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Case Report

Malignant mixed germ cell tumor of ovary-A case report

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Abstract

Mixed germ cell tumors of the ovary are rare neoplasms that often occur in young females and consist of two or more histological germ cell components. We present a rare case of an ovarian mixed germ cell tumor comprising dysgerminoma, yolk sac tumor, and residual gonadoblastoma in 8 year-old phenotypic female with abdominal pain and a pelvic mass. Histopathological evaluation revealed predominant dysgerminoma, with distinct areas of yolk sac tumor and microscopic foci of residual gonadoblastoma. The case highlights the importance of thorough histological examination for accurate diagnosis and appropriate management. This paper also includes a review of the relevant literature, discussing pathogenesis, clinical presentation, diagnostic approach, treatment strategies, and prognosis.

Keywords: Endodermal sinus tumors, Gonadoblastoma, Histopathologica.

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1. Introduction

Germ cell tumors (GCTs) of the ovary account for approximately 20–25% of all ovarian neoplasms, with malignant GCTs comprising less than 5% of all ovarian cancers. Among these, dysgerminomas are the most common malignant GCTs, often occurring in adolescents and young adults. Yolk sac tumors (endodermal sinus tumors) are highly malignant neoplasms known for their aggressive behavior and elevated serum alpha-fetoprotein (AFP) levels. Gonadoblastoma is a rare, benign or pre-malignant gonadal tumor often associated with gonadal dysgenesis and can serve as a precursor to malignant germ cell tumors, especially dysgerminoma.[1]

Mixed germ cell tumors consist of more than one germ cell element, and combinations of dysgerminoma and yolk sac tumor are not uncommon. However, the co-existence of dysgerminoma with yolk sac tumor and residual gonadoblastoma is exceedingly rare, posing diagnostic and therapeutic challenges.[1]

We describe a unique case of such a mixed germ cell tumor and explore the histopathological and clinical features, as well as implications for diagnosis, treatment, and prognosis.

2. Case Report

A 8 year old female patient came with complain of pelvic mass and abdominal pain since 3 month. On CT scan well defined mildly homogenously enhancing with few specs of calcification in right lumbar region with possibility of teratoma likely.

On physical examination, 4 x 4 cm sized non warm, tender non mobile swelling was present over periumbilical region.

On fine needle aspiration cytology atypical malignant cell arranged in group, sheets, clusters and in singly. Individual cells are round to polygonal with high N:C ratio with highly pleomorphic nuclei with open chromatin and abundant eosinophilic vacuolated cytoplasm. Many mitotic activity seen in fluid mixed myxoid and haemorrhagic

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background. Based on this findings possibility of pleomorphic sarcoma is given and biopsy is adviced.

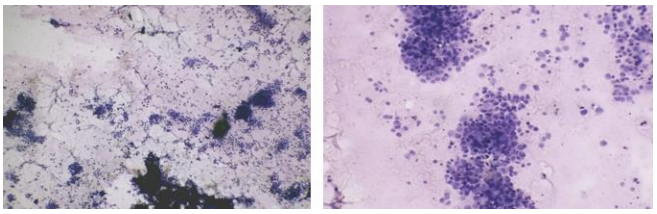

Figure 1: Right: (H & E 10 x) Cells appear in loose clusters and dispersed singly**,** large nuclei with irregular nuclear contours, Prominent nucleoli in many cells, Scant to moderate cytoplasm, mostly clear or pale; Left: (H & E 40 x) The smear is highly cellular, with loosely cohesive to dispersed cells with significant pleomorphism, Irregular nuclear membranes**,** Hyperchromatic, coarse chromatin, Cytoplasm appears scant to moderate, with amorphous to granular texture in some cells

2.1. Gross examination

Specimen consist of whitish globular well encapsulated mass measuring 10 x 8.7 x 5.8 cm with lobulated outer surface. On cut section, it is solid, lobulated, soft and tan coloured.

