Clinical Oncology: Case Reports

Case Series

A SCITECHNOL JOURNAL

SMARCA4 Deficient Tumours of Ovary and Uterus: 2 Case Reports with Review of Literature

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Abstract

Swi/Snf Related,Matrix Associated, Actin Dependent Regulator Of Chromatin,Subfamily A,Member 4 (SMARCA4-deficient) tumors are typically aggressive, characterized by undifferentiated round cells or rhabdoid features histopathologically. These tumors are rarer compared to their other epithelial counterparts and generally have a poorer prognosis. Here, we report two cases with mutations in the SMARCA4 gene.

The first case involves a 29-year-old woman with Small Cell Carcinoma of the Ovary Hypercalcemic Type (SCCOHT). She presented with lower abdominal pain, and Contrast Enhanced Compututed Tomography (CECT) imaging indicated widespread abdominopelvic disease with left supraclavicular and axillary lymph nodes. A biopsy revealed undifferentiated carcinoma with loss of Brahma-Related Gene-1 (BRG-1) and retention of Integrase Interactor-1 (INI-1) on Immunohistochemistry (IHC). Despite receiving three cycles of etoposide/carboplatin and seven cycles of a four-drug regimen (cisplatin/adriamycin/etoposide/cyclophosphamide), she succumbed to the disease while on supportive care, with an overall survival of 13 months.

The second case involves a 38-years-old woman with SMARCA4-Deficient Uterine Sarcoma (SDUS). She presented with lower abdominal pain, an enlarged uterus, thickened endometrium, and bilateral ovarian and nodal deposits. An omental biopsy revealed large tumor cells with vesicular nuclei, and IHC suggested diffuse expression of Cluster Of Differentiation 99 (CD99), with similar BRG-1 loss and INI-1 retention. She received two lines of chemotherapy (gemcitabine/docetaxel and adriamycin/ifosfamide) but unfortunately succumbed to the disease within four months of diagnosis.

Both patients presented at advanced stages and were only able to receive conventional chemotherapy due to financial constraints. Newer promising therapies need to be explored in such rare cases, where treatment protocols are still under evaluation for standard of care and efficacy, wherever resources permit.

Keywords: Rare cancers, Smarca 4 Deficient Uterine Sarcoma (SDUS), Small Cell Carcinoma of the Ovary Hypercalcemic Type (SCCOHT), (Swi/Snf Related,Matrix Associated, Actin Dependent Regulator Of Chromatin, Subfamily A, Member 4) SMARCA4 deficient.

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Received: July 14, 2024; Manuscript No: COCR-24-148451 **Editor Assigned:** July 17, 2024; PreQC Id: COCR-24-148451 (PQ) **Reviewed:** July 25, 2024; QC No: COCR-24-148451 (Q) **Revised:** July 27, 2024; Manuscript No: COCR-24-148451 (R) **Published:** August 04, 2024; DOI: 10.4173/cocr.7(6).358

Introduction

SMARCA4-deficient malignant tumors have recently been expanded to include various tumor types, such as thoracic carcinomas, sarcomas, small cell carcinomas of the ovary hypercalcemic type, malignant ovarian rhabdoid tumors, and SMARCA4-deficient undifferentiated uterine sarcomas [1,2]. These groups reportedly share common clinicopathological characteristics, including undifferentiated round cell or rhabdoid morphology, highly aggressive behavior, and poor clinical outcomes [1,2].

These tumors are associated with somatic and often germline pathogenic variants in SMARCA4, which encodes the SMARCA4 protein (BRG1), an Adenosine Triphosphatase (ATPase) and a subunit of the Switch/Sucrose Non Fermenting (Chromatin Remodeling Complex) (SWI/SNF) chromatin remodeling complex [3]. Due to their role in regulating numerous critical cellular processes, including transcriptional control, DNA repair, differentiation, cell division, and Deoxyribonucleic Acid (DNA) replication, Switch/Sucrose Non Fermenting (Chromatin Remodeling Complex) (SWI/SNF) complexes with mutant subunits are thought to contribute to cancer initiation and progression [3].

Fewer than 500 cases of Small Cell Carcinoma Of The Ovary Hypercalcemic Type (SCCOHT) and fewer than 30 cases of SMARCA4-Deficient Undifferentiated Uterine Sarcomas (SDUS) have been reported in the literature [4].

In this report, we present two rare cases: one of SCCOHT without any evident features of hypercalcemia clinically or biochemically, and another of SMARCA4-deficient uterine sarcoma.

Case Presentation

Case 1

A 29 years female, with no known comorbidities or addictions, no significant family historyof malignancy, married since 2 years, Para 1 Living 1 (P1L1) (Last child birth 15 months back) referred to us withpost operative reports and pre-operative investigations which she underwent for complaintsof abdominal pain for 4 months. The pain was in the right lower abdomen, dull boring incharacter, non colicky, radiating to whole abdomen, more on lying on the right lateralposition,with no history of altered bowel habits or dysuria or vomiting or fever or nightsweats or weight loss.

In the pre-operative investigations, we found, A Ultrasound Sonography (USG) abdomen and pelvis which showed anechogenic mass in the pelvis, related to right ovary 101 mm × 69 mm × 83 mm, with right kidney grade Ihydronephrosis and a CECT abdomen and pelvis showing 8 cm × 10 cm solid cystic mass in the pelvis, inseperable from adjacent small gut loops,grade II hydronephrosis of right kidney; multiple enlarged right external iliac, right common iliac, paraaortic, aortocaval and retrocrural lymph nodes, largest measuring 20 mm × 25 mm; Multiple enlarged nodules in the pelvis, largest measuring 15 mm × 21 mm in the Pouch of Douglas (POD) (Figures 1 and 2).

The tumor markers were as follows: Alpha Fetoprotein AFP<0.5 IU/ml, Carcinoembryonic Antigen (CEA) 1.58 ng/ml, Cancer Antigen 125 (CA 125) 76.3 IU/ml, Cancer Antigen 19.9 (CA 19.9) 35.56 U/ml,

Lactacte Dehydrogenase (LDH) 311 U/l, and B-HCG<1.2 mIU/ml, with only slightly elevated CA 125 and LDH levels. The colonoscopy report indicated examination up to the splenic flexure, revealing submucosal bulges at 15 cm-20 cm on withdrawal and a large bulge on the anterior rectal wall at 10 cm.

