Primary naso-orbital embryonal rhabdomysarcoma in a patient previously treated for breast cancer

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Abstract

Introduction: Rhabdomyosarcoma is a rare malignancy in adults, it accounts for less than 3 % of all soft tissue sarcomas. The embryonal subtype and head and neck site are common in childhood but exceedingly infrequent in adults. Its association with breast cancer was rarely described and there are several genetic mutations that appear to play a role in both of them. Also breast cancer treatments related malignancies, especially radiotherapy were suggested as a cause of development of these types of tumors in predisposed populations.

Case presentation: A 64 year-old post menopausal and hypertensive woman, presented in consultation on July 2011 with a recently appearance of right orbito-nasal mass. Her past medical history was significant for mucinous breast carcinoma diagnosed on 1992. Treatment of her breast cancer consisted of a radical left mastectomy with axillary nodal dissection lumpectomy followed by adjuvant chemotherapy (anthracycline based) and radiotherapy. Fifteen years later she presented with a local and metastatic recurrence of her breast cancer. Treatment consisted on Paclitaxel with a very good partial response, the patient then was given letrozole as a maintenance treatment. Biopsy of her orbito-nasal mass showed an emryonal rhabdomyosarcoma. No evidence of distant metastases was found. Patient underwent induction chemotherapy based on vincristin, etoposide and cyclophosphamide with a good partial response of 60%. Radiotherapy was planned; however she died due to acute hemorrhagic stroke on September 2011.

Conclusion: We report a case with unusual demographics of emryonal rhabdomyosarcoma where previous treatment for her breast cancer may play a role in developing such tumors.

Introduction

Rhabdomyosarcoma (RMS) is a highly malignant, but uncommon mesenchymal tumor that accounts for 15–20% of all soft tissue sarcomas [1]. Although RMS is the most common sarcoma in the pediatric population, it is exceedingly infrequent in adults; it represents only 3% of all soft tissue sarcomas [2]. Three histological types were described: embryonal, alveolar and pleomorphic, the first two types occur mainly in children, whereas pure pleomorphic tumors occurs in adults [3]. Embryonal subtype in adults is rare and was reported only in few case reports [4].

Although head and neck sites are common in children where they account for some 35% of cases, most series on adult disease reported that orbital presentations are distinctly uncommon (2-5%) [5-6]. Orbital presentations are among the most favorable for childhood RMS, as demonstrated in all four IRSG studies [7-8] and the relative paucity of these among adult patients might partly explain their worse overall prognosis. The overwhelming majority of orbital RMS is of the embryonal subtype [9].

RMS in adults appears to be of a worse prognosis and age at diagnosis is an independent predictor of outcome [10]. Experience with adult rhabdomyosarcoma is limited but the literature to date supports the use of multi-modality therapy with chemotherapy, surgery, and/or radiation therapy [11]

Association of breast cancer and rhabdomyosarcoma is rarely reported and there are several genetic mutations that appear to play a role in both of them [4]. Also breast cancer treatment related malignancies could be a cause of development of such sarcoma in predisposed patients [12].

We report a rare case of naso-orbital embryonal RMS occurring in a patient previously treated for breast cancer.

Case report

A 64 year-old post menopausal and hypertensive patient under diuretics, presented in consultation on July 2011 with a recently appearance of right orbital mass. Her past medical history was significant for mucinous left breast carcinoma diagnosed on 1992. It was classified pT2N1M0 according to TNM classification adopted by the AJCC, SBR 3 and hormone receptors positive. Treatment of her breast cancer consisted of a radical left mastectomy with axillar lumpectomy followed by 6 courses of adjuvant chemotherapy anthracycline based and adjuvant radiotherapy. Patient then was given Tamoxifen for 5 years. In April 2007 she presented a metastatic recurrence to cervical lymph-nodes and to lung confirmed by cervical lymph-node biopsy that showed mucinous carcinoma with positive hormone receptors at 100% rate both for ER (estrogen receptors) and PR (progesterone receptors) and HER2 negative on immunochemistry. Relapse of breast cancer disease was treated with weekly Paclitaxel at 80 mg/m2 for 32 weeks with 40% partial response then maintenance Letrozole was given since

