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Case Report

Ovarian Sertoli-Leydig cell tumors with somatic DICER1 mutations: a clinicopathologic study of 15 cases

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Abstract: Ovarian Sertoli-Leydig cell tumors (SLCTs) are a rare type of sex cord-stromal neoplasm. Approximately 60% of these tumors are associated with DICER1 mutations, which may occur in the context of the rare DICER1 syndrome. Due to the scarcity of these tumors, their comprehensive clinicopathologic spectrum and optimal management remain incompletely defined. We conducted a single-institution, retrospective clinicopathologic study on 15 patients with molecularly confirmed DICER1-related ovarian SLCTs (January 2020 - May 2025). Clinical, surgical, pathologic, and molecular data were analyzed. The median patient age at diagnosis was 21 years (range: 3-34 years). Most patients (93.3%, 14/15) were symptomatic, with abdominal distension (53.3%) and secondary amenorrhea (33.3%) being the most common presentations. The vast majority of tumors (93.3%, 14/15) were FIGO stage I, and the median largest tumor dimension was 12.0 cm. Fertility-preserving surgery was performed in 93.3% of cases; however, intraoperative tumor rupture occurred in 46.7% (7/15). Histopathologically, all tumors demonstrated classic SLCT features and were immunopositive for inhibin and calretinin. Among the cohort with somatic DICER1 mutations, only one patient (6.7%) was found to have a concurrent germline DICER1 pathogenic variant. Notably, all tumors were moderately (60.0%, 9/15) or poorly (26.7%, 4/15) differentiated, with no well-differentiated SLCTs observed. Adjuvant platinum-based chemotherapy was administered to 53.3% (8/15) of patients, primarily those with stage IC (85.7%) or higher-stage disease. After a median follow-up of 19 months, no recurrences were observed in patients with stage I disease. This study confirms that DICER1-related SLCTs predominantly occur in young women and typically present at an early stage. Our findings suggest a favorable short-term prognosis for stage I disease. We identify a strong genotype-phenotype correlation, with DICER1 mutations being exclusively associated with non-well-differentiated histology. Meticulous surgery to prevent tumor rupture is paramount, and adjuvant chemotherapy can be effectively reserved for higher-risk patients. Longer-term follow-up is needed to fully define the prognostic implications of our observations.

Keywords: DICER1, Sertoli-Leydig cell tumor, sex cord-stromal tumor, case series

Introduction

Ovarian Sertoli-Leydig cell tumors (SLCTs) are a rare type of sex cord-stromal neoplasms, accounting for less than 0.5% of all ovarian tumors and approximately 15% of malignant sex cord-stromal tumors [1, 2]. These tumors mainly affect adolescents and young adults, and most patients are diagnosed before the age of 40 years [3, 4]. Clinical manifestations usually include signs of virilization caused by androgen excess, such as hirsutism, oligomenorrhea, deepening of voice, or clitoromegaly; non-specific symptoms such as abdominal pain and distension are also frequently reported [5].

Histologically, the World Health Organization classifies SLCTs into three categories based on the degree of Sertolian differentiation: well-differentiated, moderately differentiated, and poorly differentiated. The presence of heterologous elements (such as intestinal-type mucinous epithelium) or retiform growth patterns is frequently observed and associated with more

aggressive tumor behavior [6]. Notably, the recognition of DICER1 mutations has greatly advanced our understanding of the pathogenesis of SLCT. DICER1 encodes a nuclear ribonuclease that is crucial for microRNA processing, and somatic or germline mutations of this gene have been found in most moderately and poorly differentiated SLCTs [1, 7, 8]. These tumors have been established as hallmark manifestations of DICER1 tumor predisposition syndrome, which is an autosomal dominant genetic disorder and also increases the risk of developing pleuropulmonary blastoma, cystic nephroma, thyroid neoplasms, and other rare tumors [6, 9].

