

The contribution of imaging in the diagnosis of borderline ovarian tumours: about 28 cases.

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Summary

Borderline ovarian tumors (BOTs) represent 15 to 20% of epithelial tumors of the ovary, and generally affect young women. Their prognosis is much better, with a survival of 95% at five years and 90% at 10 years. Imaging has a major role in the diagnostic, prognostic and therapeutic approach, allowing a better management, avoiding recurrences and preserving fertility in young patients. Our work is a retrospective study of 28 cases of BOTs, collected at the Mother-Child Radiology and Gyneco-obstetrics departments of the CHU HASSAN II in Fez, spread over a period of 5 years and 6 months, from January 2015 to June 2020. Which allowed us to evaluate the epidemiological and clinical profile, to describe the radiological signs of BOTs and their histological subtypes, to specify the role of imaging, and to correlate results with the anatomopathological data. Pelvic MRI was performed in 43% of our patients, and allowed characterization of BOTs and their histological subtypes with high sensitivity and specificity (17 serous, 8 mucinous and 3 mixed).

Keywords: Borderline, Ovary, MRI.

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I. Introduction

Borderline ovarian tumors (BOT) represent 15 to 20% of epithelial ovarian tumors and generally affect young women for whom fertility preservation is an important therapeutic issue [1].

This group of tumors was recognized in 1971 by the International Federation of Gynecology and Obstetrics (FIGO), as carcinomas of reduced malignancy. Adopted in 1973 by the World Health Organization (WHO) defining borderline tumors by histopathological characteristics intermediate between benign and malignant tumours. In 2003, the WHO definitively excluded the term carcinoma and introduced the denomination of "tumors with low malignant potential" or "borderline tumors of the ovary" [1].

BOTs are distinguished histologically from malignant tumors by the absence of infiltration of the ovarian stroma by tumor cells and they are distinguished from benign tumors by the presence of one or all of the following histological features: epithelial budding, pluri-stratification, significant mitotic activity with nuclear atypia [2].

BOTs have an age of onset, generally 10 years earlier than invasive ovarian tumors, with a better prognosis, a survival of 95% at five years and 90% at ten years, all stages combined. [1].

Imaging and essentially MRI plays an important role in the management of ovarian masses, allowing conservative treatment to be considered.

The aim of this retrospective study spread over a period of 5 years and 6 months from January 2015 to June 2020 on a series of 28 cases of BOT, collected in the department of Radiology and the two departments of Gynecology and Obstetrics of the CHU Hassan II of Fez, is to review our experience on borderline tumors of the ovary, By highlighting the epidemiological profile, the clinical and radiological characteristics, the radio-anatomopathological correlation, and the diagnostic difficulties.

II. Methods

Retrospective study conducted on borderline ovarian tumors in the Mother-Child Radiology department and the two Gynecology-Obstetrics departments of the CHU Hassan II in Fez. Over a period of 5 years and 6 months from January 2015 to June 2020, during which 28 cases of BOT were recorded.

The cases included in the study are patients who had BOT during the above-mentioned period, diagnosed radiologically and confirmed histologically. All patients without histological confirmation were excluded.

III. Results

In our study, there were 17 cases (60.71%) of serous BOT, 08 cases (28.57%) of mucinous BOT, and 03 cases (10.71%) of sero-mucinous BOT (mixed). The mean age was 49.50 years with an age range of 17 years to 84 years. The most represented age group was between 40 and 60 years with a percentage of 42.85% (12 patients). 11 patients (39.3%) were nulliparous, 04 patients (14.3%) primiparous and 13 patients (46.4%) multiparous. None of our patients had a family history of breast, ovarian, colon or endometrial cancer.

Chronic pelvic pain was the most frequent complaint in 16 patients (57.1%). Abdominal distension was described in 13 patients (46.4%). And only 03 patients (10.7%) had acute pelvic pain. An abdominopelvic mass was perceived in 04 patients (14.3%). The discovery was incidental in 04 patients (14.28%).

Clinical examination was unremarkable in 06 patients, 12 of our patients had a clinically palpable abdominopelvic mass ranging in size from 6 cm to 30 cm.

Ten patients were tested for ovarian tumor markers (35.71%). The results were normal in 05 patients (50%) while 05 patients (50%) had high markers.

Pelvic ultrasound (Figures 1, 2) was performed in 26 patients (92.85%), and showed an adnexal mass in all cases. The size of the masses ranged from 1.7 cm to 25 cm with a mean value of 12.29 cm. The location of the masses was unilateral in 23 patients (88.5%) and bilateral in only 03 patients (11.5%). The aspect of the cystic component was unilocular in 09 patients (06 serous BOT, 02 mucinous BOT, and 01 sero-mucinous BOT), paucilocular in 02 patients (one mucinous BOT, and one serous BOT), multilocular in 10 patients (05 serous, 04 mucinous, and one sero-mucinous BOT), and unspecified in 05 patients.

The ultrasound appearance of the ovarian masses according to the IOTA classification was indeterminate, which could be related to BOT in 16 cases (61.5%), benign in 02 cases (7.7%), and malignant in 08 cases (30.8%).