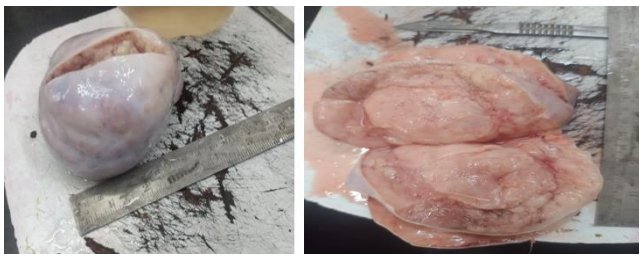

Figure 2: Left: A well-circumscribed, oval to globular mass Outer surface is smooth, glistening, and intact, with visible vascular markings and slight areas of discoloration; Right: The cut surface reveals a **s**olid, lobulated tumor with a predominantly fleshy, tan-pink to pale white appearance. Areas of soft, friable tissue with a mucoid consistency are present.

2.2. Microscopic examination

Multiple sections taken reveal varied growth pattern showing foci of trabeculae, pseudo glandular and irregularly shaped nest of cells separated by fibrous septa containing lymphocytes. The tumor cells are uniform having large nuclei, prominent nucleoli and abundant clear to finely granular cytoplasm. Stroma is delicate and loose. There are areas of small well defined tumor nests with foci of calcification present. Scattered yolk sac tumor components is also seen. Diagnosis of malignant mixed germ cell tumor (possibility of dysgerminoma with minor component of yolk sac tumor with residual gonadoblastoma) is given. IHC is advised for confirmation and typing.

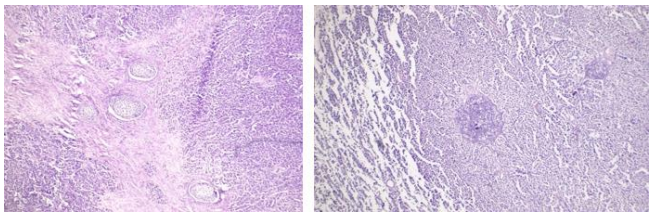

Figure 3: Left: (H &E 10x) composed of moderately to highly cellular areas arranged in sheets, nests, and microcystic/reticular patterns**.** Tumor cells are large, with round to oval nuclei**,** vesicular chromatin**,** and prominent nucleoli; Right: (H & E 10 x). The central region shows a lobulated architecture with fibrous septae. Cells are large, round to polygonal, with clear cytoplasm, central prominent nuclei, and distinct cell borders.

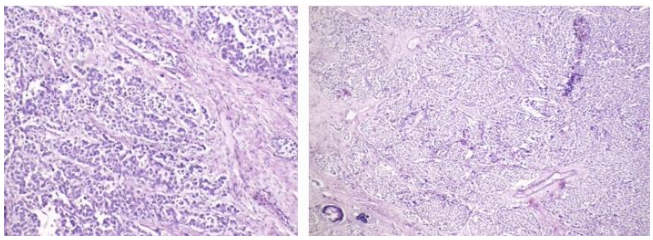

Figure 4: Left: (H & E 40 x). The image shows solid sheets and microcystic/reticular areas of tumor cells having round to oval nuclei with finely dispersed chromatin and prominent nucleoli.Moderate eosinophilic to amphophilic cytoplasm. Intervening fibrovascular septae noted between clusters. Right: (H & E 10 x) Tumor displays a reticular/microcystic pattern with interspersed glomeruloid structures characteristic of Schiller-Duval bodies

3. Discussion

The coexistence of dysgerminoma, yolk sac tumor, and residual gonadoblastoma in a single ovarian tumor is rare. Gonadoblastomas are often associated with dysgerminomas and, less frequently, with yolk sac tumors. The presence of residual gonadoblastoma suggests a possible origin from gonadal dysgenesis, even in phenotypic females with a 46, XX karyotype, although this is uncommon.[2,11]

Histologically, dysgerminomas are characterized by large, uniform cells with clear cytoplasm and central nuclei, arranged in nests separated by fibrous septa containing lymphocytes. Yolk sac tumors exhibit various patterns, including reticular, microcystic, and papillary structures, with Schiller-Duval bodies being pathognomonic. Gonadoblastomas consist of nests of germ cells and sex cord-stromal cells, often with calcifications.[3]

