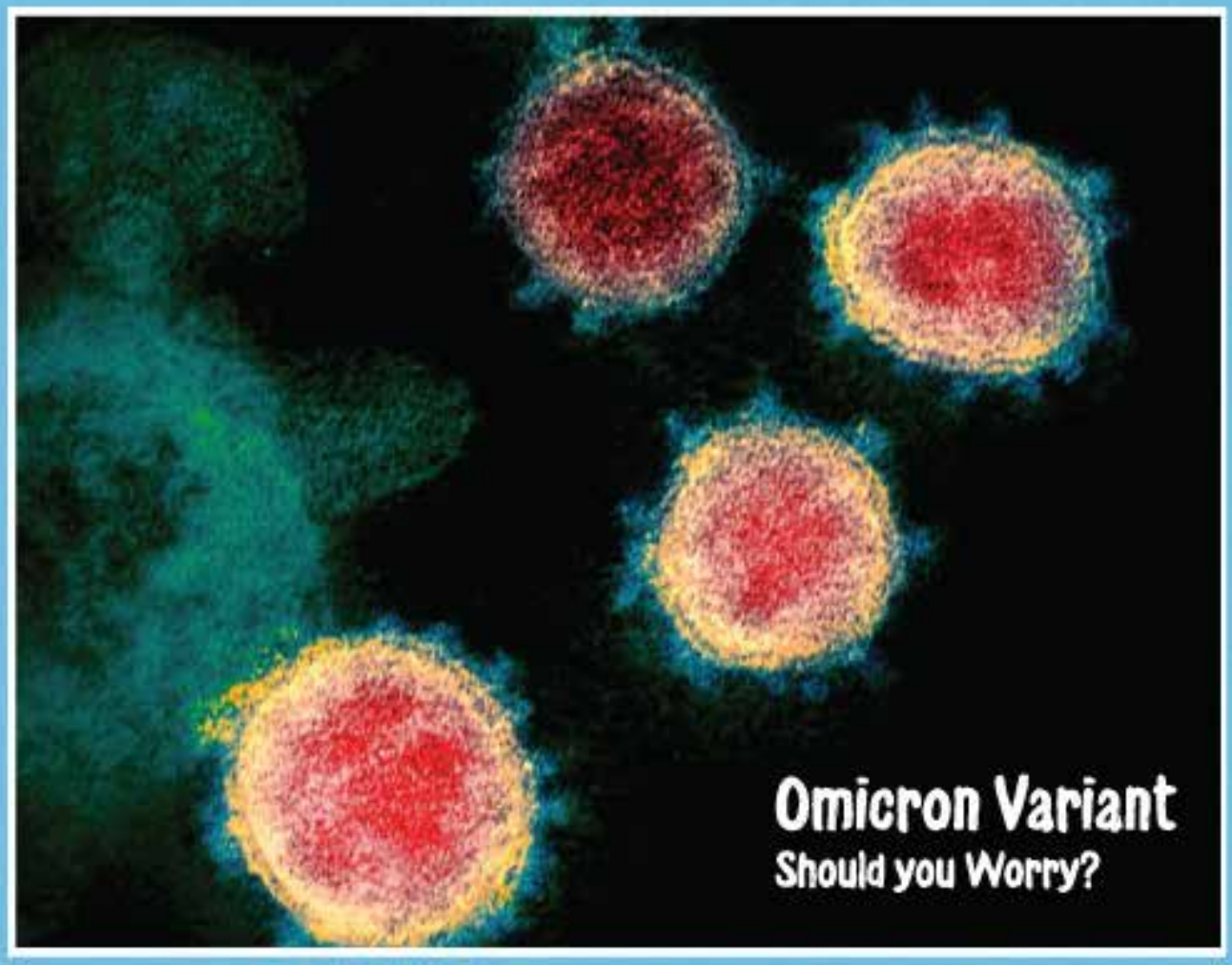
The Gulf Journal of Oncology

Indexed By PubMed and Medline Database

Issue 38, January 2022
ISSN No. 2078-2101



The Official Journal of the Gulf Federation For Cancer Control

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Case Report

Uterine Perivascular Epithelioid Cell Tumor (PEComa) in A 56–year–Old Woman

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Abstract

Perivascular epithelioid cell tumors (PEComas) are infrequent mesenchymal neoplasms. Primary uterine PEComas are extremely uncommon. To the best of knowledge, around 110 cases of uterine PEComas have been documented in the English–language literature thus far. Herein, we present the case of primary uterine PEComa in a 56–year–old Saudi woman who presented to clinical attention with a six–month history of left–sided abdominal pain. Gynecological examination showed a 5–cm solid mass involving the left adnexa. Tumor markers were normal. Computed tomography scan demonstrated a 4.2 x 4.4 x 3.4 cm superior left fundal exophytic mass. Patient underwent total abdominal hysterectomy plus bilateral salpingo–oophorectomy. Final histopathological examination demonstrated benign/uncertain malignant potential PEComa. No further adjuvant therapy was administered. At six–month follow up, the patient was asymptomatic without recurrence. In conclusion, uterine PEComas are rare. Histopathological assessment establishes the definitive diagnosis. Surgery remains the gold standard in the treatment of uterine PEComas and adjuvant therapy should be guided based on clinical and histopathological risk factors.

Keywords: Uterine perivascular epithelioid cell tumor, PEComa, Uterine sarcoma, hysterectomy

Introduction

Perivascular epithelioid cell tumors (PEComas) are infrequent mesenchymal neoplasms. They are believed to originate from perivascular epithelioid cells (PECs) that display idiosyncratic structural and immunohistochemical facets. Structurally, PEComas are comprised of epithelioid cells that exhibit predilection for perivascular distribution. Immunohistochemically, PEComas are immunoreactive for melanocytic and muscle markers. To date, there are no recognized normal equivalent cells to PECs.[1,2]