Pelvic MRI was performed in 12 patients (43%). The size of the masses ranged from 4.6 cm to 20 cm with a mean value of 13.6 cm. The location of the masses was unilateral in 09 patients (75%) and bilateral in only 03 patients (25%). The size of the endocystic vegetations was specified in 07 patients (58.33%). The size varied between 5 mm and 35.5 mm with a mean value of 19.5 mm. The vegetations were in hypersignal T2. The appearance of the cystic component was unilocular in 05 patients (04 serous, and 01 mucinous), paucilocular in 02 patients who had a serous BOT, multilocular in 04 patients (02 mucinous, and 02 serous), unspecified in one patient. 01 patient (8.3%) had benign criteria, 08 patients (66.7%) had criteria suggesting a borderline tumor, and 03 patients (25%) had malignant criteria.

The MRI criteria pointing to borderline ovarian tumors found in our patients are summarized in Table 1, with demonstrative MRI images (Figures 3, 4, 5, 6).

CT was performed in 18 cases (64.3%). The size of the ovarian masses ranged from 4.7 cm to 33 cm with a mean value of 18.58 cm. The location of the masses was unilateral in 15 patients (83.3%) and bilateral in 03 patients (16.7%). Endocystic vegetations were found in 04 patients (22.3%) with a size ranging from 16 mm to 30 mm with a mean value of 22.5 mm. The aspect of the cystic component was unilocular in 04 cases corresponding to a serous BOT, paucilocular in 04 cases corresponding to serous BOT, multilocular in 05 cases including 02 cases of mucinous BOT, 02 cases of mixed BOT (sero-mucinous), 01 case of serous BOT, and unspecified on the CT reports done in private practice in 05 cases.

The CT appearance of the ovarian masses (Figures 6) was in favor of benign lesions in 04 cases, malignant in 02 cases, 06 cases had criteria pointing to a borderline tumor of the ovary, and undetermined in 06 cases due to lack of information in the external scanner reports.

In our series the tumors were classified stage I in 23 cases (82.14%), 13 classified I a, 5 classified I b (bilateral) and 5 classified I c (ascites or exocystic vegetation), stage III in 04 cases (14.28%), 02 classified III a and 02 classified III b. One patient had a serous BOT with a micropapillary component and foci of microinvasion.

The treatment was radical in 19 patients (67.8%), and conservative in 09 patients (32.2%). 08 patients were reoperated after the final anatomopathological examination. 05 patients received adjuvant treatment consisting of complementary chemotherapy, due to the presence of a micropapillary component and/or a focus of micro-invasion and/or a peritoneal implant.

The anatomopathological result showed a **serous BOT** in 17 patients (60.71%), a **mucinous BOT** in 08 patients (28.57%), and a **mixed BOT** in 03 patients (10.71%).

Lymph node curage was unremarkable in 02 cases, and in favour of a nonspecific reactive adenitis for an adenectomy in 01 cases. 11 patients had benefited from an additional appendectomy, whose anatomopathological results showed a case of appendicular mucocele, a case of chronic appendicitis.

IV. Discussion

BOTs are rare epithelial tumors, representing 15 to 20% of epithelial tumors of the ovary, with a low invasive potential, their discovery in a period of genital activity poses a problem of fertility preservation. The different imaging techniques such as transvaginal ultrasound with Doppler, CT and especially MRI allow a better characterization of these masses and a good differentiation of the histological subtypes (serous and mucinous) in order to avoid unnecessary surgery, especially in young women wishing to become pregnant [3].

In the literature, the mean age of onset of BOT is ten to twenty years earlier than that of ovarian carcinoma [4, 5]. Anfinan N et al. reported that the mean age of patients at the time of diagnosis was 46 years with an age range that varied between 16 to 80 years [4].

In our study, the average age of our patients was 49.5 years with an age interval that varies between 17 and 84 years. The most represented age group was between 40 and 60 years (43%).

There are no specific clinical signs of BOT. It is either an incidental finding of an ovarian tumor during a gynecological or ultrasound examination or non-specific clinical signs most often related to pelvic pain, increased abdominal volume, perception of a mass by the patient and/or menstrual disorders.

For tumor markers, our study found a rate similar to that of the literature, the CA 125 positivity rate was higher in serous BOT (4/5, 80%) than in mucinous BOT (1/5, 20%). A normal CA 125 level does not rule out BOT [5]. Preoperative CA 19-9 levels are higher in mucinous BOT.

Accurate pre-operative diagnosis of ovarian tumors is essential for appropriate treatment. Currently, new imaging techniques make it possible to characterize lesions, and to reduce the indications for diagnostic surgery in favor of controlled surgery for both malignant and benign tumours.

Ultrasound is the first-line imaging technique for characterizing of ovarian masses, suprapubic ultrasound is supplemented by transvaginal ultrasound except for contraindications such as virginity.

