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CASE REPORT

Struma Ovarii with Papillary Thyroid Carcinoma and Metastasis to the Appendix: A Case Report and Literature Review

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Abstract: Struma ovarii is an infrequent type of teratoma arising from the ovary accounting for only 2% of all ovarian teratomas. These tumors have a benign biology with rare malignant transformation in about 3% of cases. The most common malignant transformation that arises from struma ovarii is papillary thyroid carcinoma. These neoplasms act in the same way as those arising from the thyroid gland, but due to the rarity of their occurrence there is still a debate over therapeutic options. We present a case of a 41-year-old Ethiopian Para IX woman presented with abdominal swelling for four years, accompanied by dull pain, satiety, and weight loss. Her vital signs were normal, and her abdominal examination revealed a large abdominopelvic mass. Her CA-125 was elevated, and her blood count, organ function tests, and serum electrolyte levels were normal. Abdominal ultrasound revealed a complex abdominopelvic mass with cystic and solid components, possibly ovarian teratoma. The patient underwent surgery, revealing a 14 by 10 cm right ovarian mass and a 3×3 cm appendiceal mass. Subsequently, total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, and appendectomy was done. Histopathologic evaluation revealed follicular proliferation of enlarged cells, with no papillary growth pattern. The case was diagnosed as malignant struma ovarii, a follicular variant of papillary thyroid carcinoma (FVPTC) with secondary deposits on the appendix. A complete thyroidectomy was done after the histopathology diagnosis. Malignant struma ovarii is rare making it challenging to treat since there are no established prognosticating histopathologic or clinical characteristics. The tumor size and metastasis determine the surgical treatment scope. Large-scale investigations are essential for prognostication and treatment options considering pathologic traits.

Keywords: struma ovarii, papillary carcinoma, malignant, appendix, metastasis, teratoma

Introduction

Ovarian germ cell tumors are fairly common neoplasms accounting for about 20% of all ovarian tumors.[1] Different types of germ cell tumors include Dysgerminoma, Teratoma, Yolk sac tumor, embryonal carcinoma, and choriocarcinoma. Mature cystic teratoma is the most common type of ovarian teratoma. It is composed of mature components that represent the three germ layers – the ectoderm, the mesoderm, and the endoderm with the former being the predominating component in almost all cases; 15% of teratoma cases have thyroid tissue as a component.[2,3] When thyroid tissue makes up more than 50% of the teratoma, struma ovarii is diagnosed.[2,4–6] Only 2% of adult teratomas are struma ovarii and less than 5% of struma ovarii exhibit malignant transformation.[1–4,7–10] Here we present a case of papillary thyroid carcinoma as a malignant transformation of the thyroid tissue of a struma ovarii with a metastatic deposit to the appendix along with a review of relevant previous works in the literature.

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Case Presentation

A 41-year-old Para IX Ethiopian woman presented with abdominal swelling of 04 years duration with associated dull aching abdominal pain, early satiety, and significant weight loss. The swelling was initially small but progressively enlarged. She has irregular menses coming every 2 to 4 weeks. Otherwise, she had no history of foul-smelling vaginal discharge, vomiting, diarrhea, or bowel habit changes. She had no history of any known chronic illness.

On physical examination, her vital signs were within normal limits. She had no lymphadenopathy. Her chest was clear and resonant. Abdominal examination revealed a huge abdominopelvic mass, which was non-tender and firm in consistency. On pelvic examination, the cervix is firm and irregular but no visible mass, discharge, or cervical motion tenderness.

Upon investigation, her CA-125 is elevated (61.3 U/mL). Her complete blood count, organ function tests, and serum electrolyte levels were in the normal range. The chest x-ray was also normal. Abdominal ultrasound showed a huge and complex abdomino-pelvic mass with a cystic and solid component which had fat and calcification and ill-defined margins with an index of right adnexal mass secondary to likely ovarian teratoma.

With the assessment of abdominopelvic mass secondary to mature cystic teratoma, the patient was operated on. Intra-operatively, there was a 14 by 10 cm right ovarian mass with a smooth non-fragile capsule and a 3×3 cm mass on the appendix with a firm attachment to the ovarian mass. The ovarian mass had attachments with the overlying peritoneum, bladder, uterus, and ipsilateral fallopian tube. About 100 mL of ascites fluid was also found. The solid organs appeared normal. Therefore, total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, and appendectomy were done. Postoperatively the patient had a smooth course and she was discharged from the hospital with a stable condition.