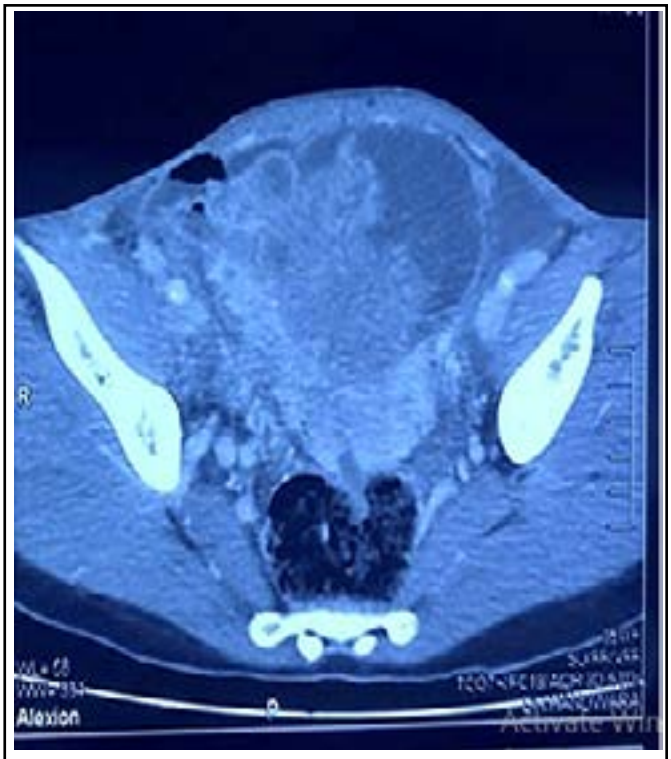

Figure 1: CECT abdomen and pelvis showing the large solid cystic mass in the pelvis.

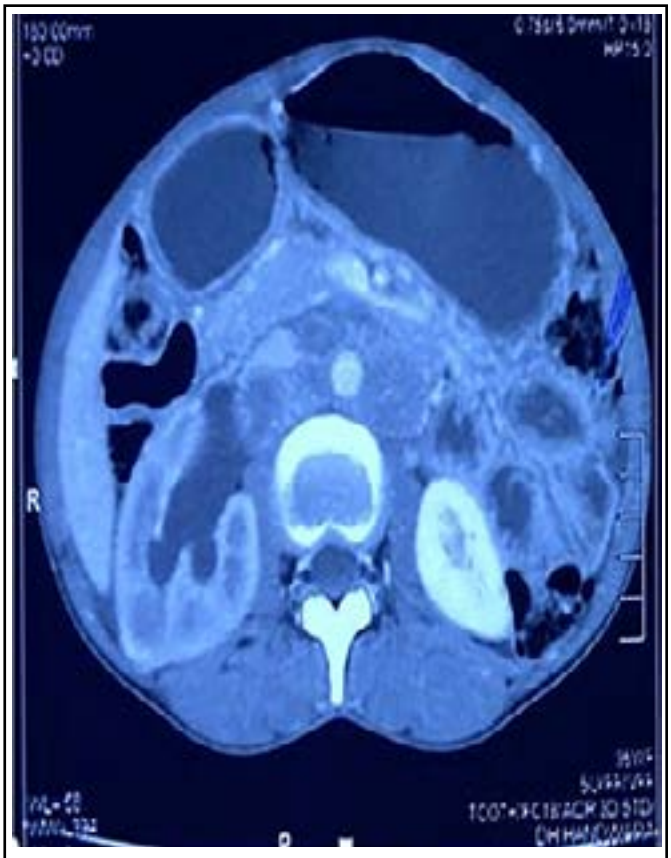

Figure 2: CECT abdomen and pelvis showing multiple enlarged lymph nodes and nodules.

The diagnostic laparotomy report noted intraoperative findings of a 15 cm × 10 cm globular mass adherent to the small bowel, urinary bladder, and vessels. Biopsies were taken from the right pelvic mass and right iliac nodes. Histopathological reports of both the mass and right iliac node indicated deposits of malignant tumor with necrosis, suggestive of poorly differentiated carcinoma.With this background, the patient was referred to our institute and examined. On examination, her general condition was fair Eastern Cooperative Oncology Group Performance Status (ECOG-PS 1), though she appeared emaciated. A firm, fixed nodal mass measuring 6 cm × 8 cm was observed in the left supraclavicular region, and multiple mobile nodes, the largest being 5 cm × 4 cm, were found in the left axilla. Her abdomen showed a healed surgical site, and the rest of the examination was normal.

Further evaluation at our institute included a normal upper Gastro-Intestinal (GI) endoscopy. A review of the biopsy with IHC of the right iliac node showed SMARCA4-deficient undifferentiated carcinoma. The tumor cells expressed Cytokeratin (CK) and Epithelial Membrane Antigen (EMA) focally but did not express PAX8, WT1, p53, CK7, CK20, or Epstein-Barr Encoding Region (EBERs). INI-1 expression was retained, while BRG-1 expression was lost, leading to an impression of small cell carcinoma of the ovary with hypercalcemia (Figures 3 and 4).

Baseline investigations revealed microcytic hypochromic anemia (Hb 8.8 g/dl). A CECT scan of the neck, chest, abdomen, and pelvis performed at our institute revealed a 15 cm × 11 cm × 12 cm solid cystic lesion in the abdomino-pelvic cavity with multiple adjacent enhancing pelvic deposits, the largest measuring 30 mm × 28 mm. Additionally, there were multiple enlarged retroperitoneal nodes, the largest measuring 28 mm × 40 mm, evidence of grade II hydronephrosis of the right kidney, and multiple enlarged internal, external, and common iliac nodes, the largest being 15 mm × 14 mm in the external iliac region. The scan also showed a 40 mm × 40 mm left supraclavicular node, 26 mm × 24 mm left axillary nodes, and multiple enlarged level II and level III cervical nodes, the largest measuring 10 mm × 9 mm (Figures 5 and 6).

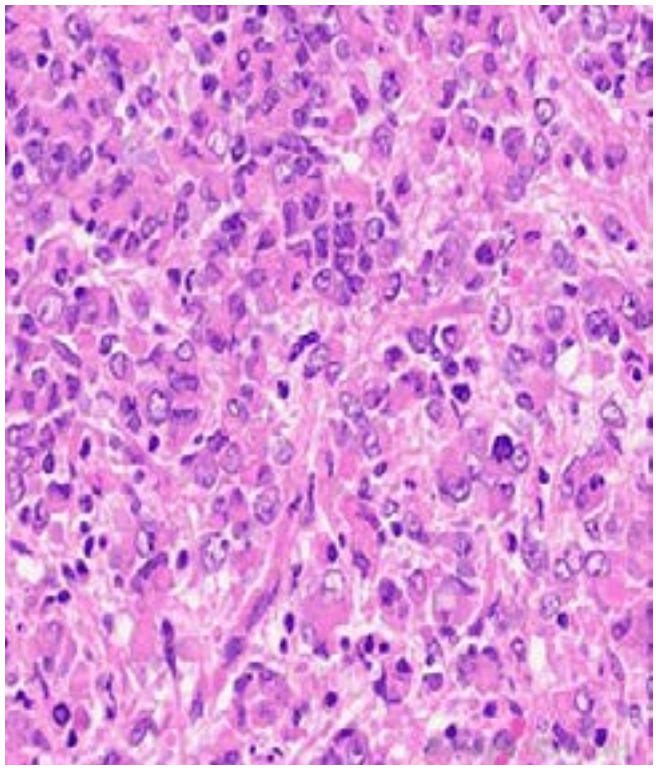

Figure 3: Histoathology slide showing the large tumour cells with vesicular nuclei and small nucleoli.