The association between SLCT and DICER1 syndrome was initially established through the International Pleuropulmonary Blastoma Registry, and subsequently this research was further advanced by the International Ovarian and Testicular Stromal Tumor Registry [6, 10]. It is estimated that approximately 60% of patients with moderately or poorly differentiated SLCT carry a germline DICER1 pathogenic variant [9, 11]. This understanding has informed the development of surveillance guidelines, which now recommend regular pelvic ultrasound examinations for individuals with known DICER1 mutations.

Due to the rarity of SLCT, the current optimal treatment strategy has not yet been fully established. The majority of patients are in the early stage (FIGO stage I), and young patients usually opt for fertility-preserving surgeries. Adjuvant chemotherapy (typically platinum-based drugs) is only applicable to higher-stage or poorly-differentiated tumors, but the relevant evidence is still limited. Recent studies have shown that the germline DICER1 status may affect the risk of recurrence, possibly due to early detection in monitored patients, although biological factors may also play a role [9].

However, due to the low incidence rate of DICER1-related SLCT, its clinicopathologic spectrum, prognostic determinants, and optimal treatment methods have not been fully described. To address this gap, we conducted a retrospective analysis of 15 cases of DICER1-related ovarian SLCT diagnosed and treated at our institution between January 2020 and May 2025. This study aims to comprehensively describe the clinical and pathological characteristics, treatment methods, and long-term prognosis of this rare disease, with the intention of providing a reference for future clinical practice and optimizing risk-adaptive treatment strategies.

Materials and methods

All DICER1-related cases of ovarian Sertoli-Leydig cell tumors (SLCTs) were retrieved from the archives of the Department of Anatomy and Pathology at West China Second University Hospital, Sichuan University. This retrospective study included patients diagnosed between January 2020 and May 2025. Demographic, clinical, laboratory, surgical, histopathological, and follow-up data of the patients were collected from electronic medical records, and imaging examination results were reviewed through the picture archiving and communication system (PACS). The analyzed variables included the age at diagnosis of the patients, symptom manifestations, tumor size, surgical methods and procedures, administration of adjuvant chemotherapy, and clinical outcomes. Tumor staging was assigned according to the International Federation of Gynecology and Obstetrics (FIGO) criteria.

All surgical specimens were independently reviewed by two specialized gynecologic pathologists to confirm the diagnosis of SLCT based on World Health Organization (WHO) criteria. Tumors were classified histologically as well-differentiated, intermediately differentiated, or poorly differentiated. Additional histologic features were systematically documented.

Exclusion criteria were as follows: (1) cases in which the diagnosis was not confirmed by both gynecologic pathologists; (2) cases with unavailable DICER1 genetic testing results; and (3) patients with known mosaicism for a loss-of-function variant or an RNase IIIb missense variant in DICER1.

Results

A total of twenty patients were initially identified. Following histopathological review, one case was excluded due to diagnostic disagreement between the two specialized pathologists. Additionally, two cases were excluded due to a lack of DICER1 genetic testing results, and two more were excluded because of known

mosaicism for DICER1 variants (one with a loss-of-function variant and the other with an RNase IIIb missense variant). Ultimately, 15 patients who met the inclusion criteria were included in the analysis.

Clinical characteristics

Patient clinical characteristics are summarized in **Table 1**. The median age at diagnosis was 21 years (range: 3-34 years). All tumors were unilateral, with a predilection for the left ovary (66.7%, 10/15). Most patients (93.3%, 14/15) were symptomatic at diagnosis, and one tumor (6.7%) was incidentally detected during pregnancy. The most common symptoms were abdominal distension (53.3%, 8/15), secondary amenorrhea (33.3%, 5/15), and abdominal pain (6.7%, 1/15). Serum tumor marker analysis showed elevated AFP in 53.3% (8/15) of cases, while CA125 and CA19-9 were elevated in 13.3% (2/15) and 6.7% (1/15), respectively.