A set of descriptive terms was proposed by the IOTA (International Ovarian Tumor Analysis) group as early as 2000 [6]:

Septum: is defined as a fine tissue-like echogenic structure crossing the cyst from one edge to the other without discontinuity. It is incomplete if it appears interrupted in certain slice.

Solid structure: corresponds to an echogenic formation evoking the presence of a tissue component. The diffuse parietal thickening, a regular septum and the normal ovarian stroma located outside the cyst are not considered as solid structure.

Vegetation or papillary structure: is a focal solid formation protruding into the cavity of a cyst from its wall and having a height equal to or greater than 3 mm. It may be regular or irregular.

Internal wall: can be regular or irregular.

The IOTA classification is based on 2 main criteria (uni or multilocular, solid or liquid lesion) [7]. The IOTA group has validated 5 ultrasound criteria of benignity (B) and 5 criteria of malignancy (M) allowing the clinician to be guided towards a malignant or benign lesion:

_If one or more M criteria apply in the absence of B criteria, the mass is classified as Malignant.

_If one or more B criteria apply in the absence of M criteria, the mass is classified as benign.

_If M criteria and B criteria apply, the mass cannot be classified.

_If none of the criteria is applicable, the mass cannot be classified.

Ultrasound characteristics of borderline ovarian tumors: [6]

➤ **Borderline serous cystadenoma**, which is bilateral in one third of cases, affects young women (30 to 50 years old) or even adolescents and represents 50-60% of borderline tumours. It is a cystic lesion most often uni- or paucilocular, of variable size often greater than 50 mm, containing endocystic vegetations of more than 7 mm. more or less numerous, without a solid portion, with a central color or power Doppler flux confirmed by spectral recording. The presence of a crescent sign confirms the ovarian origin and reduces the risk of invasive lesion.

False negatives are represented by the absence of detection of vegetations or vascularization and false positives by the confluence of the vascularized vegetations making suspect a solid portion. The absence of a solid portion is a major differential diagnostic element to eliminate serous carcinoma.

➤ **Borderline mucinous cystadenoma** accounts for 40% of borderline tumors. Two types were classically described (WHO 2003). The endocervical type (15%) with an average age of 30 years and the intestinal type (85%) occurring at an average age of 45 years [6]. Fruscella et al. [80] recently clarified the sonographic aspects pointing to intestinal and endocervical type lesions:

✓ **Endocervical lesions** are often bilateral (40%) and look similar to borderline serous lesions with a relatively small size and few locules. These lesions are usually unilocular cystic with numerous vascularized vegetations;

✓ **Intestinal-type lesions** are often unilateral (90%), of viscous content related to intracystic mucin, larger in size 15 to 30 cm, multilocular with a number of locules greater than 10, and solid lesions less frequently observed. These borderline intestinal tumors are responsible, with appendicular tumors, for the majority of pseudomyxomas of the peritoneum. The ultrasound appearance is that of a heterogeneous mixed partitioned pelvic mass that can simulate an agglutination of intestinal loops.

Tumors remaining indeterminate after ultrasound performed by an experienced operator were largely represented by borderline ovarian tumors [8]. In our study, the majority of patients (16 cases), had an indeterminate ultrasound appearance suggesting BOT.

When the tumor is complex or larger than 70 mm, transvaginal ultrasound TVUS cannot accurately detect and analyze solid tissue far from the probe, and MRI is useful in this context [9].

The MRI protocol must include morphological sequences, axial T1 and T2 in orthogonal planes (axial, sagittal and coronal) associated with so-called “functional” imaging sequences, diffusion and perfusion. The latter, usefully complementing the morphological analysis in order to better approach the anatomopathologic *gold standard*.

To characterize an adnexal mass on MRI, it is recommended to include a malignancy risk score (type ADNEX MR/O-RADS) in the report and to formulate an anatomopathological hypothesis. This ADNEX MR score, combining morphological and functional criteria, demonstrated a sensitivity of 94.9% and a specificity of 97.5% to predict malignancy with a high level of reproducibility regardless of the reader’s experience [10].

In addition to the morphological criteria previously described on ultrasound, the vegetations of BOT present in intermediate T2 hypersignal, are enhanced mainly according to a type 2 curve, and are restrictive in diffusion [10].

To differentiate BOTs from malignant ovarian tumors, it is important to be able to distinguish vegetation from a solid portion. The vegetation corresponds to a papillary structure with an acute connection angle to the cystic wall, while the solid portion corresponds to a thickening of the wall.

Low- and high-grade invasive tumors more rarely present with vegetations (32.3% and 7% respectively) with tissue portion sizes twice as large (50 mm and 62 mm respectively versus 26 mm) as that of BOT [11].

These are tumors with potential for malignancy that are usually localized to the ovary. However, somewhat paradoxically, these tumors may be associated with distant dissemination in the form of non-invasive peritoneal implants or lymphadenopathy [12].

In the case of mucinous BOT (intestinal type), a primary of the digestive tract, pancreato-biliary or urachus must be eliminated, the most frequent primary lesion being the primary appendicular mucinous lesion [13].