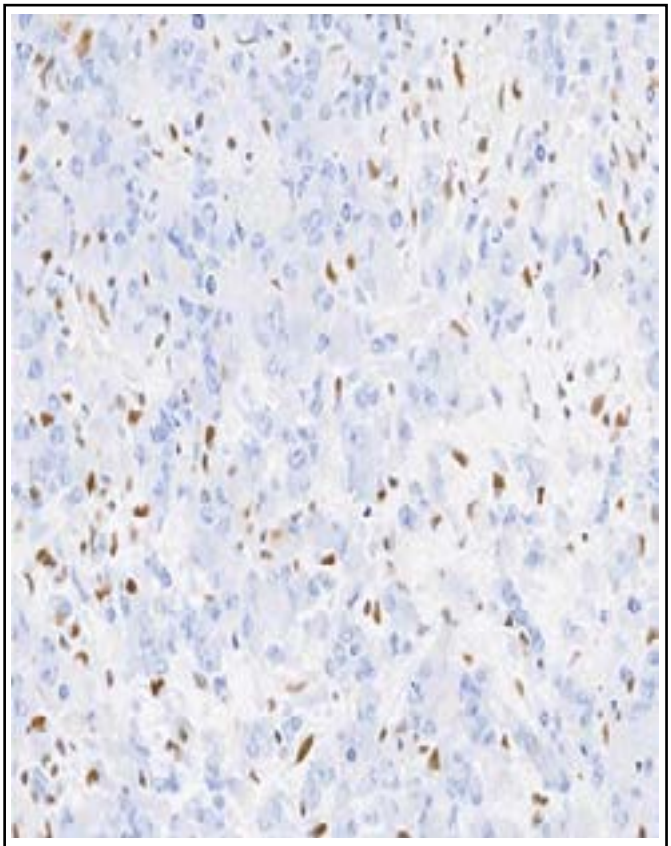

Figure 4: IHC showing the loss of BRG-1.

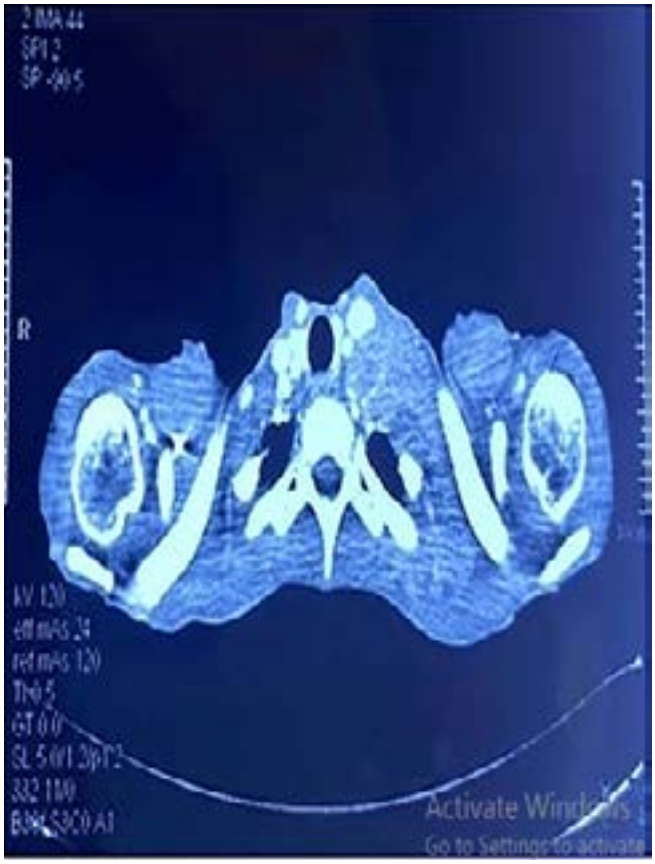

Figure 5: Contrast Enhanced Compututed Tomography (CECT) showing enlarged cervical and axillary nodes.

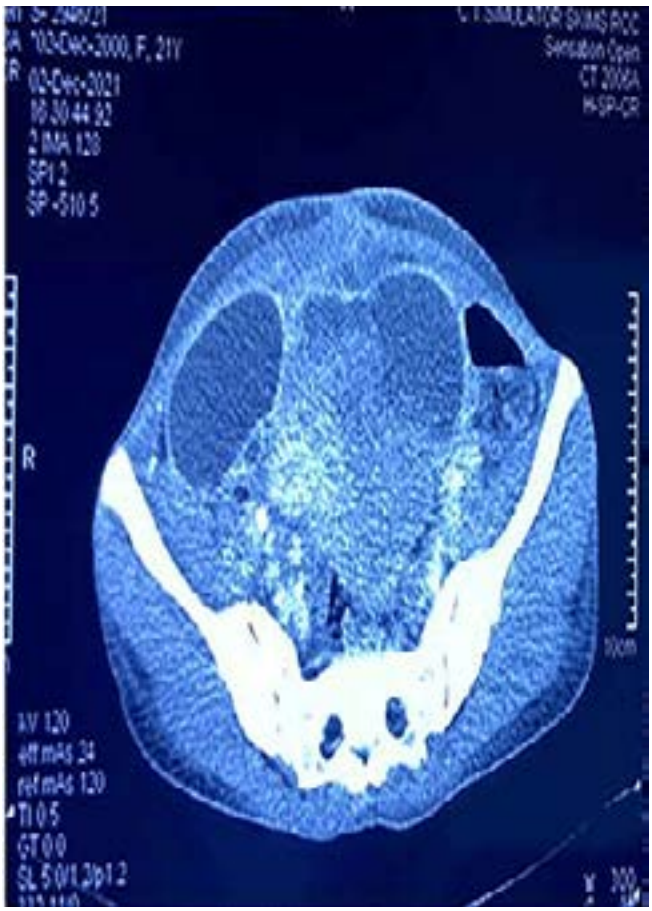

Figure 6: CECT showing large pelvic lesion with deposits.

A lymph node biopsy of the left axilla showed reactive lymph nodes with sinus histiocytosis. The bone scan was normal. The patient received three cycles of chemotherapy with etoposide and carboplatin. The chemotherapy was well tolerated, though she experienced one episode of febrile neutropenia (grade 4) and grade 3 mucositis during the second week of cycle 1, which was managed with antibiotics and supportive care.The increase in the size of the left supraclavicular lymph nodes suggested clinical progression, prompting a repeat CECT and a biopsy of the left supraclavicular lymph node. Histopathology and immunohistochemistry of the neck node revealed that the tumor cells expressed synaptophysin, showed dot positivity for EMA and focal positivity for cytokeratin, and exhibited loss of BRG-1 (SMARCA4) expression, consistent with SMARCA4-deficient carcinoma.