Surgical management and staging

Surgical management and staging data are summarized in **Table 2**. The majority of patients (93.3%, 14/15) presented with FIGO stage I disease, including 46.7% (7/15) with stage IA and 46.7% (7/15) with stage IC. One patient (6.7%, 1/15) had advanced-stage (IV) disease. A laparoscopic approach was utilized in 53.3% (8/15) of cases, while laparotomy was performed in 46.7% (7/15). Salpingo-oophorectomy was the most common surgical procedure (93.3%, 14/15), with ovarian cystectomy performed in only one case (6.7%, 1/15). Lymphadenectomy was conducted in 33.3% (5/15) of patients, omentectomy in 60.0% (9/15), and hysterectomy with bilateral salpingo-oophorectomy in 13.3% (2/15). One of the patients undergoing hysterectomy and bilateral salpingo-oophorectomy had FIGO stage IV disease. The median maximal tumor diameter was 12.0 cm (range: 3.3-25.0 cm). Pre-operative tumor rupture occurred in one case (6.7%, 1/15), and intra-operative rupture was noted in 46.7% (7/15). The pre-operatively ruptured cyst measured approximately 20 cm in diameter, while the cysts that ruptured intraoperatively ranged from 9.4 cm to 20 cm.

Histopathologic and molecular features

All tumors exhibited characteristic histological features of ovarian Sertoli-Leydig cell tumors. Histologic examination revealed nests of tumor cells within an edematous, hypocellular stroma (**Figure 1A**). These nests consisted of a variable admixture of neoplastic Sertoli cells, displaying ovoid to spindled nuclei with scant cytoplasm, and a minor component of Leydig cells with round nuclei and abundant eosinophilic cytoplasm (**Figure 1B**). Immunohistochemically, the tumor cells exhibited cytoplasmic and membranous immunoreactivity for inhibin (**Figure 2A**) and calretinin (**Figure 2B**), nuclear positivity for forkhead box L2 (FOXL2) (**Figure 2C**) and steroidogenic factor-1 (SF-1) (**Figure 2D**), as well as membranous staining for desmin (**Figure 2F**). In contrast, the neoplastic cells were negative for epithelial membrane antigen (EMA) (**Figure 2E**). According to histological differentiation, 60.0% (9/15) of tumors were moderately differentiated, and 26.7% (4/15) were poorly differentiated (**Table 3**). Notably, a retiform pattern (**Figure 1C**) was identified in two (13.3%) moderately differentiated tumors, and heterologous elements (**Figure 1D**) were present in one (6.7%) moderately differentiated case. Somatic DICER1 RNase IIIb hotspot mutations were identified in all fifteen patients. Only one patient (6.7%) was found to carry a concurrent germline DICER1 pathogenic or likely pathogenic (P/LP) variant. All DICER1-mutated tumors in this cohort were either moderately or poorly differentiated; no well-differentiated Sertoli-Leydig cell tumors were observed.

Postoperative treatment

Adjuvant chemotherapy was administered to 53.3% (8/15) of patients, all of whom had moderately or poorly differentiated tumors (**Table 3**). Chemotherapy was given to 14.3% (1/7) of patients with stage IA disease (data unavailable for one IA case), 85.7% (6/7) with stage IC (data unavailable for one IC case), and 100% (1/1) of those with stage II-IV disease. All patients who received chemotherapy were treated with a paclitaxel and carboplatin-based regimen.

Survival outcomes

The median follow-up duration was 19 months (range: 5-36 months). Among stage I patients with available follow-up data, no recurrences were observed. However, this follow-up period is relatively short for a tumor with known recurrence timelines extending beyond five years. Follow-up information was unavailable for three