PEComas can virtually involve any system of the human body.[2] In a recent systematic review of 114 PEComas arising in the female reproductive system, the uterus was the most frequently involved site (n=82, 58.6%).[3] To the best of knowledge, around 110 cases of uterine PEComas have been documented in the English–language literature thus far.[4] Owing to its rare frequency and overlapping structural and immunohistochemical characteristics, diagnosis of uterine PEComas is often delayed and missed.[5]

Herein, we present the case of primary uterine PEComa in a 56–year–old Saudi woman who presented to clinical attention with a six–month history of left–sided abdominal pain.

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Case Presentation

A 56–year–old Saudi nulliparous woman presented to clinic with a six–month history of left–sided abdominal pain. The abdominal pain was associated with decreased appetite and weight loss. The patient denied any vaginal or rectal bleeding. Past medical and surgical histories were insignificant. Abdominal examination revealed tenderness in the left lower quadrant. Gynecological examination showed a solid mass of roughly 5 cm involving the left adnexa.

Laboratory tests for tumor markers, including alpha–fetoprotein (AFP), cancer antigen 125 (CA 125), cancer antigen 15–3 (CA 15–3), cancer antigen 19–9 (CA 19–9) and carcinoembryonic antigen (CEA), were within normal limits.

Computed tomography (CT) scan demonstrated a normal sized uterus. There was a 4.2 x 4.4 x 3.4 cm superior left fundal exophytic mass (Figure 1). No other lesions were identified.

In view of a possible neoplastic mass, total abdominal hysterectomy plus bilateral salpingo–oophorectomy was performed. The uterus, cervix, bilateral fallopian tubes and ovaries weighed 19 grams and measured 4 x 3 x 2 cm. The anterior uterine wall showed a probable neoplastic mass measuring 5.5 x 4.1 x 2.5 cm with a tan solid cut surface.

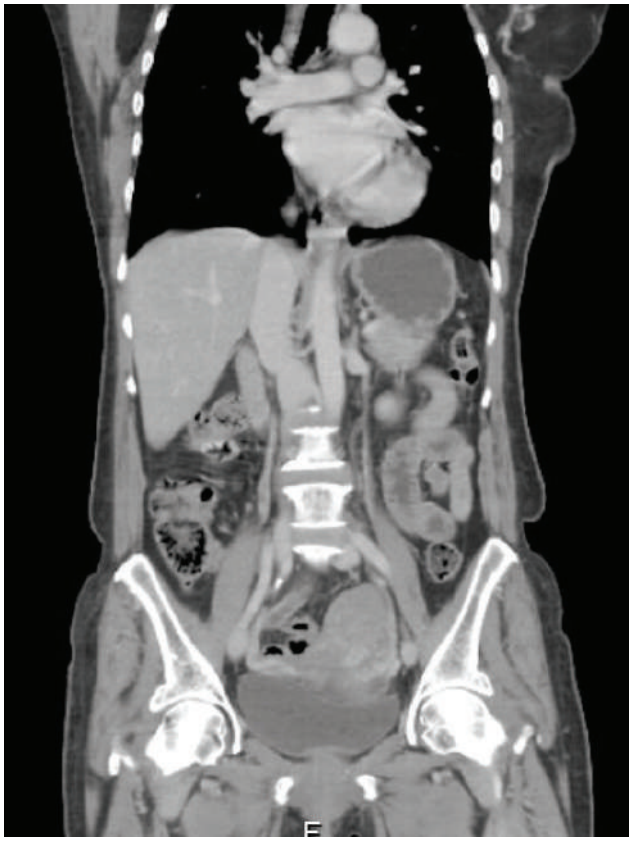

Figure 1. Computed tomography scan showing a 4.2 x 4.4 x 3.4 cm superior left fundal exophytic mass.