The repeat CECT scan of the neck, chest, abdomen, and pelvis showed disease progression, with an increase in the size of nodules in the Pouch of Douglas (POD) and pelvis, as well as the cervical lymph nodes. New findings included multiple deposits posterolateral to the psoas muscles and a few mediastinal nodes, the largest measuring 10 mm × 6 mm (Figures 7 and 8).

The patient was started on a four-drug protocol with cisplatin, adriamycin, etoposide, and cyclophosphamide. After three cycles, a repeat CECT scan of the whole body was performed. She tolerated the cycles fairly well, experiencing one episode of febrile neutropenia (grade 4) and grade 3 gastrointestinal toxicity in the form of vomiting during the second week of cycle 2. The other cycles were uneventful. Clinically, there was a good response with no palpable cervical or axillary lymph nodes. The CECT scan showed a decrease in the size of all lesions. In view of the partial response, the patient received four more cycles of the same chemotherapy. During the last cycle, she developed grade 4 neutropenia, grade 4 thrombocytopenia, and fever with Lower Respiratory Tract Infection (LRTI) symptoms. A High-Resolution CT

(HRCT) of the chest suggested ground-glass opacities, likely fungal pneumonia, which was managed with antibiotics and antifungals.

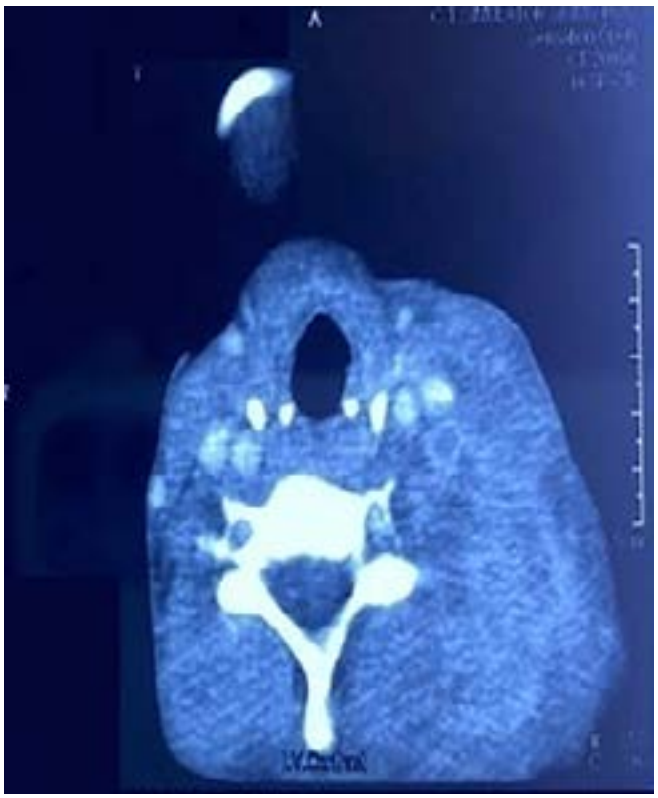

Figure 7: CECT showing enlarged cervical nodes.

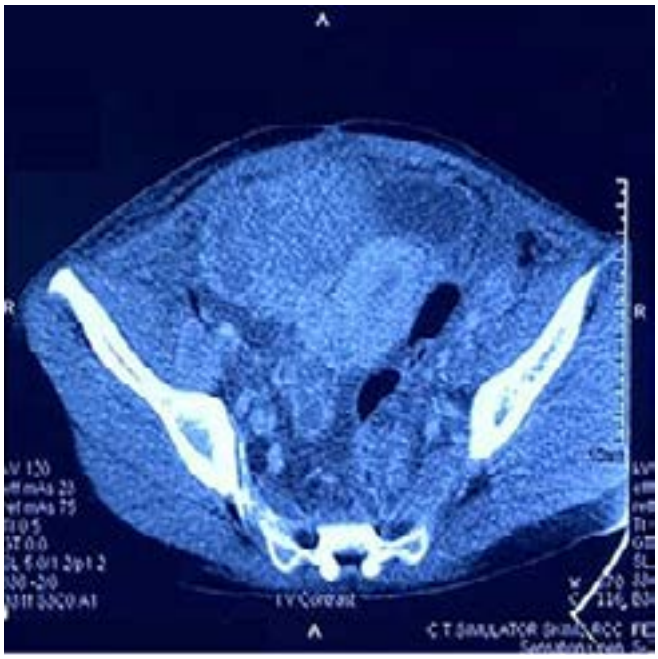

Figure 8: CECT showing increased size of pelvic mass.

After these seven cycles, the patient showed a palpable lump in the hypogastrium. An Ultrasound Sonography (USG) of the abdomen and pelvis revealed a large heterogeneous mass in the pelvis measuring 7.8 cm × 7 cm with internal vascularity, indicating an increase in size compared to the last imaging. Given the clinical and radiological progression of the disease, a drop in the patient's performance status, and prior toxicities, she was placed on best supportive care. The patient subsequently developed bilateral hydronephrosis and pedal edema, succumbing to the disease after a 13 month battle.

Case 2

A 38-years-old unmarried female, with no known comorbidities or addictions and no significant family history of malignancy, was referred to us from the surgical oncology department. She was initially evaluated for complaints of lower abdominal pain for 2 months.There were no complaints such as vaginal bleeding, altered bowel habits, dysuria, vomiting, fever, or weight loss. Initial evaluation with Ultrasound Sonography (USG) revealed a bulky uterus with multiple large heterogeneous lesions in both walls, the largest measuring 15 cm × 11.1 cm, suggestive of fibroids, with a 30 mm hyperplastic endometrium. She underwent laparotomy based on these findings, which revealed a uterus enlarged to the size of 20 weeks' gestation, with a nodular surface and friable surface deposits, as well as bilateral cystic ovaries suggestive of sarcoma. The procedure was closed without intervention.

Subsequently, an Magnetic Resonance Imaging (MRI) was performed, showing an enlarged uterus measuring 19 cm × 15 cm × 12 cm with T2-weighted heterogeneous hyperintense myometrial signal intensity lesions infiltrating the entire myometrium, including both anterior and posterior walls, and extending into the cervical stroma up to the external os. Serosal irregularities and lobulations were noted with adherence to the anterior abdominal wall. Bilateral parametrial invasion was evident with adherence to small bowel loops and the sigmoid colon. Diffusion-Weighted Imaging (DWI) showed restriction within the altered signal intensity lesion. The endometrium measured 29 mm in thickness with multiple submucosal T2-weighted hypointense areas, the largest measuring 22 mm. Both ovaries exhibited T2-weighted hyperintense signals and DWI-restricting deposits, measuring 55 mm × 46 mm on the right side and 30 mm × 29 mm on the left side, with both ovaries also showing unilocular cysts. Multiple enlarged para-aortic, right internal iliac, and left external iliac nodes were observed, with the largest measuring 33 mm × 31 mm. There were also a few deposits in the Pouch Of Douglas (POD) with no evidence of ascites. A CECT scan of the chest, abdomen, and pelvis confirmed these findings, with no evidence of extra-abdominal spread of the disease (Figures 9-11).