Typical borderline mucinous tumors are:

- voluminous,
- Multilocular, with loculi presenting variable signal intensity in T1 and T2 weighting
- The septa usually appear numerous, thick and irregular.

In total, our series had radiological characteristics very similar to those of the literature. 12 of our patients benefited from an MRI, which made it possible to specify the borderline character of the ovarian tumors in 8 cases (66.7%).

In our work, the serous BOTs were in the majority of cases, unilocular and paucilocular cystic masses containing endocystic vegetations with a diameter greater than 3 mm, in T2 hypersignal, restrictive in diffusion and significantly enhanced according to a curve type 2 after injection. Mucinous tumors presented as large cystic lesions, multilocular with different signal from the loculi on T1 and T2 weighting.

MRI is a powerful examination to characterize ovarian masses with sensitivity in our study:

- Of 100% taking into consideration the results of the examinations carried out at the Fez University Hospital.

- 67% taking into account all the results of the examinations carried out at the CHU and externally.

During the 5 years and 6 months of our work, we only found 05 cases of radiological false positives, the most atypical of which are represented by the following 02 cases with anatomopathological results not in favor of borderline tumour.

✓ A case of ovarian tuberculosis (Figure 7), which simulated ovarian cancer. We must always think of pelvic tuberculosis each time it is a young patient coming from a country where tuberculosis is endemic or having an immunosuppression.

✓ A case of a Granulosa cell tumor, its preoperative imaging diagnosis is a challenge, given its great morphological variability and the lack of epidemiological and semiological data in the radiological literature.

CT is an irradiating technique that should be offered only as third-line after pelvic MRI due to a low PPV of around 60%. It allows the characterization of mature cystic teratomas. It is recommended to perform a thoraco-abdomino-pelvic scan with injection for the pretherapeutic extension assessment. In case of contraindications to the injection of iodinated contrast agent, abdominal and pelvic MRI can be proposed, supplemented by a chest CT scan without injection.

PET-CT (Positron Emission Tomography) can be useful to look for recurrences in patients with elevated tumor markers with normal ultrasound and MRI.

Limites

The study excludes patients operated on the data of the ultrasound made by a non-radiologist doctor who mentioned another often benign diagnosis.

V. Conclusion

Borderline ovarian tumors (BOT) represent 15 to 20% of malignant ovarian tumors and occur in a one third of cases in women under 40 years who have not always accomplished their pregnancy plan.

In the majority of cases, BOTs are discovered at an early stage, defined by damage limited to one or two ovaries (FIGO I stage). The survival rate is high with an overall survival greater than 94% at 10 years. The risk of recurrence in the invasive form is low, varying between 0.5 and 3.8%.

BOTs are characterized by non-specific clinical symptoms, incidental discovery during a gynecological or radiological examination, or non-specific clinical signs, pelvic pain, an increase in abdominal volume associated or not with the perception of an abdominal mass.

The development of different imaging techniques allows a better characterization of ovarian masses by diagnosing borderline, benign and malignant tumors as well as a good differentiation of the histological subtypes of BOT (serous, mucinous and others).

Endovaginal and/or suprapubic ultrasound is the first-line examination when for ovarian lesion, and its classification must be based on the international criteria defined by the IOTA group.

Magnetic resonance imaging (MRI) is indicated as a second line to characterize indeterminate or large masses poorly explored in their entirety by ultrasound, thus allowing differentiation of the histological subtypes of BOT and optimizing therapeutic management, particularly surgery.

Computed tomography (CT) is the reference examination for the assessment of extension and resectability.

Choosing the right treatment for each patient is a great challenge for the practitioner. The use of conservative treatment is recommended for young women wishing to become pregnant, with close and regular monitoring.

Monitoring is based on a combination of clinical examination, dosage of tumor markers, in particular CA 125 if initially high, and ultrasound.

In general, the management and the follow-up of BOT are multidisciplinary, involving radiologist, surgeon, pathologist and oncologist with an excellent prognosis.

What we already know about this topic

- MRI is necessary for tissue characterization of ovarian masses.
- The vegetations of BOT present in intermediate T2 hypersignal, restrictive in diffusion, and are enhanced according to a type 2 curve.
- Mucinous cystadenoma of the endocervical type resembles to borderline serous cystadenoma.

What this study adds:

- Ultrasound and scanner can be the cause of false negatives in case of small vegetations.
- Serous borderline tumor of the ovary may have a multiloculated component.
- We must always think of pelvic tuberculosis, which can be the cause of false positives, each time it is a young patient coming from a country where tuberculosis is endemic or having an immunosuppression.

