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CASE REPORT

An unusual case of undifferentiated pleomorphic vulval sarcoma

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ABSTRACT

Vulvar sarcomas are one of the rarer female genital tract malignancies, characterized by nonspecific signs and symptoms often leading to clinical misdiagnosis which increases the morbidity and mortality. It presents in 5th to 6th decade of life. Undifferentiated pleomorphic sarcomas (UPS) previously known as malignant fibrous histiocytoma (MFH) are the rarest of vulval sarcomas and hence least suspected initially. It is advised to keep vulvar sarcomas as a clinical differential in cases of non specific vulval swellings in order to establish an early accurate diagnosis to expedite its management. We present an unusual and rare case which was clinically misdiagnosed as a benign vulval swelling in a 26 year old married female who presented with painless vulval swelling for 1 year. It was provisionally diagnosed as malignant mesenchymal neoplasm on fine needle aspiration cytology which later was confirmed as UPS on after evaluating a judicious panel of immunohistochemistry markers where a myogenic, vascular and neurogenic origin was ruled out. Patient was treated with wide local excision and adjuvant platinum based chemotherapy which showed good response with no signs of reoccurrence or metastasis in a follow up period of 6 months.

Keywords: Malignant fibrous histiocytoma, vulval sarcoma, female reproductive tract malignancy.

Female genital tract malignancies are one of the leading causes of morbidity and mortality among women of all age groups. Vulvar cancers are representing 0.6% of all cancers in women and 4% of all female reproductive tract malignancies [1]. Vulval sarcomas (VS) comprise approximately 1-3% of all vulvar cancers and are characterized by nonspecific signs and symptoms which lead to late presentation at an advanced stage. Due to such variable presentations they are at times clinically misdiagnosed most commonly as Bartholin's cysts or abscesses which delays warranted diagnostic modalities leading to late definite diagnosis and hence poor clinical outcome as tend to grow aggressively and have high metastatic potential. VS have high mortality rate with median age of presentation being 50 years. Leiomyo-sarcomas are the commonest and undifferentiated pleomorphic sarcoma (UPS) is rarest of vulval sarcomas [2].

UPS was first described in 1964. The most common sites of involvement include lower extremities (mainly thigh), upper arms, retroperitoneum, viscera, head and neck with reproductive tract presentation being exceedingly rare. Distant metastases are common (most frequent being the lung). It is important to consider vulvar sarcomas in the clinical differentials because of non-specific presentation in order to establish an early accurate diagnosis and appropriate treatment. UPS is a diagnosis of exclusion after excluding a vascular, epithelial, myogenic or neural origin via immunohistochemistry. We present an unusual and rare case of UPS at an unusual site in a young female.

Case

An otherwise healthy 26 years old para 2 woman was presented with a painless gradually progressive mass in vulva, (with unremarkable menstrual history) for last one year. Local examination did not reveal any loco-regional lymphadenopathy. Clinically a benign growth was suspected.

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Blood work was within normal limits. USG showed increased internal vascularity.

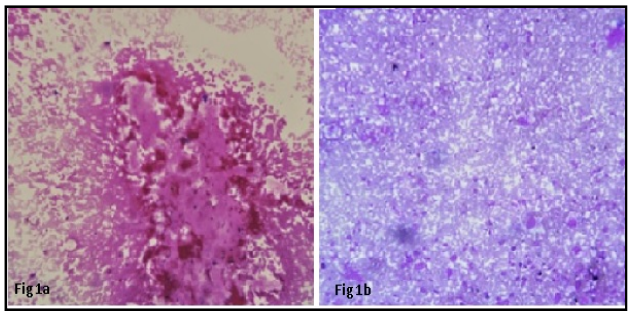

Figure 1: FNA smears were cellular showing atypical pleomorphic cells lying in a myxoid background (a) H and E 10x; (b) Giemsa 10x

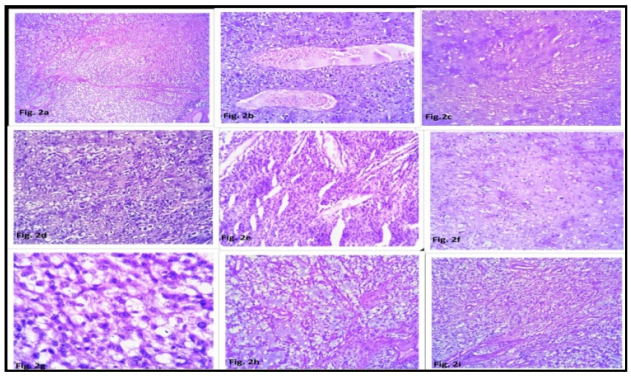

Figure 2: a) H and E 10x nodular arrangement of the tumor, b) H and E 10x well vascularized area, c) H and E 10x necrosis, d) H and E 40x tumor cells showing vesicular nuclei, e) H and E 10x angiosarcoma like areas, f) H and E 10x chondroid metaplasia, g) H and E 10x epithelioid cells, h) H and E 10x myxoid degeneration, i) H and E 10x spindled cell areas.