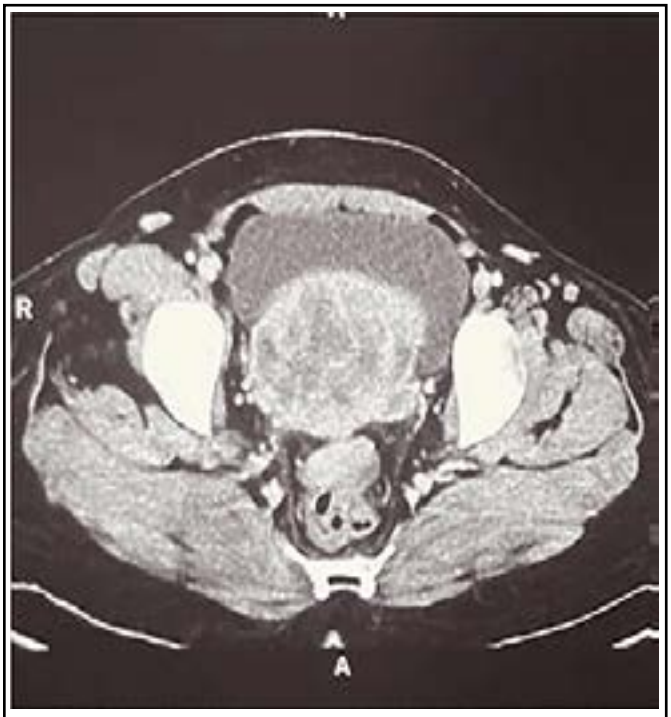

Figure 9: CECT showing uterine mass and lymph nodes.

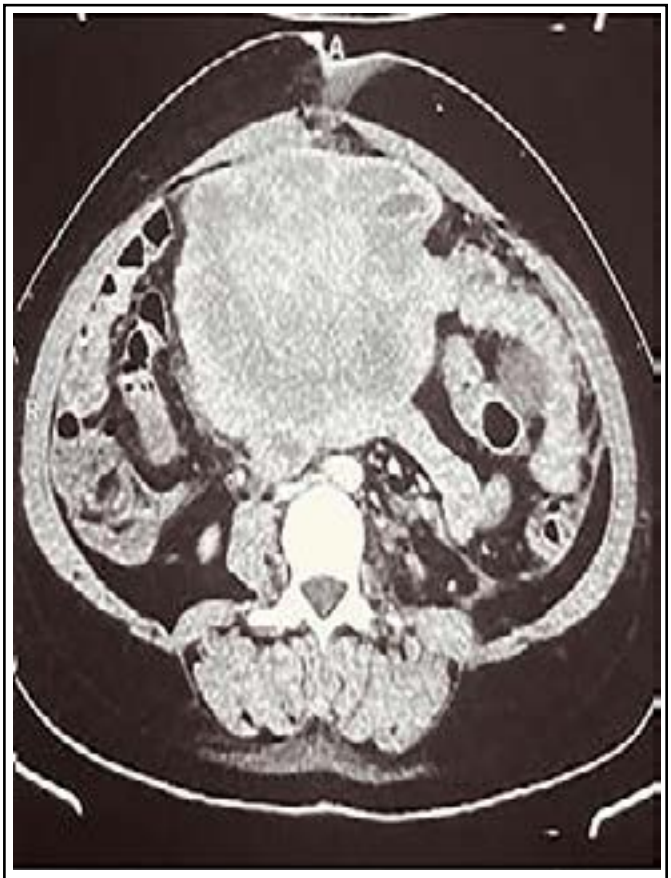

Figure 10: CECT showing uterine mass and lymph nodes.

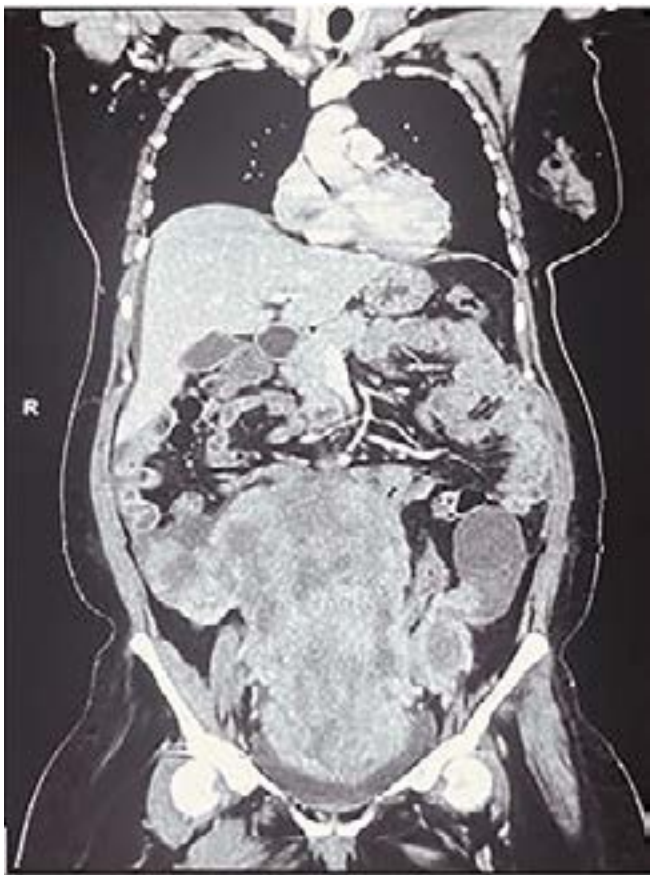

Figure 11: CECT abdomen and pelvic axial section showing the extend of uterine lesion.

Blood investigations revealed the following levels: CEA 1.42 ng/ml, CA 19.9 8.5 U/ml, Beta-Human Chorionic Gonadotropin (B-HCG) 0.25 mIU/ml, CA 125 788 IU/ml, AFP 2.83 ng/ml, and LDH 353 U/l. Based on these reports, she underwent re-exploratory laparotomy with omental and pelvic peritoneal biopsy at our institute's surgical oncology department. Intraoperatively, a 15 cm × 15 cm mass replacing the uterus, bilateral ovarian composite cysts, pelvic and peritoneal deposits, and mild ascites were found.

Histopathological examination of the pelvic and omental deposits revealed monomorphic malignant tumor cells arranged in chords and sheets. The tumor cells were large with vesicular nuclei, small nucleoli, and very scanty cytoplasm. Immunohistochemistry showed diffuse expression of Cluster Of Differentiation 99 (CD99) and complete loss of BRG-1 expression. There was no expression of CK, Epithelial Membrane Antigen (EMA), PAX-8, cyclin-D1, CD-10, PR, SMA, desmin, S-100, CD34, Leucocyte Common Antigen (LCA), synaptophysin, WT-1, Transducin-Like Enhancer of Split-1 (TLE-1), NKX2.2, or Bcl6 Corepressor (BCOR). INI-1 expression was retained, suggesting a diagnosis of high-grade malignant tumor of SMARCA4-deficient type (Figures 12-14).

