagnose ES.[9] CD-99 though sensitive is not specific and is also elevated in lymphoma, rhabdomyosarcoma, and epithelial neuroendocrine carcinoma.[10] In our case, a small round blue cell tumor found on histopathology was confirmed as extraskeletal ES of vulva by IHC study, which showed strong positive membrane staining for CD-99 and FLI-1 and negative staining for CD-45/desmin/pancytokeratin. Cytogenetic studies to demonstrate translocation "*t*" (11;22) (q24;q12) were not done in our case due to the non-availability of the facility. The management of the ESFT requires a multidisciplinary systemic approach, usually consisting of surgery, radiotherapy, and multiagent chemotherapy. Multiagent regimens based on ifosfamide showed improved 5-year overall survival rates in the non-metastatic cases.[11] Similarly, our patient underwent enucleation of the left labial cyst. Based on the high grade of tumor, she was given nine cycles of adjuvant chemotherapy of alternating VAC-IE regimen and was disease free during post-chemotherapy, 1-year follow-up. EES is highly aggressive tumor, which has worse prognosis and poorer 5-year survival rate (38% vs. 75%) than their skeletal counterpart.[1] Hematogenous metastasis to lungs, bones, and bone marrow is common with the lung being most common (25%). One case of extrapulmonary intracranial metastasis has been reported by Yip *et al*.[12] NPC is disease of complex etiology, which follows bimodal peak of age at diagnosis, particularly in low-risk population. The first peak is in late adolescence/early adulthood (ages 15–24 years) and a second peak in the elderly (65–79 years).[13] Most common presentation in NPC is painless neck swelling, whereas cranial nerve involvement as an initial presentation is very rare and is seen in only 7.8% and the most frequently affected cranial nerves are V and VI.[14] During the 1st year of follow-up following completion of adjuvant chemotherapy, our patient did not show any sign of locoregional recurrence or distant metastasis, but she presented after 1 year with features of multiple cranial nerve palsies (CN VI, IX, X, and XII). CECT of the base of skull and nasopharynx showed contrast-enhancing heterogeneous mass lesion involving the left nasopharynx, sphenoid sinus, and cavernous sinus. This was initially suspected to be a base of skull metastasis from primary vulvar ES; however, biopsy from the nasopharyngeal lesion revealed it to be a well-differentiated squamous cell carcinoma. She was planned for EBRT to nasopharynx by telecobalt-60 unit to a total dose of 70gy/35#.

CONCLUSION

Metachronous NPC in a primary EES of vulva has not been reported so far. We report this rare case, which presented to us as a diagnostic dilemma. Hence, any case of primary sarcoma presenting with a separate lesion should be adequately investigated. Primary vulvar ES is a rare and inadequately studied malignancy. Further clinical studies are needed to understand its disease behavior and to establish a standard multidisciplinary treatment protocol.

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