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Case series

# Diverse case series of granulomatous peritonitis mimicking advanced ovarian cancer

Rachel L. Furuya [a,*], Bobbie J. Rimel [b], Richard Tsai [c], Rebecca Ann Brooks [d], L. Stewart Massad [e], Premal H. Thaker [e,1], John D. Pfeifer [f,1]

[a] Department of Obstetrics and Gynecology, Washington University School of Medicine, MSC 8064-37-1005, 660 S. Euclid Ave, St. Louis, MO 63110, USA
[b] Division of Gynecologic Oncology, Samuel Oschin Comprehensive Cancer Institute, Cedars-Sinai Medical Center, 127 S San Vicente Blvd, Los Angeles, CA 90048, USA
[c] Mallinckrodt Institute of Radiology, Washington University School of Medicine, 510 S Kingshighway Blvd, St. Louis, MO 63110, USA
[d] Division of Gynecologic Oncology, University of California Davis Comprehensive Cancer Center, 4501 X Street, Sacramento, CA 95817, USA
[e] Division of Gynecologic Oncology and Alvin J. Siteman Cancer Center, Washington University School of Medicine, 4500 Forest Park Avenue, Saint Louis, MO 63108, USA
[f] Department of Pathology and Immunology, Washington University School of Medicine, 660. S Euclid Ave., St. Louis, MO 63110, USA

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ABSTRACT

*Background:* Epithelial ovarian cancer commonly presents with vague symptoms that delay diagnosis until disease is advanced. Granulomatous peritonitis is a term used to describe granulomatous inflammation within the peritoneal cavity and mimics advanced stage ovarian cancer clinically and on imaging. The goal of this study was to examine the frequency and characteristics of cases of granulomatous peritonitis mimicking ovarian cancer at a single institution and to describe the etiology in this population.

*Methods:* Eight cases were identified with pathology conformation of granulomatous disease and absence of cancer. The etiologies include pelvic tuberculosis, ruptured dermoid cyst, ruptured hemorrhagic corpus luteum, prior endometriosis surgery, xanthogranulomatous inflammation and three cases of tubo-ovarian abscesses.

*Results:* Seven of the eight had pelvic masses on imaging studies; one patient had presumed carcinomatosis without an adnexal mass on CT scan. Preoperative CA-125 was elevated in four of the eight patients, with a range of 30.8 to 228 U/mL. All had some form of surgical management with at least one ovary removed.

*Conclusion:* Clinicians should be aware of this disease to improve diagnosis and direct appropriate patient management.

## 1. Background

Epithelial ovarian cancer most commonly presents with vague symptoms such as bloating, constipation, abdominal pain, and increasing abdominal girth. Absent of effective screening tools, ovarian cancer is usually diagnosed at advanced stages. While physical exam findings, imaging studies, and serum level of CA-125 can raise clinical suspicion, diagnosis requires tissue biopsy. Previously, those with suspected ovarian cancer almost uniformly underwent surgical debulking. Although there has been paradigm shift towards neoadjuvant chemotherapy when tumor burden or comorbidities are high, many patients will still receive primary cytoreductive surgery. (Koirala et al., 2020) Preoperative biopsy is rarely performed for those patients. There are cases that present with the classic signs, symptoms, imaging findings, and lab abnormalities consistent with the diagnosis of ovarian cancer, but operative exploration sometimes reveals another disease process is responsible for these findings.

Granulomatous peritonitis is a term used to describe granulomatous inflammation within the peritoneal cavity. Granulomatous inflammation is defined by the presence of histocytes, often with T lymphocytes, and can be the result of numerous etiologies including infectious agents, allergic reactions, foreign materials, bowel contents, and autoimmune disease. (Levy et al., 2009) Histologic patterns can help narrow the etiologic differential diagnosis. (Shah et al., 2017) Granulomas are

* Corresponding author.
*E-mail addresses:* furuyar@wustl.edu (R.L. Furuya), bobbie.rimel@cshs.org (B.J. Rimel), r.tsai@wustl.edu (R. Tsai), rebrooks@ucdavis.edu (R.A. Brooks), massadl@wustl.edu (L. Stewart Massad), thakerp@wustl.edu (P.H. Thaker), jdpfeifer@wustl.edu (J.D. Pfeifer).
[1] Both Drs. Thaker and Pfeifer are co-senior authors on the manuscript.