Upon referral to the medical oncology department, the patient had an Eastern Cooperative Oncology Group Performance Status (ECOG) performance status of 2, with a large globular mass palpable in the abdomen suggesting a uterus size equivalent to 24 weeks of gestation. Following relevant blood tests, the patient's case was discussed in a multidisciplinary tumor board, and based on literature review, a decision was made to initiate gemcitabine-docetaxel chemotherapy.

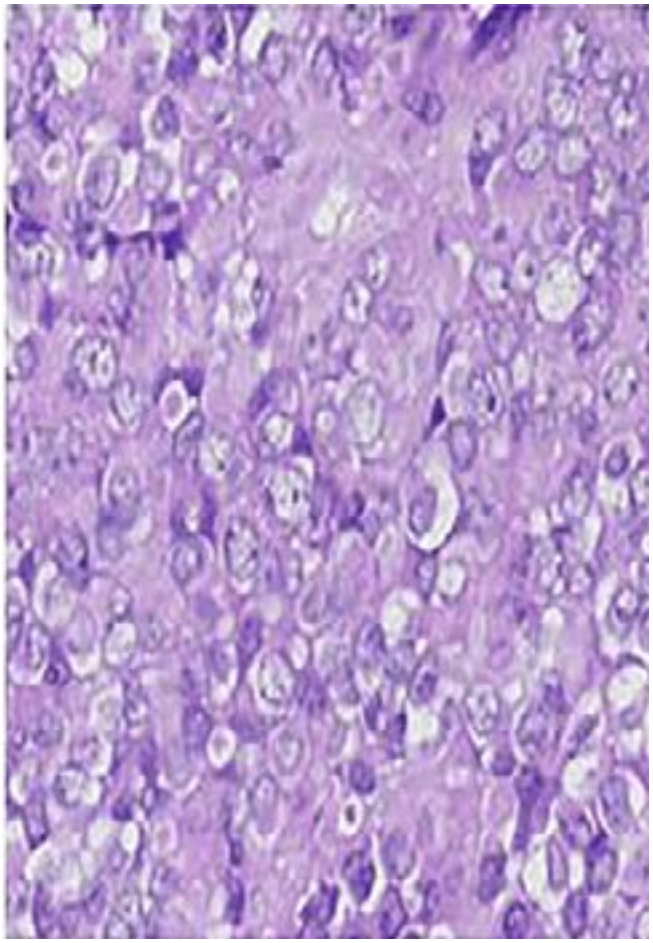

Figure 12: Histopathology slide showing large tumour cells with vesicular nuclei, small nucleoli and scanty cytoplasm.

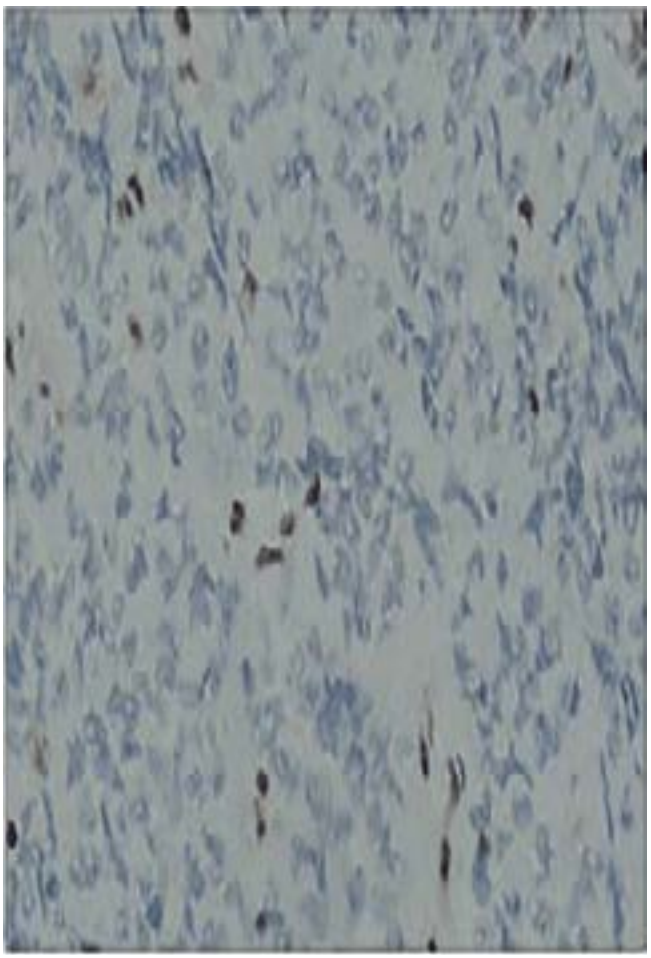

Figure 13: IHC showing loss of BRG-1 in the tumour cells.

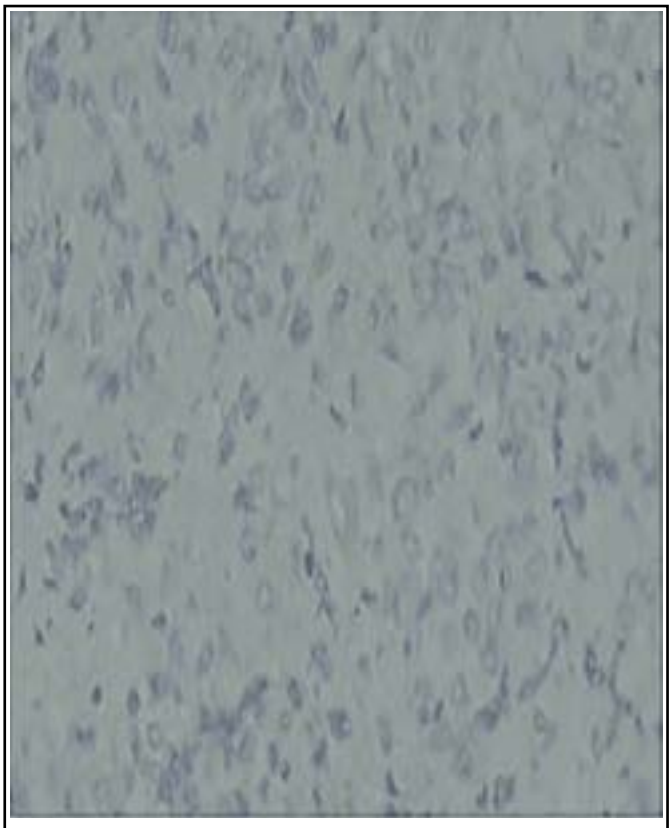

Figure 14: Negative IHC for EMA.