Conflicts of interest

The authors have declared that they have no conflict of interest

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Tables and figures

Table 1: Distribution of patients according to predictive MRI criteria for borderline ovarian tumors

MRI CRITERIA PREDICTIVE OF BORDERLINE TUMOR	NUMBER OF CASES (12 cases)	%
Endocystic vegetations	09	75
Hypersignal T2 of the vegetations	09	75
Restriction of spreading vegetation	06	50
Size of endocystic vegetations >3mm	07	58.3
Type 2 enhancement curve for vegetation	05	41.6
Thick wall	01	8.3
Intraperitoneal effusion of low abundance	06	50
Peritoneal carcinomatosis	02	16.6
Lymphadenopathy	01	8.3

Figure 1: Endovaginal ultrasound showing a cystic lesion in the ovary with a crescent sign (white arrow) and containing vascularized vegetation on Doppler (star)

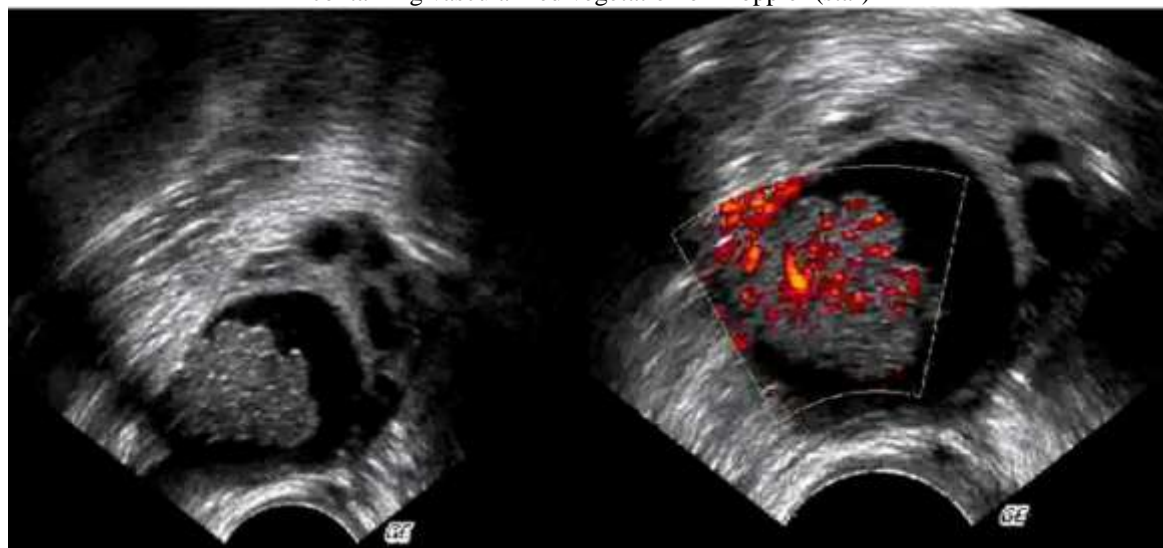


Figure 2: Endovaginal ultrasound showing a multilocular ovarian cystic lesion containing several septa and some vegetations

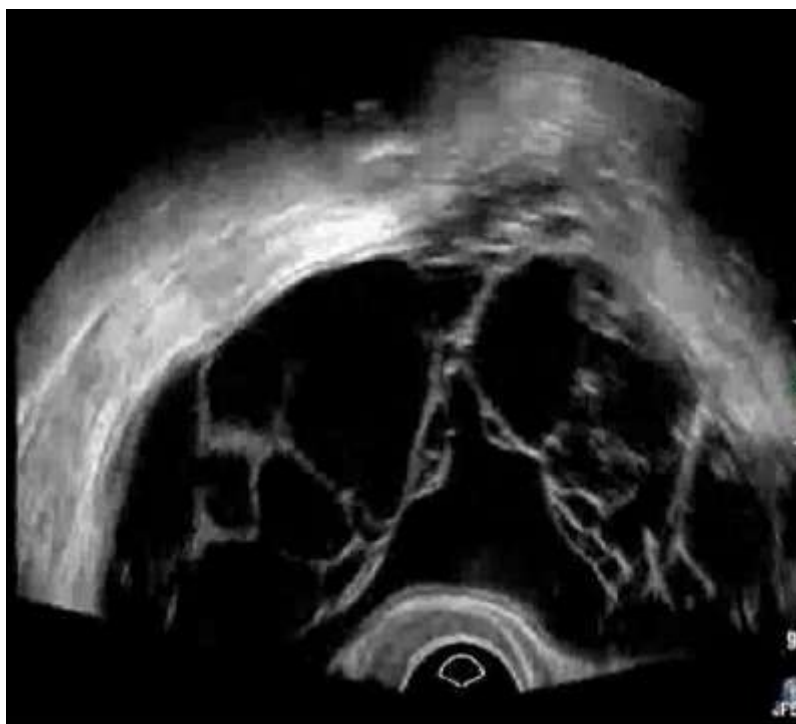


Figure 3: Pelvic MRI: Right unilocular cystic mass, containing vegetation (white arrow) in T2 hypersignal, restrictive in diffusion, and weakly enhanced after contrast, according to a type 2 curve. **Appearance of a borderline ovarian serous cystadenoma**
Anapath: borderline serous cystadenoma