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divided into two broad categories: foreign body granulomas and immune granulomas. Foreign body, also known as giant cell, granulomas form around materials that are too large for phagocytosis and not immunogenic; thus, they do not elicit T cell-mediated response. Macrophages accumulate, release cytokines, and fuse to form giant cells around the material surface, forming a granuloma. Immune granulomas are caused by agents that produce a persistent T-cell mediated response and are further subdivided into necrotizing granulomas, prototypically tuberculosis, or non-necrotizing granulomas, such as sarcoidosis (Shah et al., 2017).

There are several reports of granulomatous peritonitis presenting like ovarian cancer with many being diagnosed at the time of surgery and some even undergoing extensive abdominal surgery for presumed ovarian cancer, with its associated risk and morbidity. Including peritoneal granulomatosis in a preoperative differential diagnosis may help physicians to diagnose these rare cases prior to operative intervention. The goal of this study was to examine the frequency and characteristics of cases of granulomatous peritonitis mimicking ovarian cancer at a single institution and to determine what diseases are represented in this population.

## 2. Methods

Cases were identified from the files of the Lauren V. Ackerman Laboratory of Surgical Pathology at Washington University St. Louis via a search for the pathologic diagnoses of "granulomatous" or "granulomas" of the abdomen, uterus, tubes, or ovaries between January 1, 1982 and July 31, 2024. Further chart review identified those patients whose initial differential diagnosis included ovarian cancer. Women older than 18 years of age at time of diagnosis with peritoneal granulomatosis confirmed by histology at the time of surgery, without evidence of ovarian cancer, who had initial treatment and diagnosis at our institution, and who had full documentation of initial treatment in the medical record formed the basis of our study. Institutional IRB exemption was obtained for the retrospective medical record review. The most recent case was added to the cohort with patient consent (case 8). It was not possible to obtain consent from others given time from diagnosis and/or the patients were lost to follow up. No identifying information was used for these cases.

Hematoxylin and eosin (H&E) stained sections (both actual intraoperative frozen sections as well as permanent sections) were produced via standard methods. All cases were reviewed by a pathologist with subspecialty expertise in gynecologic pathology (JDP). Computed tomography (CT) imaging for the most recent case was provided for reference.

## 3. Results

Eight patients meeting the inclusion criteria were identified (Table 1). Seven of the eight had pelvic masses on imaging studies ranging from 2.5 cm to 15 cm in largest diameter; one patient (case 3) had presumed carcinomatosis without an adnexal mass on computerized tomography (CT) scan. Preoperative CA-125 ranged from 30.8 to 228 U/mL and was elevated above the upper limit of normal (35) in four of the eight patients. Seven patients underwent exploratory laparotomy, and 4 of 8 had frozen section analysis performed. All patients had at least one ovary and tube removed; six of the eight patients had removal of both tubes and ovaries, and hysterectomy was done in five of the eight patients. Two patients required a bowel resection: one for a small bowel obstruction and one for bowel perforation requiring a second operation.

Pathologic evaluation confirmed the diagnosis of granulomatous peritonitis in all cases and confirmed that none of the patients suffered from malignancy. Final pathology aligned with intra-operative pathology report in all four cases that had frozen section assessment. Acid fast bacilli were identified in case 3 with caseating granulomatous inflammation (Fig. 1). Non-caseating granulomas were associated with a ruptured dermoid cyst in case 4 (Fig. 1). In case 5, the granulomas were associated with a ruptured hemorrhagic corpus luteum (Fig. 1); in three cases the granulomas were associated with tubo-ovarian abscesses (TOA) (cases 1, 2 and 7). In case 6, the granulomatous inflammation was attributed to previous surgery for endometriosis (Fig. 1). Case 8 was found to have extensive xanthogranulomatous inflammation of the left ovary and fallopian tube as seen in Fig. 2. CT imaging of case 8 (Fig. 3) demonstrated left adnexal mass, lymphadenopathy, and peritoneal nodularity.