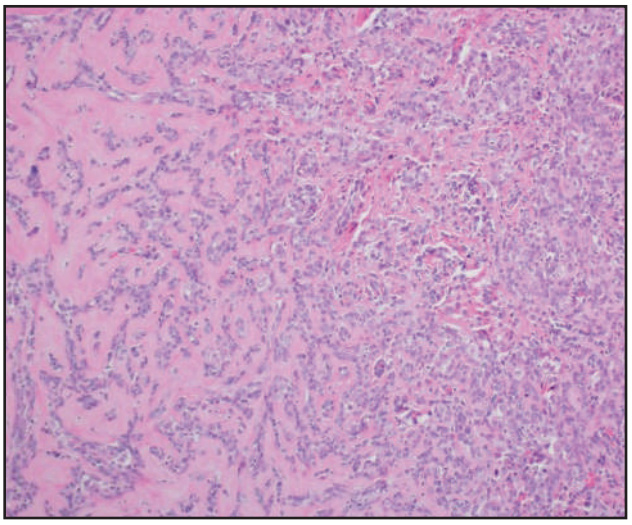

Figure 2. Hematoxylin and eosin stain of the uterine mass showing neoplastic proliferation of epithelioid and spindle cells arranged in cords, sheets and nests with perivascular growth pattern and hyalinized stroma.

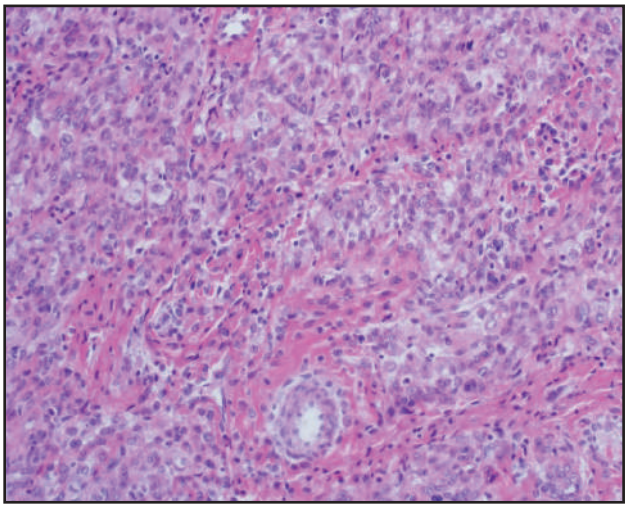

Figure 3. Hematoxylin and eosin stain of the uterine mass showing the neoplastic cells with eosinophilic granular cytoplasm, mild pleomorphism and some visible nucleoli. No necrosis or lymphovascular space invasion were observed.

Histopathological examination of the uterine wall mass demonstrated neoplastic proliferation of epithelioid and spindle cells arranged in cords, sheets and nests with perivascular growth pattern and hyalinized stroma (Figure 2). The neoplastic cells had eosinophilic granular cytoplasm, mild pleomorphism and some visible nucleoli (Figure 3). No necrosis or lymphovascular space invasion were observed. Rare mitosis of less than 1/50 high high–power field (HPF) was noted. Qualitatively, immunohistochemical (IHC) studies of neoplastic cells revealed strong positivity for HMB45 (Figure 4A). Weak

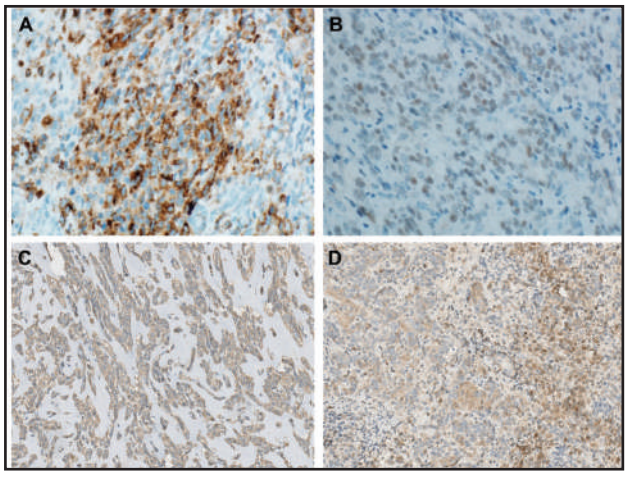

Figure 4. Immunohistochemistry of the neoplastic cells showing strong positivity for (A) HMB45, (B) transcription factor E3 (TFE3), (C) smooth muscle actin (SMA), and (D) microphthalmia transcription factor (MiTF).