June 2009. In the actual presentation, her performance status was 1, physical examination showed a right large naso-orbital mass with ptosis (fig1). No palpable cervical lymph-node and no breast recurrence were noticed. Biopsy of the orbital mass showed an embryonal rhabdomyosarcoma with pleomorphic round and polygonal cells in a fibro-myxoid matrix. On immunochemistry, both anti desmine and anti-myogenine were positive (fig2). Nasal and orbital CT scan showed a right ethmoidal mass with bone lyses and necrotic cervical maxillary lymph-nodes (fig3). Clinical and biological workup didn't show any sign of metastatic sites or progressive breast cancer disease. A curative strategy was decided by the medical staff and the patient underwent induction chemotherapy based on vincristin, etoposide and cyclophosphamide. Three courses were completed with a good partial response of 60%. Radiotherapy was planned; however she died due to acute hemorrhagic stroke on September 2011.

Discussion

Three main reasons to present this interesting observation. First, is the unusual demographics and localization of emryonal RMS in our patient [4]. Second one is the association of RMS with breast cancer could suggest the probable presence of genetic disorders [13]. And the third one is breast cancer treatment related disorders; especially radiotherapy and hormonal therapy may play a role in developing sarcomas in predisposed patients. [12, 13].

Embryonal RMS is generally regarded as a neoplasm occurring primarily during childhood, although there have been few reports of this neoplasm in adults [14]. A very similar case was reported by Morris of sino-orbital RMS occurring in 64 year-old woman previously treated for breast cancer, but it was of the alveolar subtype [4].

In childhood head and neck RMS localization is predominant, patient prognosis and response to chemotherapy are correlated closely with the histologic subtype. In contrast, adult RMS arises predominantly in the extremities, head and neck localization remains extremely rare in adults and prognosis does not depend on histological subtype [3].

The association of breast cancer with RMS could suggest the presence of genetic disorders as Li-Fraumeni syndrome. Breast cancer is the most common tumor in women with Li-Fraumeni Syndrome (LFS), an inherited cancer syndrome associated with germline mutations in the TP53 tumor suppressor gene. However the clinical presentation of our patient doesn't fit criteria of diagnosing this syndrome especially the age of occurrence of the first cancer which should be under 36 year-old and the absence of familial history of multiple cancers [15]. Improvement in diagnosing and treating cancers has led to the increased likelihood of being diagnosed with a second primary cancer. These second cancers may be the result of lifestyle choices, genetics, environmental exposures and late effects of treatment [16]. In a large Australian cohort study had shown that the relative risk of developing a second malignancy after breast cancer treatment is 1.86 [17]. Cumulative incidence of second primary malignancy after radiotherapy can reach 20 %, 40 years after treatment. Relative risk is around 1.1 in adult patients. Pathogeny and risk factors are not yet fully understood [18]. In a large series of 376,825 breast cancer patient survivors, examining the risk of developing non-hematological malignancies, sarcomas represents less than 2 %. [13]. There is evidence that radiation induced cancers may occur outside of the site of irradiation. In a recently published review of all available data of sarcoma radiotherapy induced in patient treated for breast cancers some prognostic factors influence their occurrence as the dose and techniques of radiotherapy and a deleterious BRCA-1 mutation . [19]

Some authors have suggested a causative role of Tamoxifen in the development of uterine sarcomas in previous reports. About 66 cases of sarcomas were reported among them only 3 cases of uterine RMS were reported. To the best of our knowledge there is no previous extra-uterine RMS reports incriminating Tamoxifen in the pathogeny of RMS. [12]

In a reported case of uterine RMS in a patient previously treated with Anstrozole, authors made carefully the hypothesis of the probable role of third generation aromatase inhibitors [12]. Our patient received both Tamoxifen and aromatase inhibitors which was Letrozole and we cannot confirm the attribution of RMS to such therapies.

Given the rarity of RMS in adults, controlled randomized trials are not feasible and thus treatments modalities are not well codified. Many authors reported that adults RMS is inherently different from pediatric patients and that prognosis seems to be worse in adults [5]. However others concluded that there is no major difference in outcome between adults and children with RMS if adults are treated according to pediatrics guidelines; also the response rate to chemotherapy seems to be the same if the same regimens are used [11]. There was a good partial response in our patient to induction chemotherapy based on pediatric protocols; unfortunately we couldn't evaluate the outcome due to the incidental death following the acute hemorrhagic stroke. However, the presence of concurrent metastatic breast cancer would influence the outcome even if the treatment has had been completed.