Four required no further treatment after surgery (Table 1). Case 2 and 7 received post-operative antibiotics for TOA. Case 7′s initial surgery was complicated by multiple adhesions and was found to have a bowel perforation post-operatively requiring a second operation and bowel resection. Case 3 was treated for tuberculosis with isoniazid, rifampin, pyrazinamide, and ethambutol. Case 8 underwent an extensive but negative work up for rheumatologic disease. After a median follow up of 47 months (range 0–228 months), none developed gynecologic malignancy.

## 4. Discussion

This study found that granulomatous peritonitis is a rare mimicker of ovarian cancer with only eight cases identified in a high-volume center over more than 42 years. All patients had some form of operative management with seven undergoing laparotomy and all having at least one ovary removed. These cases identify a diverse array of etiologies that exemplify the need to keep a broad differential.

Peritoneal tuberculosis is the most well-reported cause of peritoneal granulomatosis mistaken for ovarian cancer worldwide. Overlap in symptomology, laboratory findings, and imaging make it difficult to distinguish preoperatively. There are several case series, in addition to many case reports, that retrospectively describe common findings for patients with peritoneal tuberculosis mimicking ovarian cancer. (Koc et al., 2006; Oge et al., 2012; Bilgin et al., 2001; Xi et al., 2010; Wu et al., 2011) The four identified case series all report a mean elevation in CA-125 (range 286 to 565 U/mL) with almost all patients having ascites, pelvic masses, or both. In three of the series, most patients with ascites underwent paracentesis which yielded inconclusive results. All four series found that diagnosis was almost exclusively made at time of surgery or postoperatively with many patients having had extensive presumed debulking. In our study, only one patient was diagnosed with peritoneal tuberculosis (case 3). The patient presented with vague symptoms of bloating, constipation, increasing abdominal pain, and weight loss. As expected, based on prior studies, CA 125 was elevated to 228 U/ml. CT demonstrated carcinomatosis but did not show ascites or a pelvic mass. In this case, frozen section was performed showing granulomatous disease. Unfortunately, the patient still underwent significant debulking surgery with final diagnosis demonstrating tuberculosis. It is important to note that, in addition to previously mentioned symptoms, this patient also had night sweats, dry cough, and a positive purified protein derivative (PPD) without a chest radiograph performed. Although peritoneal tuberculosis is well described globally, it is uncommon in the population our institution serves.

In addition to tuberculosis, there are rare reports of other infectious etiologies resulting in granulomatous peritonitis that have been mistaken for ovarian cancer. In our study, three patients (cases 1, 2, and 7) were found to have ruptured TOAs at the epicenter of their granulomatous reaction. TOAs are most commonly polymicrobial; however, there are case reports of actinomycosis and *Enterobius vermicularis* TOAs resulting in granulomatous peritonitis. (Khan et al., 1981; Craggs et al., 2009; Kim et al., 2004) All three patients underwent laparotomies with one requiring bowel resection at time of initial operation (case 2) and one requiring a reoperation with bowel resection (case 7) noted in Table 1.

Non-infectious etiologies underlie a subset of cases of granulomatous peritonitis, as highlighted by our case series. Our cohort had two cases of