positivity of neoplastic cells were noted for transcription factor E3 (TFE3), smooth muscle actin (SMA) and microphthalmia transcription factor (MiTF) (Figure 4B–D). Conversely, the neoplastic cells stained negative for melanA, h–caldesmin, inhibin, pan cytokeratin (PAN–CK), cluster of differentiation 10 (CD10) and cluster of differentiation 99 (CD99). The final histopathological diagnosis was consistent with primary uterine PEComa with benign/uncertain malignant potential.

The patient had an uneventful postoperative course. In consideration of the benign/uncertain malignant potential of the neoplastic lesion, the tumor board meeting recommended a consensus to proceed with close follow up with CT imaging in three and six months and no further adjuvant therapy would be administered. At six months follow up, the patient was asymptomatic without any evidence of recurrence.

Discussion

Herein, we reported the first case of primary uterine PEComa in Saudi Arabia, specifically, and the Middle East, generally. Our case report enriches the scarce literature on the topic of uterine PEComa (roughly 110 cases).[4]

PEC, the cell origin of PEComa, was first coined by Apitz and colleagues and formerly was categorized as an 'abnormal myoblast'. However, in early 1990s, Bonetti and partners suggested the notion 'perivascular epithelioid' to categorize a miscellaneous cluster of mesenchymal neoplasms that shared morphologically and immunohistochemically epithelioid cells with a perivascular distribution.[6] Currently, PEComas encompass a large group of neoplasms comprising clear cell sugar tumor, clear cell myomelanocytic tumor of the falciform ligament/ligamentum teres, angiomyolipoma and lymphangioleiomyomatosis.

Histopathological variants of PEComa include tumors with varying components of epithelioid tumor cells, spindled neoplastic cells or extensive stromal hyalinization (sclerosing PEComa).[2,7] Immunohistochemically, PEComas distinctively coexpress both melanocytic (for example, HMB45, MiTF and melanA) and muscle (SMA, desmin and h–caldesmon) markers.[4,5,8] HMB45 is the most consistent sensitive marker to diagnose PEComa based on two systematic reviews.[3,8] Molecularly, several genetic alterations have been implicated in the pathogenesis of PEComas including tuberous sclerosis complex (TSC) mutations, TFE3 rearrangements and RAD51B fusions.[2,4,5]

A gynecologic–specific scheme has been formulated to predict PEComas that are highly inclined to possess an aggressive biological behavior based on five substantial histopathological features. These histopathological features comprise tumor size ≥ 5 cm, high–grade nuclear atypia, necrosis, lymphovascular space invasion and high mitotic figures >1/50 HPFs). A definitive malignant potential of PEComa is established when ≥4 or ≥3 histopathological features are identified as suggested by Schoolmeester et al.[8] and Benette et al.[4], respectively. Otherwise, PEComa will be categorized as a neoplasm of benign/uncertain malignant potential.[4,8]

At the present time, there is no universally agreed upon consensus regarding the optimal management of PEComa of gynecologic origin. This is largely ascribed to the comparatively small number of cases reported and absence of randomized clinical studies.[4,5,8] The bulk of patients with female reproductive system PEComa are seldom diagnosed preoperatively.[3] Surgical resection with neoplasm–free margins is the primary course of management.[4,5,8] The therapeutic impact of cytotoxic therapy (for example, doxorubicin, vincristine and ifosfamide) and radiotherapy is uncertain.[3] Targeted therapy with mammalian target of rapamycin (mTOR) inhibitors exhibited encouraging therapeutic responses in select reports.[2–5,8,9] Long–term follow up of uterine PEComas is paramount since our knowledge of this condition is still limited.

Conclusion

In conclusion, our knowledge of uterine PEComas and its management and prognosis is not adequately matured. This is mostly attributable to the rare incidence of PEComa, absence of consensus guidelines and lack of long–term follow up data. A tumor board management approach is recommended. Surgery remains the gold standard in the

treatment and adjuvant therapy should be guided based on clinical and histopathological risk factors.

Acknowledgment

None

Funding

None

Conflict of interest

The authors declare that they have no conflicts of interest.

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