She tolerated the first two cycles of chemotherapy well but was subsequently lost to follow-up. During telephonic follow-up, it was noted that the patient completed the remainder of her chemotherapy at a private hospital. Unfortunately, she experienced disease progression after three cycles of the regimen. An alternative chemotherapy regimen containing Adriamycin and ifosfamide was attempted, but the patient succumbed to the disease during the second cycle of this treatment.

Discussion

Small Cell Carcinoma Of The Ovary Hypercalcemic Type (SCCOHT) is an aggressive cancer, with long-term survival rates of 30% in early-stage cases. They represent less than 0.01% of all ovarian cancers [5]. Recently, germline and/or somatic mutations in SMARCA4, a member of the SWI/SNF chromatin remodeling complex, have been identified as the main underlying molecular alteration in these cases, facilitating diagnosis through Immunohistochemistry (IHC) for loss of SMARCA4 expression (also known as BRG1) [2,6]. Since the discovery of this defining molecular alteration, SMARCA4-deficient sarcomas have also been reported in other anatomic sites where SMARCA4-deficient tumors, including atypical teratoid or rhabdoid tumors of the CNS, thoracic sarcomas, and undifferentiated uterine sarcomas, have been reported [7].

Smarca4 Deficient Uterine Sarcoma (SDUS) usually occurs in patients with a median age of 33 years, slightly higher than the median age of 24 years in SCCOHT [8]. Our patients presented within these respective age groups.In SCCOHT cases, the age range at diagnosis varies widely from 7 months to 56 years [9]. Clinical features often include young age, hypercalcemia in two-thirds of cases, and advanced stage in approximately one-third of patients. Our patient had normocalcemia but was 29 years old with an advanced stage, consistent with our case. Tumor markers typically used in epithelial ovarian cancers are not informative in SCCOHT; our patient had nonspecifically raised CA125 and Lactacte Dehydrogenase (LDH) levels. Radiological imaging characteristics are generally nonspecific [10]. Histologically, SCCOHT is characterized by small cell populations, prototypical small blue round cells with high nuclear atypia, numerous mitoses, and frequent necrosis. The growth pattern is typically solid and trabecular, often with distinctive follicle-like spaces. Immunohistochemically, Small Cell Carcinoma of the Ovary Hypercalcemic Type (SCCOHTs) are positive for vimentin and show focal expression of epithelial markers. BRG1 protein, encoded by the SMARCA4 gene, is almost always absent. In our case, there was focal expression of CK and EMA, with retained INI-1 expression and loss of BRG-1 expression.

In SDUS, young women are predominantly affected, with a mean age of 33 years, significantly younger than patients with undifferentiated endometrial carcinomas (mean age 61 years) [11]. Clinical manifestations are nonspecific, and imaging characteristics are not well defined. MRI is useful for assessing local invasion, particularly with T2-weighted sequences for detecting myometrial invasion [12]. CT scans are more useful for staging rather than diagnosis [13]. Diagnosis is based on histology and loss of SMARCA4 staining with anti-SMARCA4 antibodies [9]. Histologically, SDUS shows diffuse sheets of medium to large epithelioid cells with areas of rhabdoid morphology, corded architecture, stromal hyalinization, and focal phyllodiform architecture. SDUS is microsatellite stable and lacks significant expression of epithelial markers like keratin, EMA, and claudin-4 [9].

Treatment of SCCOHT is stage-dependent, following International Federation of Gynecology and Obstetrics (FIGO) guidelines for ovarian cancer staging. A multimodal approach, determined in a multidisciplinary tumor board, is essential [14]. In early stages, radical surgery akin to high-grade epithelial ovarian cancers is recommended. Adjuvant chemotherapy typically includes cisplatin and etoposide, although variations exist in clinical practice.External beam radiother-

apy is commonly recommended for SCCOHT, similar to its use in small cell lung cancer and other small cell cancers. Most patients with SCCOHT respond to chemotherapy regimens that combine agents such as cisplatin, etoposide, doxorubicin, bleomycin, cyclophosphamide, and vinblastine [14]. Approaches to early-stage SCCOHT vary widely: some advocate fertility-sparing surgery followed by adjuvant chemotherapy, while others propose radical staging surgery with pelvic and paraaortic lymphadenectomy. For advanced stages, neoadjuvant chemotherapy followed by radical staging surgery is often preferred. Due to its highly aggressive nature, prognosis remains very poor, with a 1-year survival rate around 50% in advanced cases [15]. Despite attempts at aggressive surgical management combined with chemotherapy and sometimes radiotherapy, outcomes are often discouraging [16].

Interestingly, studies have found that despite being a low mutation burden cancer, the majority of SCCOHTs demonstrate PD-L1 expression and strong associated T cell infiltration, suggesting potential for immunotherapy approaches [17]. Our patient received two lines of aggressive chemotherapy due to metastatic disease at presentation, showing partial response to a 4-drug protocol initially but succumbing to the disease within 13 months of diagnosis.

In SDUS, characteristics such as lymphovascular invasion, extrauterine spread, and metastasis at presentation are commonly observed [9]. As a relatively new entity, treatment guidelines are still evolving. Total abdominal hysterectomy with or without bilateral salpingo-oophorectomy is considered standard for uterine sarcomas, with ovarian preservation tailored to individual clinical scenarios [13,18]. Adjuvant chemotherapy options include gemcitabine-docetaxel or anthracycline-ifosfamide-based regimens [4]. Despite aggressive surgical intervention, the median survival for SDUS is typically 9 months, significantly shorter than that for undifferentiated endometrial carcinomas (36 months) [9]. Lower SMARCA4 expression has been associated with increased sensitivity to cisplatin, although outcomes remain poor overall [19]. Our patient received both gemcitabine-docetaxel-based and anthracycline-ifosfamide-based chemotherapy regimens.

Perioperative radiotherapy has shown potential in studies to improve outcomes for uterine sarcomas [20]. Emerging therapies such as Cyclin Dependent Kinases 4 And 6 (CDK4/6) inhibitors, Enhancer Of Zeste 2 Polycomb Repressive Complex 2 Subunit (EZH2) inhibitors, and immune checkpoint inhibitors have demonstrated promising results in SCCOHT cases and should be further evaluated for effectiveness in SDUS [9,11,18].

Conclusion

While prognosis hinges on early and precise identification, followed by radical resection with clear margins whenever possible. Given the on-going evaluation of treatment protocols for their standardization and efficacy, timely intervention and effective management of chemother-apy-related toxicities are critical for patient care. Continued research, collaborative efforts among healthcare professionals, and the develop-ment of standardized treatment strategies should be actively promot-ed to advance patient outcomes in these challenging malignancies.

Acknowledgements

We thank the entire department of Medical Oncology,SKIMS,Srinagar,including nurses and supporting staff.We also thank our patients and their families who gave us consent for publication of these cases.We also thank our Radiology department and Pathology department for the providing and interpreting the images for this chapter.

Funding

None.