Table 1. Clinical features of DICER1-related ovarian Sertoli-Leydig cell tumor

Case Number	Age	Laterality	How diagnosed	Presenting symptom	Preoperative AFP	Preoperative CA125	Preoperative CA19-9	Preoperative hCG
1	14	Left	Symptomatic	Abdominal distention	Normal	Normal	Normal	Normal
2	19	Left	Symptomatic	Abdominal distention	Normal	Normal	Normal	Normal
3	17	Left	Symptomatic	Abdominal pain	Elevated	Normal	Normal	Normal
4	27	Right	Routine check-up	Secondary amenorrhea	Elevated	Normal	Normal	Normall
5	30	Right	Pregnancy	Abdominal distention	Elevated	Elevated	Normal	Normal
6	29	Left	Symptomatic	Abdominal distention	Elevated	Normal	Normal	Normal
7	15	Left	Routine check-up	Secondary amenorrhea	Elevated	Normal	Elevated	Normal
8	23	Right	Symptomatic	Abdominal distention	Normal	Normal	Normal	Normal
9	13	Left	Routine check-up	Secondary amenorrhea	Normal	Normal	Normal	Normal
10	14	Left	Routine check-up	Secondary amenorrhea	Normal	Normal	Normal	Normal
11	3	Right	Symptomatic	Abdominal distention	Elevated	Normal	Normal	Normal
12	22	Left	Incidental	No symptoms or signs	Normal	Normal	Normal	Normal
13	34	Left	Routine check-up	Secondary amenorrhea	Normal	Normal	Normal	Normal
14	21	Right	Symptomatic	Abdominal distention	Elevated	Elevated	Normal	Normal
15	29	Left	Symptomatic	Abdominal distention	Elevated	Normal	Normal	Normal

Table 2. Surgical data of DICER1-related ovarian Sertoli-Leydig cell tumor

Case Number	Surgical approach	Tumor size (cm)	Rupture	Surgical procedure	FIGO stage
1	Laparotomy	25.0	No rupture	Salpingo-oophorectomy + omentectomy + lymphadenectomy	IA
2	Laparoscopic	15.0	Intra-Operative	Salpingo-oophorectomy	IC1
3	Laparotomy	18.0	No rupture	Salpingo-oophorectomy	IA
4	Laparoscopic	11.7	Intra-Operative	Salpingo-oophorectomy + omentectomy	IC1
5	Laparotomy	20.0	Pre-Operative	Salpingo-oophorectomy + Omentectomy + lymphadenectomy	IC2
6	Laparotomy	18.8	Intra-Operative	Salpingo-oophorectomy + Omentectomy + lymphadenectomy	IC1
7	Laparoscopic	8.5	No rupture	Salpingo-oophorectomy + Omentectomy	IA
8	Laparoscopic	10.0	Intra-Operative	Salpingo-oophorectomy + Omentectomy	IC1
9	Laparoscopic	3.3	No rupture	Cystectomy	IA
10	Laparotomy	17.5	Intra-Operative	Salpingo-oophorectomy + Omentectomy	IC1
11	Laparotomy	12	No rupture	Salpingo-oophorectomy	IA
12	Laparoscopic	7.4	No rupture	Salpingo-oophorectomy	IA
13	Laparoscopic	5.6	No rupture	Hysterectomy + Bilateral salpingo-oophorectomy + Omentectomy + lymphadenectomy	IA
14	Laparotomy	20.0	Intra-Operative	Hysterectomy + Bilateral salpingo-oophorectomy + Omentectomy + lymphadenectomy	IV
15	Laparoscopic	9.4	Intra-Operative	Salpingo-oophorectomy	IC1

FIGO, International Federation of Gynecology and Obstetrics; SLCT, Sertoli-Leydig cell tumor.

patients: one with stage IV disease who was lost to follow-up after surgery and one cycle of chemotherapy at our institution, and two others with stage IA and IC1 disease, respectively. The loss to follow-up of the sole advanced-stage case particularly limits conclusions regarding outcomes for higher-stage DICER1-mutant SLCTs.