**Table 1**
Cases of granulomatous peritonitis mimicking ovarian cancer.

| Case Number | Presenting symptoms | CA- 125 | Preoperative Imaging | Chest X-Ray | Surgical Procedure | Surgical Findings | Histologic Findings | Microbiology | Diagnosis | Treatment |
|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Left lower quadrant abdominal pain | 6 | CT A/P: complex, multilobulated, and multiloculated, left-sided pelvic mass measuring 5 × 6 cm near sigmoid colon. | Not performed | EL, resection of pelvic mass, left salpingo-oophorectomy | 7–8 cm left sided simple ovarian mass arising from left ovarian remnant and fallopian tube. | FS: not performed<br>Fallopian tube with non-caseating granulomas and peritubal adhesions. Large focus of non-caseating granuloma in peritubal soft tissue. | Not performed | Tubo-ovarian abscess | No further treatment |
| 2 | Abdominal bloating | 24 | MRI A/P: complex 10 × 10 cm mass in left adnexa | Normal | EL, TAH, BSO, segmental colon resection | Inflammatory mass fixed to left pelvis encompassing left adnexa and sigmoid colon | FS: not performed<br>Left ovary with severe chronic granulomatous inflammation, with microabscesses - consistent with tubo-ovarian abscess with fistulous tract to colon | Negative AFB | Tubo-ovarian abscess | Antibiotics |
| 3 | Abdominal pain, bloating, constipation, increasing abdominal girth, weight loss, night sweats, history of positive PPD, dry cough | 228 | CT A/P: carcinomatosis | Not performed | EL, TAH, BSO, omentectomy, anterior abdominal wall biopsy | Intraperitoneal granulomatosis, suspect tuberculosis | FS: anterior abdominal wall specimen with caseating granulomas<br>Fallopian tubes. ovaries, uterus, endometrium and omentum with caseating granulomatous inflammation. A single acid-fast organism identified. | Positive AFB | Pelvic tuberculosis | INH, rifampin, PZA, ethambutol |
| 4 | Abdominal pain and discomfort | 143 | CT A/P: large hypodense, 5 × 6 cm pelvic mass posterior to uterus and anterior to rectum | Normal | EL, TAH, BSO, peritoneal biopsies | Samll 4 cm uterus, 6 cm right ovarian mass, left ovarian mass with sebaceous fluid and hair. Extensive pelvic adhesions, Peritoneal studding. | FS: granulomatous inflammation, dermoid tumors, peritoneal inflammation<br>Peritoneal nodules, granulomatous inflammation, uterus myometrium granulomatous inflammation. Bilateral dermoids on ovaries, ruptured dermoid leaking granulomatous inflammation | AFB negative | Ruptured dermoid cyst | No further treatment |
| 5 | Diffuse abdominal pain, nausea, vomitting | Not collected | CT A/P: large (15x9 cm) multiloculated cystic mass compatible with ovarian neoplasm and partial SBO. | Not performed | EL, TAH, BSO, small bowel resection | Dense adhesions, dilated tubes | FS: not performed<br>Ruptured hemorrhagic corpus lutea, dilated fallopian tube with focal non-caseated granulomas | GMS and AFB negative | Ruptured hemorrhagic corpus luteal cyst | No further treatment |
| 6 | Abdominal pain | 9 | CT A/P: left adnexal mass measuring 5x6 cm and small 3x2.5 cm right ovarian cyst. | Normal | EL, BSO, left ureterolysis | Bilateral adnexal masses | FS: benign<br>Necrotizing palisading granulomas, focal endometriosis, non-polarizable foreign body giant cells | none | Prior endometriosis surgery | No further treatment |
| 7 | Increasing abdominal girth, shortness of breath, pulmonary embolus | 30.8 | CT A/P: Left ovary obliterated by adnexal mass 7 × 6 × 8cm, bilateral hydronephrosis, multiple colon and rectal adhesions. | Hyperinflated | EL, TAH, BSO | Normal right tube and ovary, normal uterus, left ovary replaced by abscess, multiple adhesions | FS: not performed<br>Left tube and ovary −granulomatous inflammation, positive for abscess | AFB and GMS stains negative | Tubo-ovarian abscess | Reoperation for post-operative colon perforation. Right colectomy and ileostomy, ICU |

(*continued on next page*)