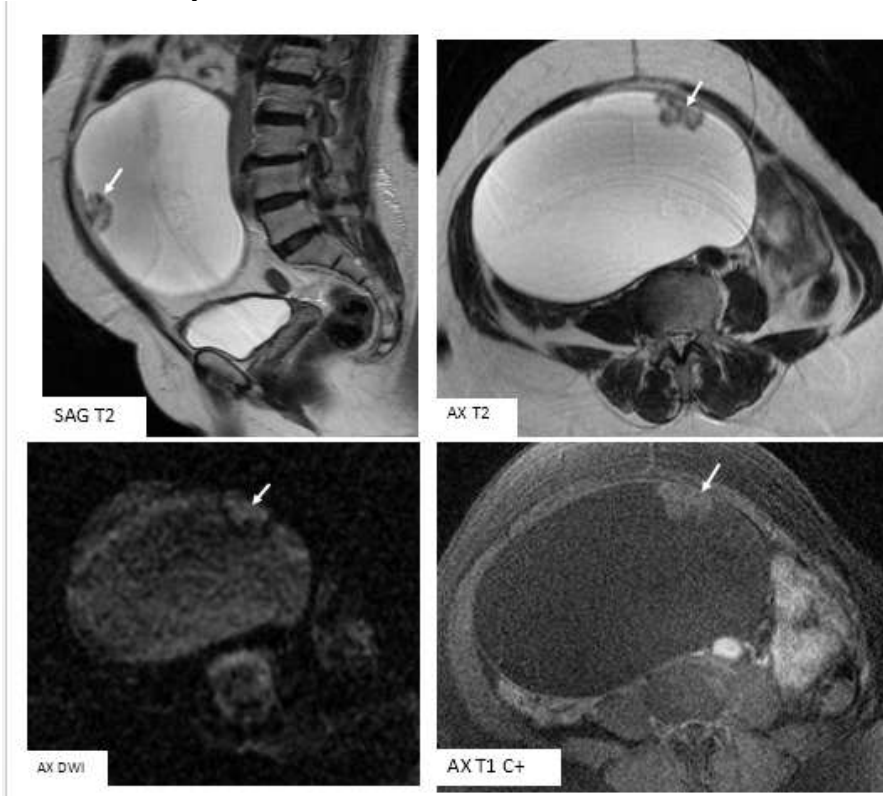


Figure 4: Pelvic MRI: large right bilocular cystic mass (black arrow showing a septum), containing several endocystic vegetations (white arrow) in hypersignal T2, restrictive in diffusion, and weakly enhanced after contrast, according to a type 2 curve, with a minimal effusion at the level of the cul-de-sac of Douglas (white star). **Appearance of a micropapillary borderline ovarian serous cystadenoma.**
Anapath: Serous TOB with micropapillary component.