Discussion

Ovarian Sertoli-Leydig cell tumors (SLCTs) are rare sex cord-stromal neoplasms, constituting only 0.2-0.5% of all ovarian cancers and predominantly affecting young women [12, 13]. Owing to their rarity, the available literature on SLCTs remains limited. Notably, a younger age

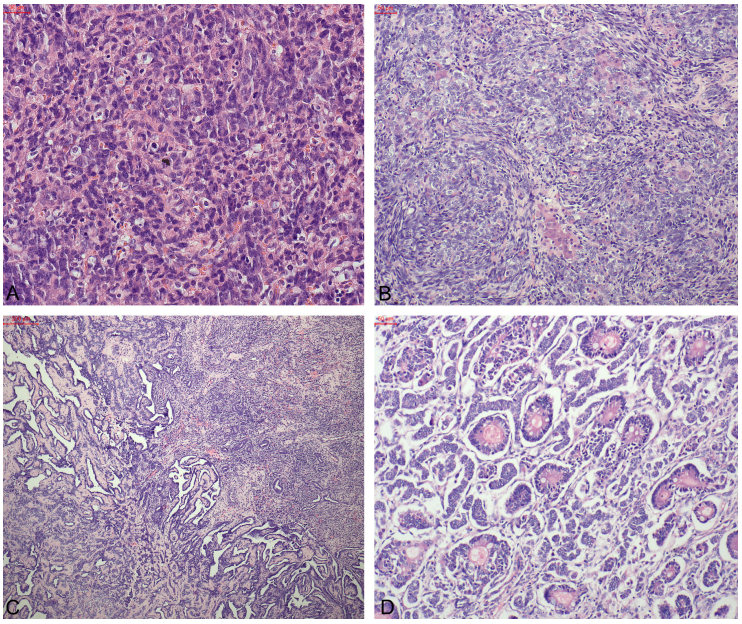

Figure 1. Histopathological features of ovarian Sertoli-Leydig cell tumors (hematoxylin and eosin staining). A. Nests of spindle-shaped tumor cells within an edematous, hypocellular stroma (original magnification ×200). B. Intermediate-magnification view demonstrates a mixture of Sertoli cells with ovoid to spindled nuclei and scant cytoplasm, and Leydig cells featuring round nuclei and abundant eosinophilic cytoplasm (original magnification ×100). C. A moderately differentiated tumor exhibiting a retiform pattern (original magnification ×40). D. A moderately differentiated tumor containing heterologous elements (original magnification ×100).

at diagnosis is a recognized feature of DICER1-mutant SLCTs. While the reported age range for SLCTs is broad (1-82 years) with a mean of 25 years [13, 14], our cohort exhibited a even younger median age of 21 years, further supporting this association. Consistent with previous reports, most patients (93%) presented with symptomatic disease [6]. SLCTs can usually be diagnosed at an early stage and are confined to a single ovary [13, 15]. In this series of cases, 14 out of 15 patients (93.3%) had stage I disease, with all tumors being unilateral and predominantly on the left side (66.7%), consistent with the established epidemiological pattern.

The most common clinical manifestations of ovarian SLCTs are irregular bleeding, abdominal masses, or amenorrhea [16, 17]. Excessive androgen levels typically cause virilizing signs, including oligomenorrhea, hirsutism, and voice deepening, which are observable in up to 60% of patients, especially those with moderately or poorly differentiated tumors [17, 18]. Without virilization, patients typically experience non-specific symptoms such as abdominal distension, mass, or pelvic pain [19]. In our cohort, the main symptoms of abdominal distension and menstrual irregularities (including secondary amenorrhea) were caused by the mass effect of these characteristic large tumors (median diameter: 12.0 cm) and their hormone-producing capacity. A key finding was the early stage at diagnosis, with 93% of cases being limited to FIGO stage I, which is consistent with the established disease behavior and indicates a potentially favorable prognosis when managed with timely intervention [6].

Imaging examinations are crucial for evaluating ovarian SLCTs. Ultrasound examination can detect larger masses and may show thickening of the endometrium, indicating possible high estrogen levels [17]. More advanced examination methods, such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET), are particularly useful for identifying smaller lesions or metastatic disease [19]. Serum tumor markers have supplementary diagnostic value, with frequent elevation of alpha-fetoprotein (AFP), testosterone, estrogens, cancer antigen 125 (CA-125), cancer antigen 19-9 (CA 19-9), or human chorionic gonadotropin (hCG) [17]. Combining characteristic imaging features with the serum tumor marker profile can significantly improve the accuracy of preoperative diagnosis.