**Table 1** (*continued*)

| Case Number | Presenting symptoms | CA- 125 | Preoperative Imaging | Chest X-Ray | Surgical Procedure | Surgical Findings | Histologic Findings | Microbiology | Diagnosis | Treatment |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | | | | | | admit, abscess drain, antibiotics |
| 8 | Abdominal pain | 56.5 | CT A/P: complex 12 × 8 × 9 mass left hemipelvis, lymphadenopathy, peritoneal carcinomatosis | Not performed | Diagnostic laparoscopy, left salpingo-oophorectomy, pelvic lymph node biopsy, omental and peritoneal biopsy | Large cystic left adnexal mass, ruptured intraoperatively with thick yellow fluid (consistent with pus vs other inflammatory response), white nodules throughout peritoneum, adhesions | FS: benign, inflammation, possible endometriosis appendix with fibrous obliteration, left ovary with extensive xanthogranulomatous inflammation, left tube with chronic salpingitis, adnexal remnant with fibroadipose tissue with xanthogranulomatous inflammation, omentum with extensive chronic inflammation | none | Xanthogranulomatous inflammation | Negative rheumatic work up. No further treatment. |

ruptured ovarian cysts. One case was a ruptured dermoid cyst, leaking sebaceous material into the abdomen (case 4) resulting in diffuse inflammatory granulomas and non-caseating granulomatous disease involving the ovary (Fig. 1). Mature cystic teratomas (dermoids) are common benign ovarian tumors, representing approximately 20 % of all ovarian tumors, but granulomatous peritonitis secondary to rupture is uncommon. (Suprasert et al., 2004) Ruptured contents including fat and hair are thought to cause a foreign body inflammatory reaction resulting in giant cell granulomas in the perineal cavity. There are a limited number of reports of ruptured dermoids mimicking ovarian cancer. Phupong *et al.* presented a patient who had an extensive staging procedure for presumed ovarian cancer as frozen pathology was not available when the surgery was performed. (Phupong et al., 2004) On the other hand, Suprasert *et al.* described two cases that were presumed advanced ovarian cancer. At the time of surgery, the tumors had hair and fat components indicating they were ruptured teratomas. (Suprasert et al., 2004) One patient still underwent a full staging procedure out of concern for malignant transformation. The patient described in this series had confirmation of granulomatous inflammation on frozen pathology but had diffuse peritoneal inflammation and underwent a major surgery (Table 1).

The second ruptured ovarian cyst in this series was a simple hemorrhagic corpus luteum (case 5). Additionally, our series describes granulomatous disease in a patient with endometriosis and a history of prior surgeries (case 6). To our knowledge, neither hemorrhagic corpus luteum nor endometriosis have been described as etiologies for diffuse granulomatous peritonitis. There are reports chemical peritonitis due to prior surgeries or cornstarch powder on surgical gloves resulting in foreign body granulomatous disease. (Phupong et al., 2004; Edlich et al., 2009) Unfortunately we have no records regarding the surgical gloves used in Case 6′s prior surgeries to determine if this could have been a contributing factor.

Xanthogranulomatous inflammation is a rare inflammatory process characterized by infiltration of granulation tissue and histiocytes, macrophages, and plasma cells that results in tissue destruction as seen in Fig. 2. It is more commonly seen in the gallbladder and kidney. Xanthogranulomatous oopheritis is rare with exact etiology unknown and can be localized or spread throughout the peritoneal cavity as was seen in Case 8. As demonstrated in Fig. 3, it can present with peritoneal nodularity and lymphadenopathy making it difficult to differentiate from metastatic disease. Associations have been made with prior infections, endometriosis, intrauterine devices, pelvic inflammatory disease, and certain pharmacologic agents. (Bhatnagar et al., 2018) The patient discussed in Case 8 did not have any of these risk factors. The patient completed a rheumatology workup without identification of a definitive cause, leaving the etiology unclear.

## 5. Conclusion

Granulomatous peritonitis can present like late-stage ovarian cancer. This review highlights diverse etiologies including tuberculosis, TOAs, ruptured ovarian cysts, and xanthogranulomatous disease and the importance of keeping a broad differential. Patients with granulomatous peritonitis, depending on etiology, may not require extensive surgical management. Clinicians should be aware of this disease to improve diagnosis, especially in the face of a history of tuberculosis. When granulomatous peritonitis is on the differential diagnosis, diagnostic laparoscopy with frozen section may be indicated before laparotomy and debulking.