Subsequently, all the removed tissue samples were brought to the Department of anatomic pathology for histopathologic evaluation. Up on gross examination, the right ovary was massively enlarged with an irregular outer surface measuring 15x12x8 cm with a cut surface of gray-white solid having multiple cystic spaces that are filled with brownish viscous fluid (Figures 1 and 2). The appendix had a nodular mass over its tip that measured 5x4x2 cm with a cut surface of tan white having multiple small nodularities and brownish foci (Figure 3). The contralateral ovary, uterus and cervix were thoroughly evaluated and showed no grossly visible abnormality.

Upon microscopic evaluation, sections taken from both the right ovary and the appendiceal mass showed predominantly follicular proliferation of enlarged follicular cells showing glassy chromatin, elongated nuclei, frequent nuclear grooving, nuclear pseudo inclusions, and nuclear overlapping. No papillary growth pattern was seen. Despite the fact that we sampled the tissue extensively, we did not find admixed teratomatous component (Figures 4–7 and Supplementary Figures 1–4) With these histomorphologic features, the case was signed out as malignant struma ovarii, a follicular

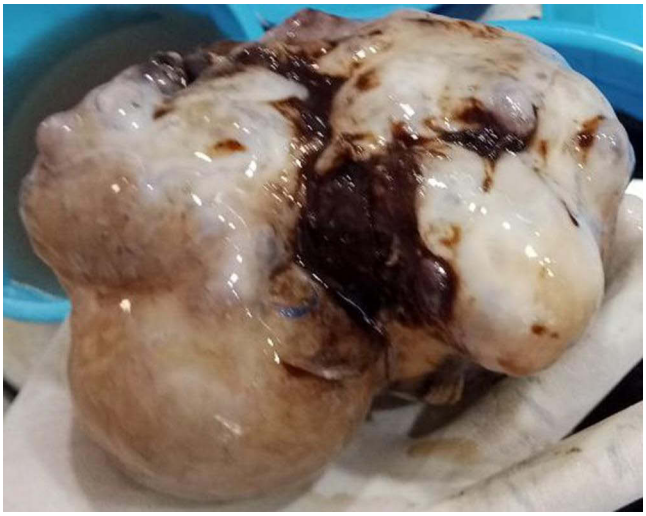

Figure 1 Gross appearance of the right ovarian mass.

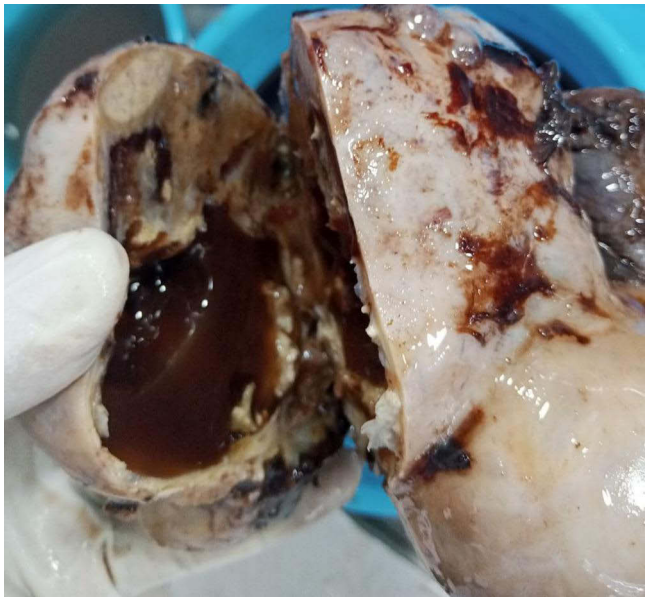

Figure 2 Cut surface of the right ovarian mass.

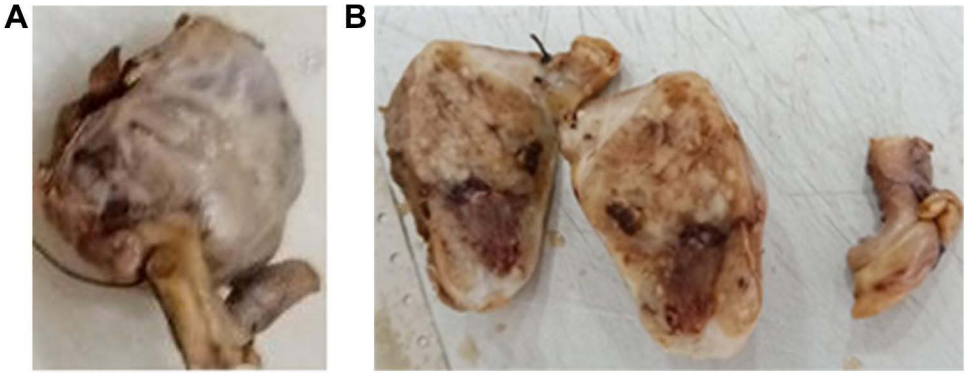

Figure 3 (**A**) Gross appearance of the appendix with a nodule over its tip. (**B**) Cut surface appearance of the appendix.