For the final diagnosis of SLCTs, just like other ovarian tumors, it requires confirmation through postoperative histopathological examination. In our series, all the tumors exhibited the typical morphological features of SLCTs, supported by consistent immunohistochemical positivity for calretinin and inhibin. Histologically, the majority (60%) were moderately differentiated, which is consistent with the existing literature reports [7]. Molecular analysis revealed that all cases had somatic DICER1 RNase IIIb hotspot mutations, and only one patient (6.7%) carried

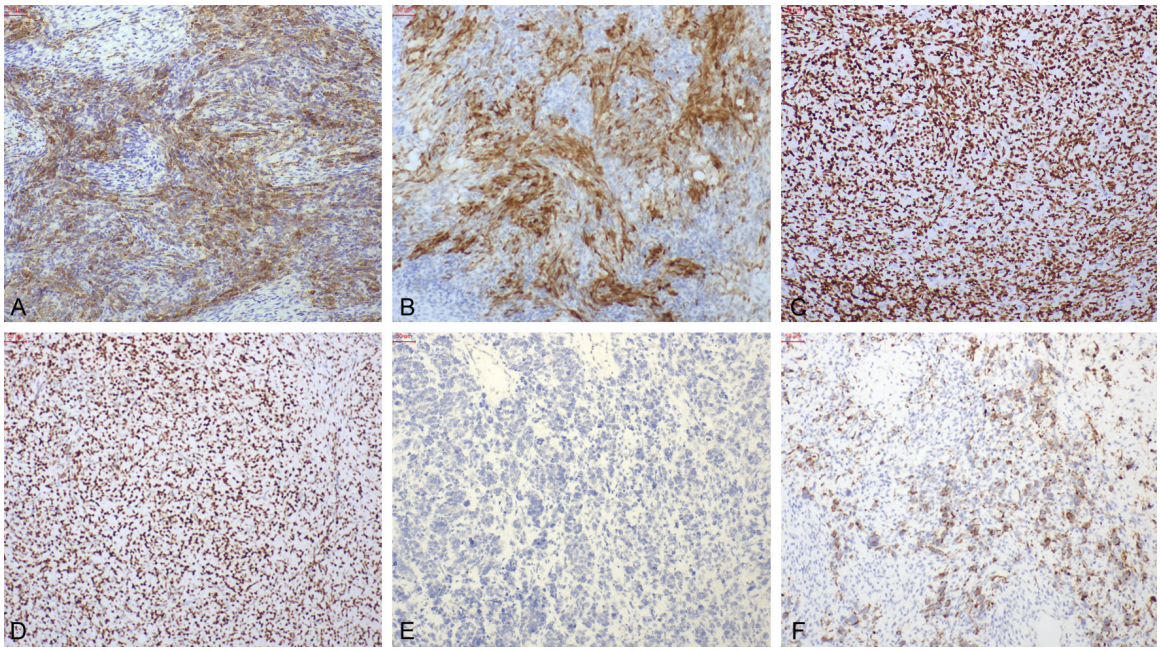

Figure 2. Immunohistochemical characterization of ovarian Sertoli-Leydig cell tumors. (A) Tumor cells exhibited strong cytoplasmic and membranous positivity for inhibin. (B) Neoplastic cells showed cytoplasmic and membranous staining for calretinin. (C) Nuclear immunoreactivity for forkhead box l2 (FOXL2) was observed. (D) Tumor cells demonstrated Nuclear staining for steroidogenic factor-1 (SF-1). (E) The neoplastic cells were negative for epithelial membrane antigen (EMA). (F) Focal cytoplasmic staining for desmin was present. Original magnification: ×100 (A-F).

concomitant germline DICER1 pathogenic variant. Compared with previous report [9], this lower germline mutation rate may reflect referral bias, regional genetic differences, or our focus on somatic detection methods. It is noteworthy that all DICER1-mutated tumors showed moderate or poor differentiation, and no well-differentiated cases were observed. This significant genotype-phenotype correlation further supports the hypothesis that well-differentiated SLCTs may arise through DICER1-independent pathways, providing a theoretical basis for their independent classification [7].