Conclusion

Since our patient received many treatments and no genetic investigation was undergone, we cannot conclude on the most determinant factor in developing such a rare tumor. But we think that radiation may play a major role in this clinical presentation.

Abbreviations

CT: computed tomography
IHC: immunohistochemistry
AJCC: American Joint Committee on Cancer
IRSG: Intergroup Rhabdomyosarcoma Study Group
HER2: Human Epidermal Growth Factor Receptor 2

Consent

Written informed consent was obtained from the patient's next of kin for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

SR was involved in the analysis of the data and the literature research and wrote the manuscript. GR helped with the patient management and revision of the manuscript. MA and SK helped with the literature research. AT and HM helped with modifications and revision of the manuscript. AH and SS performed the histological examination. HE approved the treatment and analyzed the literature data. All authors read and approved the final manuscript.

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Figures

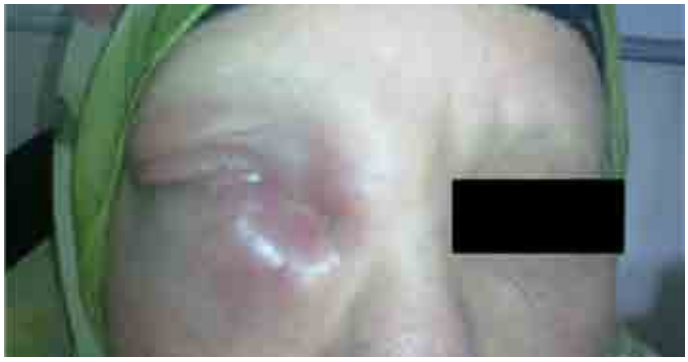

Fig. 1: Right large naso-orbital mass with ptosis.

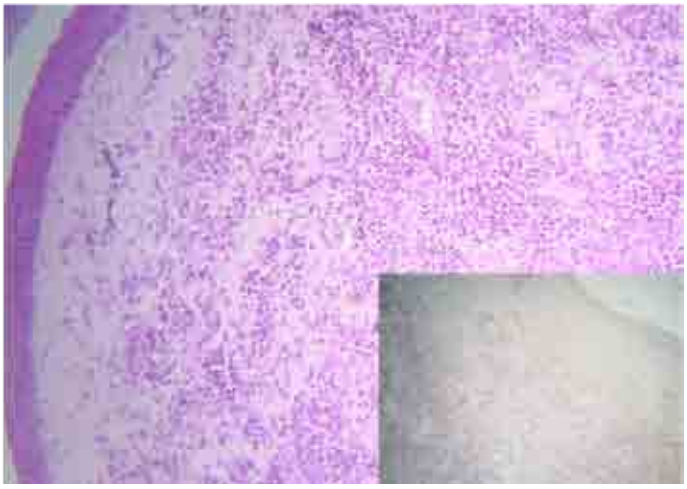

Fig. 2: HE x 100: Embryonal rhabdomyosarcoma: pleomorphic and polygonal celles in a fibro-myxoid matrix, cells are expressing nuclear myogenin.

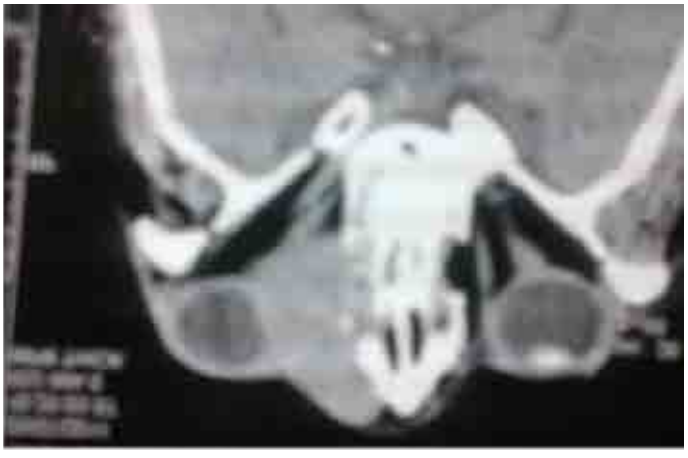

Fig. 3: Nasal and orbital CT scan showed a right ethmoidal mass with bone lysis and necrotic cervical maxillary lymph-nodes.