References

1. Rekhtman N, Montecalvo J, Chang J. C, Alex D, Ptashkin R. N, et al. (2020). SMARCA4-deficient thoracic sarcomatoid tumors represent primarily smoking-related undifferentiated carcinomas rather than primary thoracic sarcomas. J Thorac Oncol. 15:231-247.
2. Witkowski L, Carrot-Zhang J, Albrecht S, Witkowski L, Carrot-Zhang, et al. (2014). Germline and somatic SMARCA4 mutations characterize small cell carcinoma of the ovary, hypercalcemic type. Nat Genet. 46:438-443.
3. Savas S, & Skardasi G. (2018). The SWI/SNF complex subunit genes: Their functions, variations, and links to risk and survival outcomes in human cancers. Crit Rev Oncol/Hematol. 123:114-131.
4. Gao. (2023) Pathological characteristics and immune microenvironment of SMARCA4-deficient undifferentiated uterine sarcoma. Diagn Pathol.18:62.
5. Pressey J.G, Dandoy C E, Pater L. E., Rios J. S, Sisson R, et al. (2020). Small Cell Carcinoma Of The Ovary Hypercalcemic type (SCCOHT): Comprehensive management of a newly diagnosed young adult. Gynecol Oncol. 158:538-546.
6. Jelinic P, Mueller J. J, Olvera N, Dao F, Scott S N, et al. (2014). Recurrent SMARCA4 mutations in small cell carcinoma of the ovary. Nat genet, 46:424-426.
7. Yoshida A, Kobayashi E, Kubo T, Kodaira M, Motoi T, et al. (2017). Clinicopathological and molecular characterization of SMARCA4-deficient thoracic sarcomas with comparison to potentially related entities. Mod Pathol. 30:797-809.
8. Kolin D.L, Dong F, Baltay M, Lindeman N, MacConaill L, t al. (2018). SMARCA4-deficient undifferentiated uterine sarcoma (malignant rhabdoid tumor of the uterus): a clinicopathologic entity distinct from undifferentiated carcinoma. Mod Patho. 31:1442-1456.
9. Young R H, Oliva E. & Scully R E. (1994). Small cell carcinoma of the ovary, hypercalcemic type: a clinicopathological analysis of 150 cases. Am J Surg Pathol. 18:1102-1116.
10. Kommos FKF, Tessier-Cloutier B.: Small cell carcinoma of ovary,hypercalcemic type. Pathol Outlines
11. Kolin DL, Quick CM, Dong F, Fletcher CD, Stewart CJ, et al. (2020). SMARCA4-deficient uterine sarcoma and undifferentiated endometrial carcinoma are distinct clinicopathologic entities. Am J Surg Pathol. 44:263-270.
12. Santos P, & Cunha T. M. (2015). Uterine sarcomas: clinical presentation and MRI features. Diagn Interv Radiol. 21:4.
13. Tirumani SH, Ojili V, Shanbhogue AKP, Fasih N, Ryan JG, et al.(2013). Current concepts in the imaging of uterine sarcoma. Abdom Imaging, 38:397-411.
14. Ray-Coquard I, Morice P, Lorusso D, Prat J, Oaknin A, et al. (2018). Non-epithelial ovarian cancer: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up. Ann Oncol, 29:iv1-iv18.
15. Dykgraaf RH, de Jong D, van Veen M, Ewing-Graham PC, Helmerhorst TJ, & van der Burg, ME. (2009). Clinical management of ovarian small-cell carcinoma of the hypercalcemic type: a proposal for conservative surgery in an advanced stage of disease. Int J Gynecol Cancer. 19.
16. Pautier P, Ribrag V, Duvillard P, Rey A, Elghissassi I, et al. (2007). Results of a prospective dose-intensive regimen in 27 patients with small cell carcinoma of the ovary of the hypercalcemic type. Ann Oncol. 18:1985-1989.
17. Jelinic P, Ricca J, Van Oudenhove E, Olvera N, Merghoub T, et al. (2018). Immune-active microenvironment in small cell carcinoma of the ovary, hypercalcemic type: rationale for immune checkpoint blockade. JNCI: J Natl Cancer Inst. 110:787-790.
18. Tischkowitz M, Huang S, Banerjee S, Hague J, Hendricks WP, et al. (2020). Small-cell carcinoma of the ovary, hypercalcemic type–genetics, new treatment targets, and current management guidelines. Clin Cancer Res. 26:3908-3917.
19. Bell EH, Chakraborty AR, Mo X, Liu Z, Shilo K, et al. (2016). SMARCA4/BRG1 is a novel prognostic biomarker predictive of cisplatin-based chemotherapy outcomes in resected non–small cell lung cancer. Clin Cancer Res. 22:2396-2404.
20. Callegro-Filho D, Gerhenson D M, Nick A M. (2016) Small cell carcinoma of the ovary-hypercalcemic type(SCCOHT):A review of 47 cases. Gynecol Oncol. 140:53-57.

Appendices

Abbreviations

SMARCA4 - Swi/Snf Related, Matrix Associated, Actin Dependent Regulator Of Chromatin, Subfamily A, Member 4

BRG-1- Brahma-Related Gene-1

ATPase - Adenosine Triphosphatase

SWI/SNF - Switch/Sucrose Non Fermenting (Chromatin Remodeling Complex)

DNA - Deoxyribonucleic Acid

SCCOHT- Small Cell Carcinoma of the Ovary, Hypercalcemic Type

SDUS - Smarca4 Deficient Uterine Sarcoma

P1L1 - Para 1 Living 1

CECT - Contrast Enhanced Compututed Tomography

POD - Pouch of Douglas

AFP- Alpha Fetoprotein

CEA - Carcinoembryonic Antigen

CA 125 - Cancer Antigen 125

CA 19.9 - Cancer Antigen 19.9

LDH - Lactacte Dehydrogenase

B-HCG - Beta-Human Chorionic Gonadotropin

ECOG PS - Eastern Cooperative Oncology Group Performance Status

GI - Gastro-Intestinal

IHC -Immunohistochemistry

CK - Cytokeratin

EMA - Epithelial Membrane Antigen

PAX-8 - Paired-Box Gene 8

WT-1 - Wilms' Tumour -1

EBER -Epstein-Barr Encoding Region

INI-1 - Integrase Interactor-1

USG - Ultrasound Sonography

MRI - Magnetic Resonance Imaging

DWI - Diffusion Weighted Imaging

CD99 - Cluster Of Differentiation 99

CD-10 - Cluster Of Differentiation 10

PR - Progesterone Receptor

SMA - Smooth Muscle Actin

CD 34 - Cluster of differentiation 34

LCA - Leucocyte Common Antigen

TLE - Transducin-Like Enhancer Of Split-1

NKX2.2 - Nk2 Homeobox 2

BCOR - Bcl6 Corepressor

CNS - Central Nervous System

FIGO - International Federation Of Gynecology And Obstetrics

PDL-1 - Programmed cell death ligand 1

CDK4/6 - Cyclin Dependent Kinases 4 And 6

EZH2 -Enhancer Of Zeste 2 Polycomb Repressive Complex 2 Subunit

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