Due to the rarity of SLCTs, standardized treatment guidelines are lacking. Therefore, individualized management should be carried out based on tumor stage, patient age, and histological grade. Surgery is the main intervention method. For young patients with stage IA disease who wish to preserve their fertility, fertility-sparing surgery is a feasible option, as its recurrence rate is comparable to that after radical surgery (approximately 8% vs. 3% in previous studies) [13, 20]. However, the management of patients with stage IC disease is more complex. Advanced stage is a known negative prognostic factor, with one study reporting a recurrence rate of 30% and a mortality rate of 54% for stage IC SLCTs [20], highlighting the need for more evidence to optimize the surgical strategies for these cases. Our data emphasizes the critical importance of meticulous surgical staging and individualized care. The high utilization rate of fertility-preserving surgery (93%), mainly unilateral salpingo-oophorectomy, indicates that the principle of conservatism has been successfully implemented in this young population. However, the incidence of intraoperative tumor rupture is quite high (up to 46.7%), especially in larger tumors, which poses significant challenges to the surgery and highlights the necessity of adopting more refined surgical techniques to avoid deterioration of the condition and affect the treatment outcome of the tumor.

The high frequency of intraoperative tumor rupture (46.7%) in our series warrants further discussion. There are several factors that may contribute to this phenomenon. Firstly, the tumors are usually large (median diameter 12.0 cm), which increases the difficulty of removal, especially when performed through minimally

Table 3. Postoperative data of DICER1-related ovarian Sertoli-Leydig cell tumor

Case Number	Level of Differentiation	Heterologouselements	Retiform	Somatic DICER1 RNase IIIb hotspot variant	Germline DICER1 P/LP variant	Adjuvant chemotherapy	Follow-up and outcome
1	Intermediately-to-poorly	No	No	Positive	Negative	Paclitaxel plus carboplatin	No evidence of disease at 28 months
2	Poorly	No	No	Positive	Negative	N/A	N/A
3	Poorly	No	No	Positive	Negative	N/A	N/A
4	Intermediately	No	Yes	Positive	Positive	Paclitaxel plus carboplatin	No evidence of disease at 13 months
5	Intermediately	No	No	Positive	Negative	Paclitaxel plus carboplatin	No evidence of disease at 8 months
6	Intermediately	No	No	Positive	Negative	Paclitaxel plus carboplatin	No evidence of disease at 5 months
7	Intermediately	No	No	Positive	Negative	-	No evidence of disease at 18 months
8	Poorly	No	No	Positive	Negative	Paclitaxel plus carboplatin	No evidence of disease at 20 months
9	Intermediately	No	No	Positive	Negative	-	No evidence of disease at 18 months
10	Intermediately-to-poorly	No	No	Positive	Negative	Paclitaxel plus carboplatin	No evidence of disease at 25 months
11	Intermediately	No	No	Positive	Negative	-	No evidence of disease at 30 months
12	Intermediately	No	Yes	Positive	Negative	-	No evidence of disease at 32 months
13	Intermediately	No	No	Positive	Negative	-	No evidence of disease at 36 months
14	Poorly	No	No	Positive	Negative	Paclitaxel plus carboplatin	N/A
15	Intermediately	Yes	No	Positive	Negative	Paclitaxel plus carboplatin	No evidence of disease at 6 months

invasive surgery. Secondly, SLCT may contain cystic or fragile components, which makes it prone to rupture during the operation. Thirdly, the presence of adhesions or a desire to perform fertility-sparing surgery through a smaller incision may increase the complexity of the surgery. This high rupture rate underscores a significant clinical challenge. As intraoperative rupture upstages a tumor to at least stage IC, which may influence decisions regarding adjuvant therapy, meticulous surgical techniques are crucial. Surgeons should be aware of this risk, especially when managing large, cystic adnexal masses in young women. Strategies such as careful tissue handling, the use of retrieval bags, or opting for a laparotomy when minimally invasive complete resection seems unsafe can be considered.