### Consent

Written informed consent was obtained from the patient in case 8 for publication of this case series and accompanying images. Consent was not obtained from the other 7 cases due to time from case and/or patients lost to follow up. No identifying information was used for these cases.

### Author Contributions

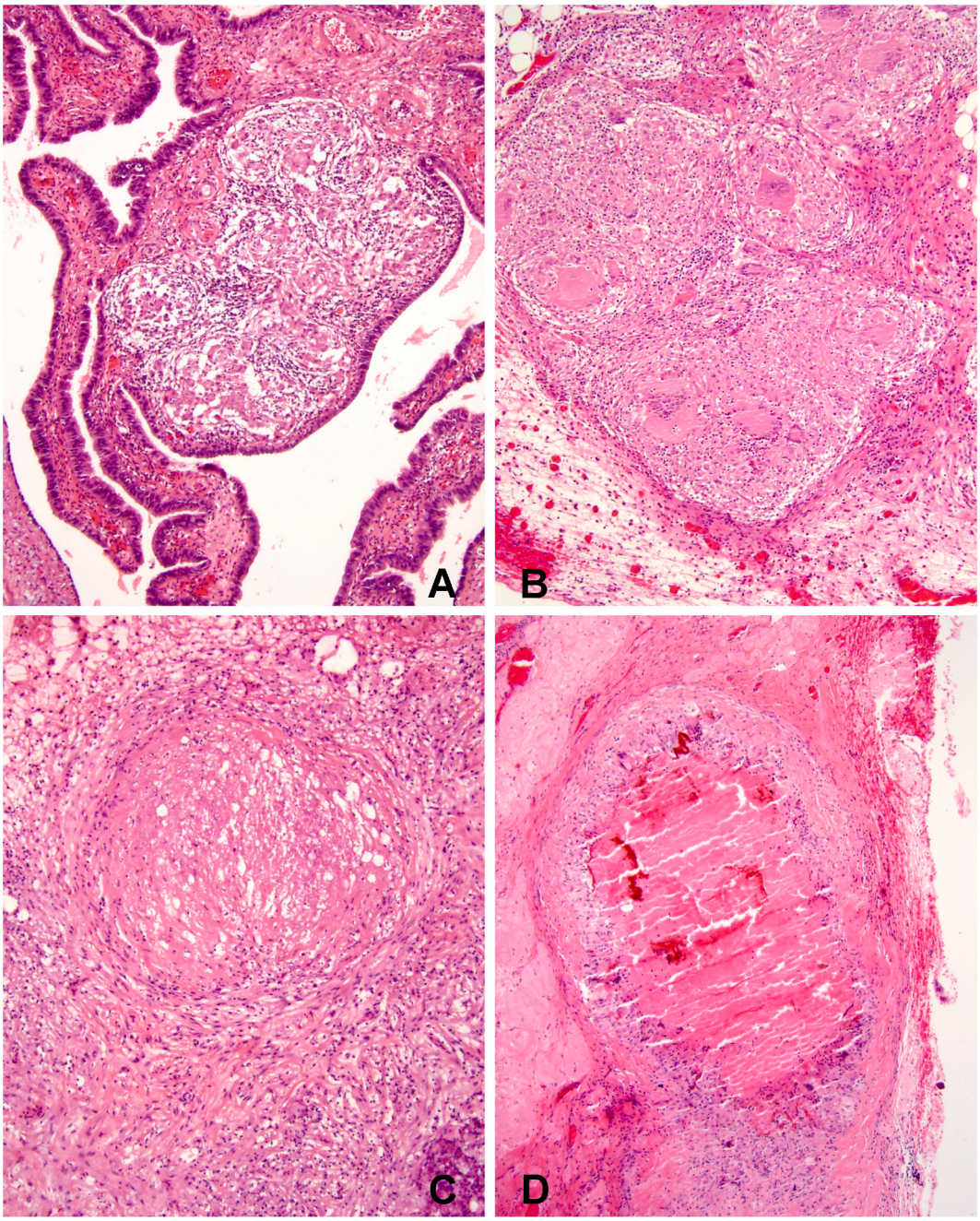


**Fig. 1.** Representative H&E stained sections of selected cases demonstrating the findings of granulomatous inflammation. Panel A: Non-necrotizing (non-caseating) granulomas involving the fallopian tube (case 5). Panel B: Focally necrotizing granulomas involving periadnexal soft tissue; note the numerous multinucleate giant cells (case 3). Panel C: Non-caseating granuloma involving the peritoneum (case 4). Panel D: Necrotizing granuloma involving the ovary (case 6).