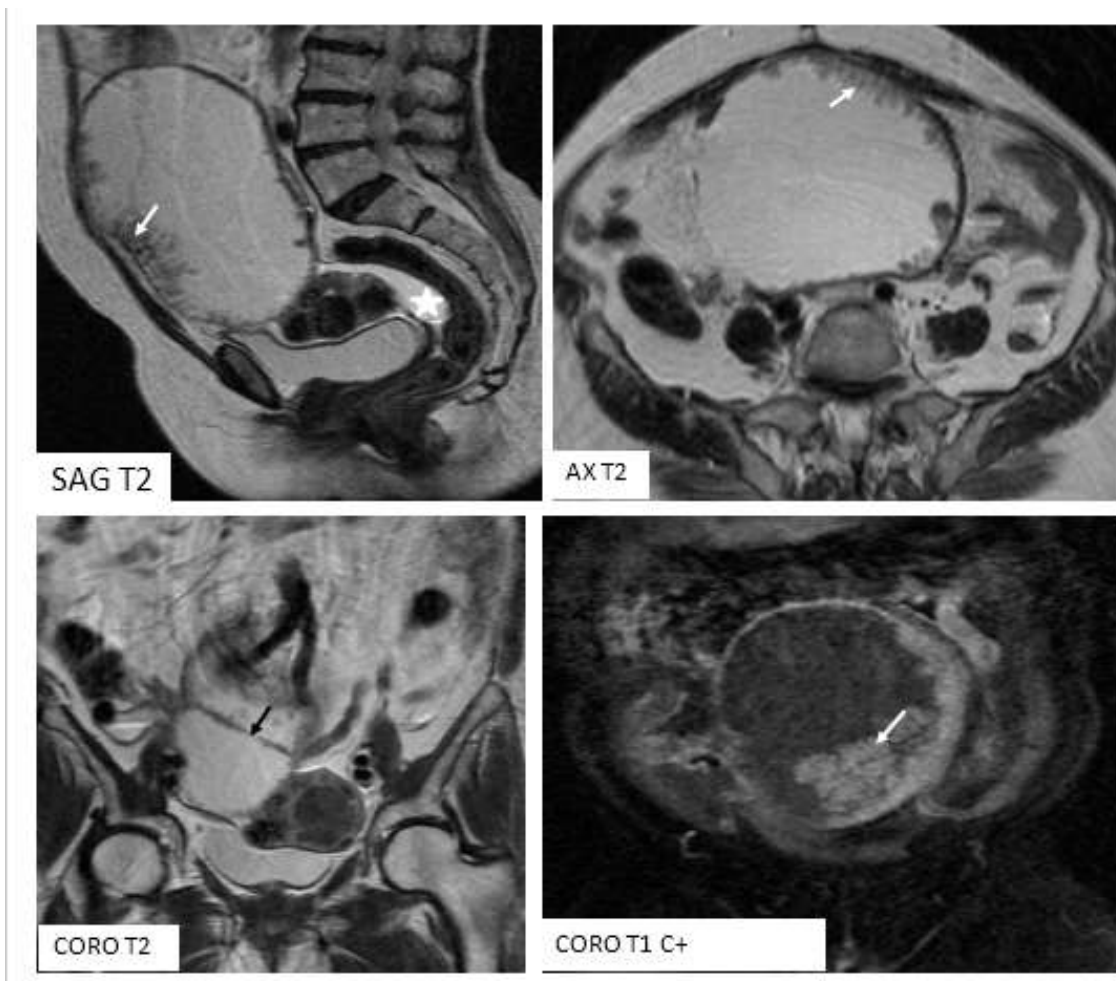


Figure 5: Non-injected pelvic MRI of a pregnant patient showing multiloculated right cystic ovarian mass, containing vegetations (white arrow) in T2 hypersignal, restrictive in diffusion, Appearance of a borderline ovarian mucinous cystadenoma.
Anapath: Right ovarian mucinous TOB

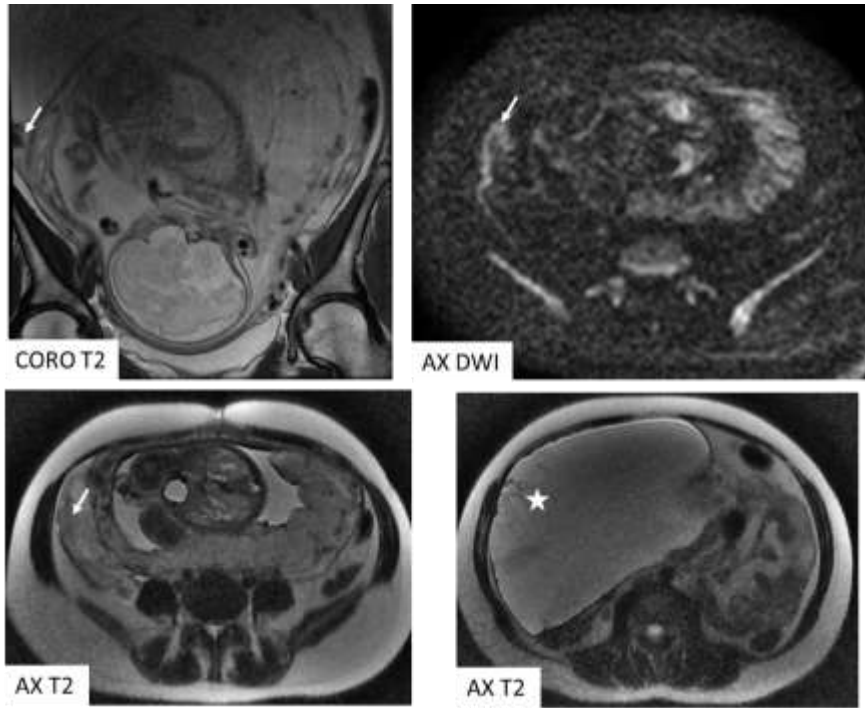


Figure 6: CT TAP in axial section (a, b) and sagittal reconstruction (c): voluminous right ovarian abdomino-pelvic mass (star), with triple component: solid, calcic and cystic mostly multiloculated with enhancement of the fleshy portion and septa after contrast. Effusion of great abundance (black arrow). Contralateral ovary increased in size and heterogeneous in relation to its age (white arrow).
Radiological aspect in favor of a mucinous right ovarian cystadenocarcinoma .
Anapath: Mucinous TOB of the right ovary