Adjuvant chemotherapy was administered based on individualized risk assessment, primarily to patients with advanced-stage or poorly differentiated tumors. Due to the lack of prospective data, the role of this therapy in SLCTs remains controversial. However, the current evidence supports its use in cases with adverse features, including moderately/poorly differentiated histology, stage IC disease, retiform pattern, or heterologous elements [18, 21, 22]. Although the bleomycin-etoposide-cisplatin (BEP) regimen is the most commonly used, there is no consensus on the optimal regimen. Other active options include paclitaxel-cisplatin (TP), ifosfamide-etoposide-cisplatin (VIP), cisplatin-vincristine-bleomycin (PVB), and cisplatin-epirubicin-cyclophosphamide (PAC) [13, 23, 24]. In our cohort, the continuous use of a platinum-based regimen (paclitaxel-carboplatin) reflects the common practice in the absence of formal guidelines. The absence of recurrences in stage I patients with available follow-up provides preliminary support for this risk-adapted approach in the short term.

The prognosis of ovarian SLCTs is usually more favorable than that of ovarian epithelial cancer, but not as good as that of granulosa cell tumors [22, 23]. The prognosis mainly depends on the tumor stage and histologic grade, and is also influenced by factors such as tumor size and the presence of heterologous elements or a retiform pattern. Approximately 20% of patients will experience disease recurrence, and the vast majority (95%) of recurrences occur within five years after diagnosis [17, 25]. Therefore, patients usually undergo regular monitoring for 2 to 5 years after surgery before being considered to have a lower risk of recurrence. In our cohort, with a median follow-up of 19 months (range: 5-36 months), no recurrences were observed among stage I patients with available data. While this short-term outcome is encouraging and aligns with the expected good prognosis for early-stage SLCTs, it must be interpreted with caution. The relatively short follow-up period is a significant limitation, as it does not cover the typical timeframe during which most recurrences are reported. Furthermore, the loss to follow-up of critical cases, most notably the only patient with stage IV disease, severely limits our ability to draw conclusions regarding outcomes for advanced-stage DICER1-mutant SLCTs. These constraints are inherent to retrospective studies of rare tumors, but they also highlight the necessity of multi-institutional collaboration in order to gain a more comprehensive understanding of the natural development process of SLCTs and the best treatment options.

This study has several limitations, including its retrospective design and the small sample size, the latter being inherent to the rarity of SLCTs. As noted, the median follow-up of 19 months is relatively short, and the loss of the stage IV case to follow-up are important constraints. These factors preclude definitive conclusions, underscoring the need for future prospective, multi-center studies with extended follow-up and systematic genetic profiling to validate our observations and refine risk-stratification approaches.

Conclusions

In conclusion, our clinicopathologic analysis of 15 cases confirms that ovarian SLCTs harboring somatic DICER1 mutations typically present in young women at an early stage. Short-term outcomes for stage I disease in our cohort were favorable, though the follow-up period is limited and longer surveillance is necessary to fully assess prognosis. We identify a strong genotype-phenotype correlation, with DICER1 mutations being exclusively associated with non-well-differentiated histology. Meticulous surgical resection, with particular care to avoid tumor rupture (a common challenge highlighted

by our data), forms the cornerstone of management. Adjuvant chemotherapy should be reserved for patients with high-risk characteristics, such as advanced-stage or poorly differentiated disease. Future studies with extended follow-up and comprehensive germline testing are needed to better understand the long-term behavior of these rare tumors and optimize treatment strategies.

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Written consent to publish this information was obtained from the patients.

Disclosure of conflict of interest

None.

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