Immunohistochemically, dysgerminomas are positive for placental alkaline phosphatase (PLAP)**,** OCT3/4**,** and c-KIT (CD117).[4,5] In contrast, yolk sac tumors express alpha-fetoprotein (AFP) and glypican-3**,** which are considered specific and sensitive markers for endodermal sinus differentiation.[5,6] Gonadoblastomas may express markers of both germ cells (such as PLAP and OCT3/4) and sex cord-

stromal cells (such as inhibin and calretinin), reflecting their mixed cellular origin.[7,8]

Management typically involves surgical resection, with fertility-sparing surgery being considered in young patients. Adjuvant chemotherapy, often with bleomycin, etoposide, and cisplatin (BEP regimen), is indicated, especially in cases with yolk sac tumor components due to their aggressive nature.[9,10]

The identification of gonadoblastoma in cases of malignant mixed germ cell tumor (MMGCT) of the ovary holds substantial clinical significance, particularly in phenotypic females. Gonadoblastoma is a rare, benign, but potentially malignant neoplasm that typically arises in dysgenetic gonads and is strongly associated with the presence of Y chromosome material. Its detection in a phenotypic female necessitates a re-evaluation of the underlying gonadal and genetic constitution, as it often indicates an unrecognized disorder of sex development (DSD), such as gonadal dysgenesis in individuals with 46,XY karyotype.[11]

From a treatment standpoint, the presence of gonadoblastoma prompts critical modifications to the management protocol. First, it mandates cytogenetic evaluation to detect occult Y chromosome sequences (e.g., via karyotyping or PCR for SRY gene). The identification of Y chromosome material confers a high risk for bilateral gonadal malignancy and justifies consideration of prophylactic contralateral gonadectomy, even in the absence of overt tumor.[12] This contrasts with standard MMGCT management, which often involves unilateral salpingo-oophorectomy with fertility preservation when possible.

Furthermore, gonadoblastoma frequently coexists with malignant germ cell tumor components, particularly dysgerminoma. Its identification should therefore prompt a comprehensive pathological review to determine the extent and histological diversity of the neoplasm, guiding adjuvant therapy decisions such as the necessity and regimen of combination chemotherapy (e.g., BEP protocol).[13]

In the context of long-term care, detecting gonadoblastoma has implications beyond oncologic treatment. It requires coordinated multidisciplinary management involving endocrinology, genetics, and psychology to address issues such as hormone replacement, gender identity, and fertility planning.

The presence of gonadoblastoma in MMGCT of the ovary in phenotypic females introduces complex therapeutic challenges that go beyond tumor eradication. These include delayed recognition of DSD, surgical decision-making around fertility, chemotherapy toxicities, coordination across specialties, and psychosocial implications. Addressing these challenges requires a proactive, multidisciplinary, and patient-centered approach that integrates oncologic care with genetic, reproductive, and psychological support.[14-17]

In cases where MMGCT includes dysgerminoma, a minor yolk sac component, and residual gonadoblastoma, several differential diagnoses must be considered to ensure accurate histopathological classification and appropriate treatment.

3.1. Pure dysgerminoma

Typically homogeneous, lacks yolk sac elements. Immunoreactive for OCT4, CD117, and PLAP [(18)].

3.2. Pure yolk sac tumor

Distinguished by Schiller-Duval bodies and AFP positivity. Often more aggressive and monomorphic histologically [(19)].

3.3. Gonadoblastoma with overgrowth of dysgerminoma

Characterized by nests of germ cells and sex cord-like elements with possible calcifications. May contain early dysgerminomatous transformation.

3.4. Embryonal carcinoma or choriocarcinoma

Rare in MMGCT but aggressive. Immunostaining for CD30 and β-hCG can help identify these components.

3.5. Sex cord-stromal tumors (e.g., Sertoli-Leydig Cell Tumor)

These tumors mimic gonadoblastoma's stromal elements but lack germ cell markers. Positive for inhibin and SF-1.

3.6. Mixed germ cell tumor without gonadoblastoma

Typically arises in phenotypically and genotypically normal females, and lacks association with DSD or Y chromosome material.

4. Conclusion

This case highlights the importance of considering mixed germ cell tumors in the differential diagnosis of ovarian masses in young females. The presence of residual gonadoblastoma within such tumors, although rare, has implications for pathogenesis and management. Comprehensive histopathological and immunohistochemical evaluation is crucial for accurate diagnosis and guiding treatment.

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6. Conflict of Interest

None.

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