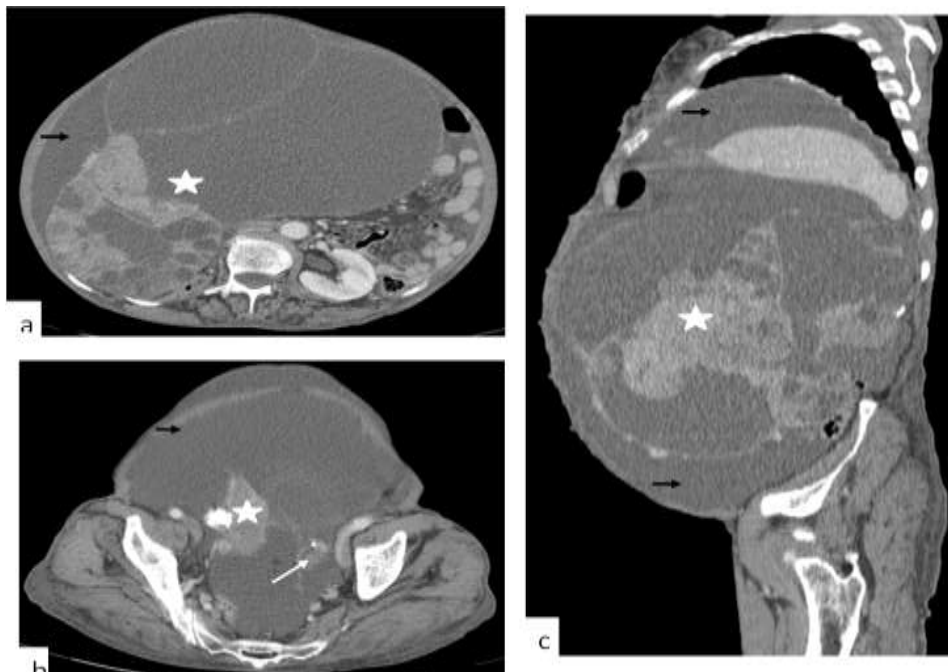
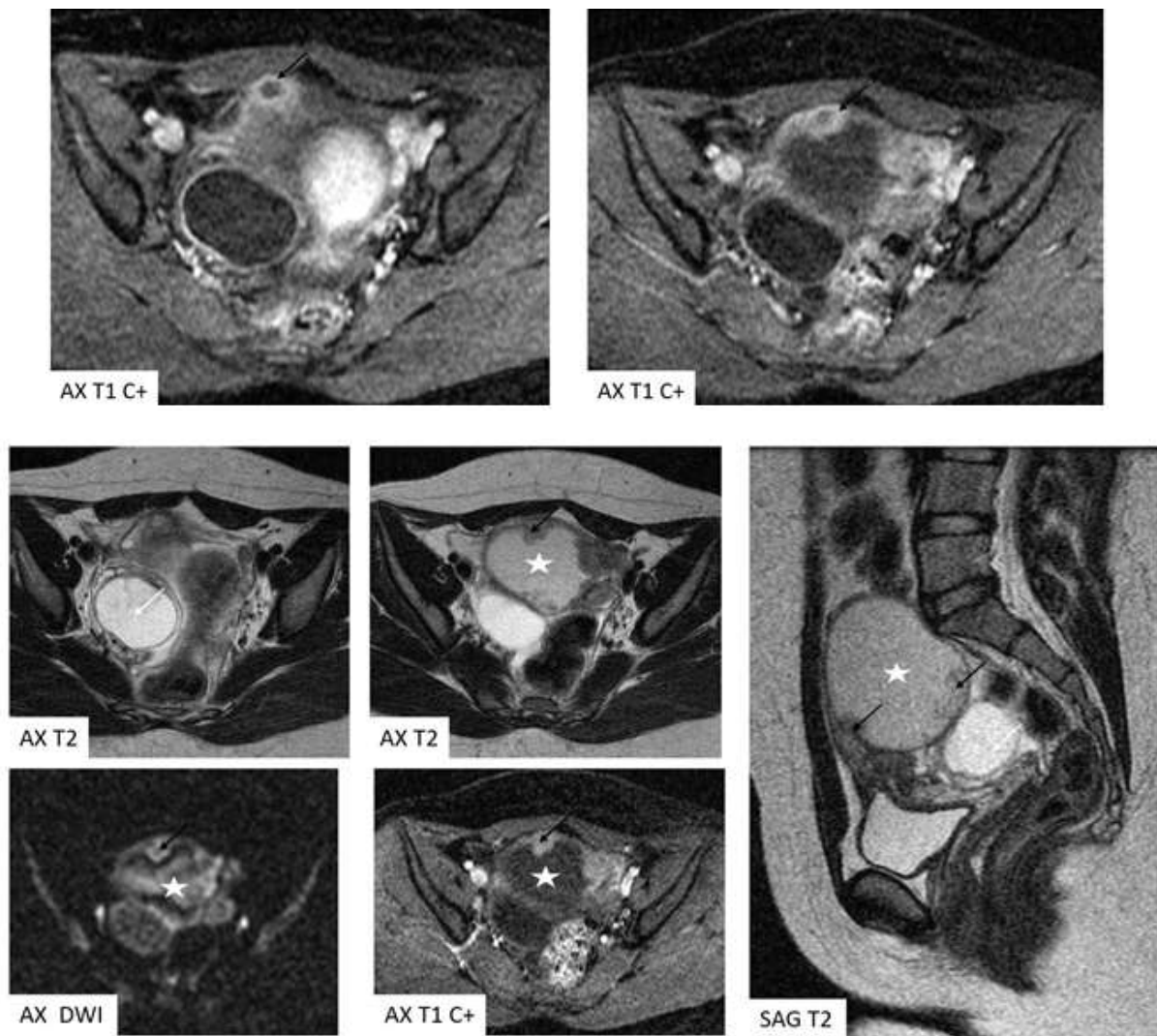


Figure 7: Pelvic MRI showing central necrosis of the vegetation (black arrow), suggesting tuberculosis.



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