Fine needle aspiration smears were paucicellular comprising of atypical cells lying in a blood mixed myxoid background. Individual atypical cells were oval to spindle shaped, moderately pleomorphic, had high nucleo-cytoplasmic ratio, vesicular chromatin, inconspicuous to conspicuous nucleoli and scant amount of cytoplasm. The smears gave an impression of malignant mesenchymal lesion (figure 1). Excisional biopsy was received as an unencapsulated grayish brown soft tissue mass measuring 8x7x6cm^3. Outer surface was smooth and congested. Cut surface was heterogeneous, solid greyish brown along with areas of haemorrhage and necrosis. Histopathology sections showed well vascularised malignant mesenchymal neoplasm displaying nodular arrangement. Differentiated areas like that of angiosarcoma, chondroid metaplasia, myxoid degeneration, spindled and epithelioid cells admixed with necrosis and inflammatory infiltrate were evident (figure 2). Positive immunoreactivity was seen with vimentin, S100, CD56, CD68. Ki67 showed 30% nuclear positivity in tumor cells (figure 3). Cd34, CK, EMA, LCA, OCT4, HMB45 showed no immunoreactivity. With no identifiable line of differentiation a diagnosis of undifferentiated pleomorphic sarcoma of vulva was signed out.

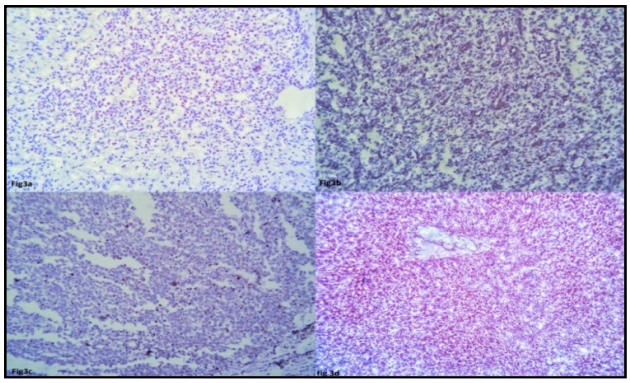

Figure 3: Immunohistochemistry 40x a) vimentin, b) S100, c) CD56, d) CD68

Discussion

UPS is and aggressive sarcoma of soft tissues which is thought arises from a primitive mesenchymal cell capable of differentiating into histiocytes, fibroblasts, myofibroblasts and osteoclasts. Its aetiology remains however prior radiation therapy is a likely risk factor in some cases [3]. It has no defining clinical feature which can delineate it from other sarcomas except that it presents as a rapidly enlarging mass.

UPS is also associated with non-specific cytogenetic aberrations having highly complex karyotype, usually triploid or tetraploid. Therefore cytogenetics does not aid in distinguishing it among other pleomorphic sarcomas [4].

A study conducted by Carneiro et al [5] found that loss of 4q31 (encompassing the *SMAD1* gene) and loss of 18q22 were independent predictors of metastasis. The RAS/MAPK pathway has been implicated in the pathogenesis of UPS, as evident by increased expression of pERK [6]. Several cases of UPS have been found to harbour either PRDM10-MED12 or PRDM10-CITED2, which could represent a unique subset of UPS [7].

Grossly the most consistent feature found in UPS is the presence of necrosis and haemorrhage. Microscopically undifferentiated soft tissue sarcomas are characterised by

presence of frequent pleomorphic cells, epithelioid like cells or spindle cells along with frequent tumor giant cells arranged in pattern less manner showing brisk mitosis, haemorrhage, necrosis and lacking any specific line of differentiation. As molecular pathology has no role in diagnosis, definite diagnosis can be reached only by histopathological examination supplemented by immune-histochemistry markers.

MFH classification was removed and replaced by UPS according to the World Health Organization (WHO) classification guidelines for soft tissue sarcomas in 2002 as it lacked true histiocytic origins [8].

Magnetic resonance imaging (MRI) is the imaging method of choice topped up by positron emission tomography-computed tomography scan to look for distant metastasis. MRI shows a high signal on T2 weighted images. UPS metastasizes to lungs or regional lymph nodes and rarely present as metastasis with unknown small primary. Both local recurrence and distant metastases often develop within 12 to 24 months of diagnosis.

UPS is best treated by wide surgical excision followed by adjuvant radiotherapy in cases of deep seated sarcomas or when negative margins are not obtained. For non-operable or metastatic sarcomas, primary radiation therapy could be an option, but chemotherapy is the preferred first-line option. In our case wide local excision of the mass was done followed by platinum based chemotherapy which showed good response. The patient is presently doing fine without any signs or symptoms of recurrence or distant metastasis 6 months after completion of treatment. In the multivariate analysis by Engellau et al [9], necrosis and local recurrence were significant predictors of metastasis within the first 2 years of diagnosis and throughout a longitudinal follow-up period, whereas only tumor depth and local recurrence were significant predictors beyond 2 years.

5 year survival is 50 - 60% for all high grade pleomorphic sarcomas. Early treatment after swift diagnosis with wide local resection and postoperative chemotherapy or radiotherapy at an early stage ensures better clinical outcome.

Differentials considered in our case were malignant peripheral nerve sheath tumor, epithelioid sarcoma, malignant melanoma, angiosarcoma, germ cell tumor (embryonal), rhabdomyosarcoma and myeloid sarcoma.

Approximately 100 cases of vulvar sarcoma and only very few of UPS could be found on literature review [10].

Conclusion

Because of lack of substantial studies, data is very limited to correctly predict the prognosis of patients. UPS should always be referred to a tertiary care centre for primary biopsy, expert pathological diagnosis and multidisciplinary treatment. Hasty decision to blindly excise the mass without knowledge of its histological nature is strongly discouraged as it would lead to increased risks of death due to positive resection margins and reoccurrences. As UPS present mostly at later stages, any patient presenting with rapidly increasing mass, a timely biopsy will not only hasten the diagnosis but also expedite the management of this cancer thus improving patient's clinical outcome. Any line of differentiation should be meticulous looked microscopically which calls of extensive sampling of the tumor and judicious use of immunohistochemistry. A multidisciplinary treatment protocol along with close follow up is advised for these notorious sarcomas which are infamous for local recurrences and distant metastasis.

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