All authors listed provided significant contributions to the manuscript. R.L. Furuya assisted in conceptualization, writing the original draft, and reviewing and editing. R. Tsai assisted with visualization, data curation, and reviewing and editing. B.R. Rimel, R.A. Brooks, and L.S. Massad assisted in data curation and reviewing and editing. P.H. Thaker and J.D. Pfeifer assisted in data curation, reviewing and editing and supervising the team.

## CRediT authorship contribution statement

**Rachel L. Furuya:** Conceptualization, Writing – original draft, Writing – review & editing. **Bobbie J. Rimel:** Data curation, Writing – review & editing. **Richard Tsai:** Data curation, Visualization, Writing – review & editing. **Rebecca Ann Brooks:** Data curation, Writing – review & editing. **L. Stewart Massad:** Data curation, Writing – review & editing. **Premal H. Thaker:** Data curation, Supervision, Writing – review & editing. **John D. Pfeifer:** Data curation, Supervision, Writing – review & editing.

## Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: Some of the authors are editorial board members of Gynecologic Oncology Reports and were not involved in editorial review or decision to publish the article. Some of the authors declared potential competing interests which were listed on their conflict of interest forms.

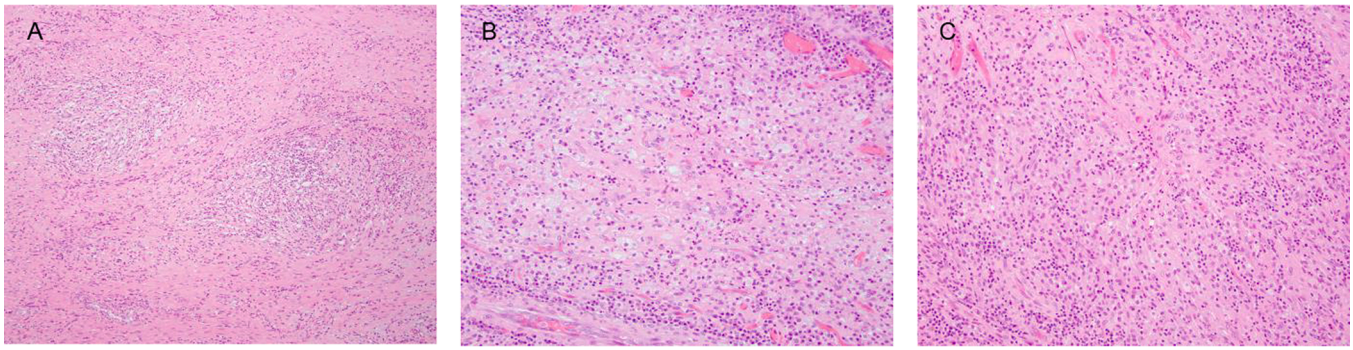


**Fig. 2.** Granulomatous peritonitis with a xanthogranulomatous pattern. A: Scattered non-caseating granulomas in a background of inflamed fibrotic stroma. B: Vague granuloma with prominent lipid-laden macrophages (xanthoma cells). C: Areas of confluent chronic inflammatory cells and xanthoma cells.

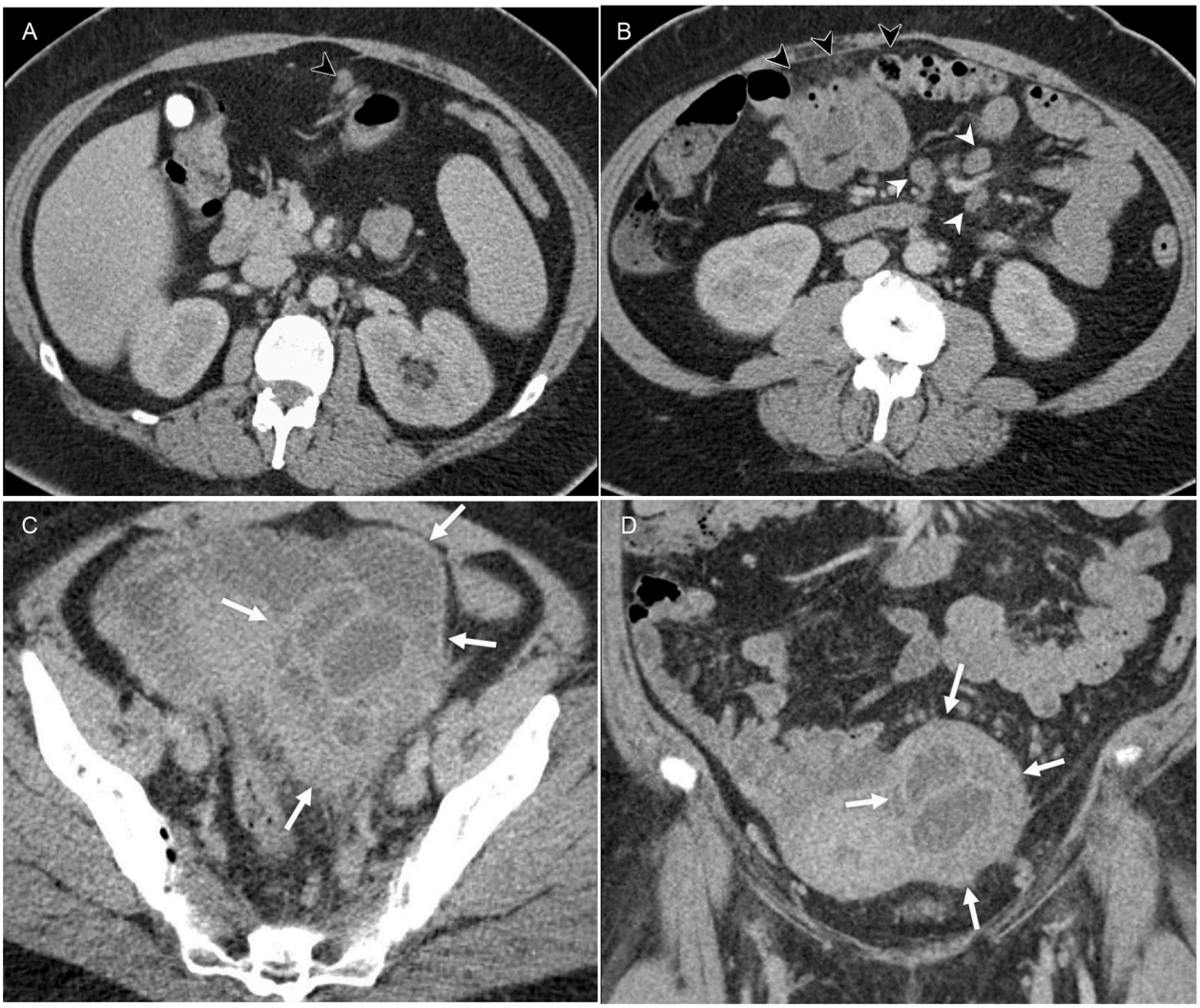


**Fig. 3.** 38-year-old female with ovarian mass. Axial (A, B, and C), and (D) coronal post-contrast CT images of the abdomen and pelvis demonstrate a complex, multiloculated, left adnexal cystic and solid mass with surrounding inflammatory changes (white arrows). Studding and nodularity of the greater omentum was also present (black arrows). Enlarged mesenteric lymph nodes were also seen throughout the abdomen (white arrowheads).

## Data availability

Data will be made available on request.

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