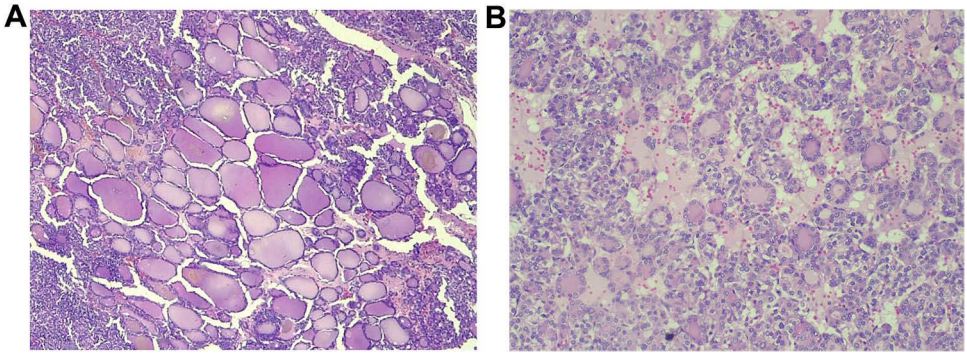

Figure 4 (**A**) Low power view (40x) from the right ovary showing predominantly follicular growth pattern. (**B**) Medium power view (200x) from the right ovary showing predominantly follicular growth pattern.

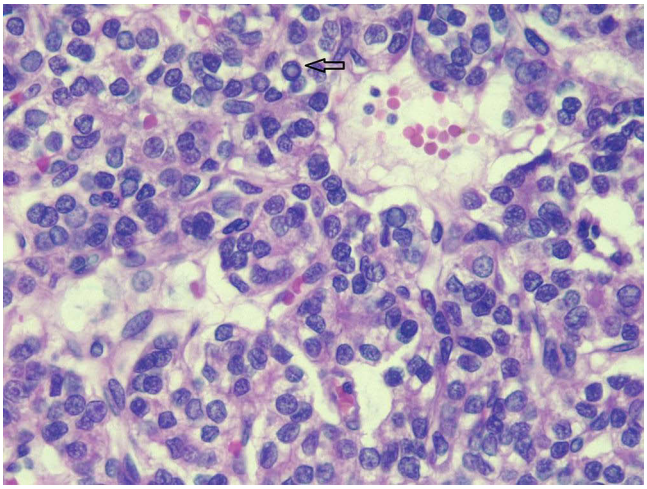

Figure 5 High power view (600x) showing classic cytomorphologic features of PTC with washed out chromatin, nuclear elongation, grooving and pseudo inclusions (arrows).

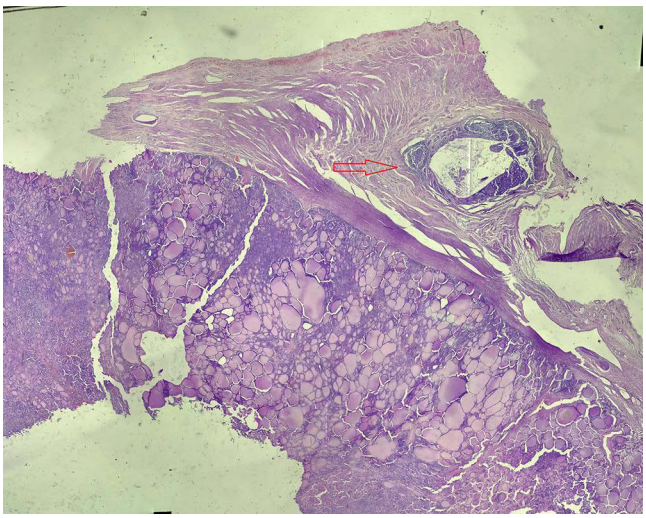

Figure 6 Microscopic view of appendiceal mass with apparent metastatic thyroid tissue that has pushed the appendiceal mucosa (arrow).

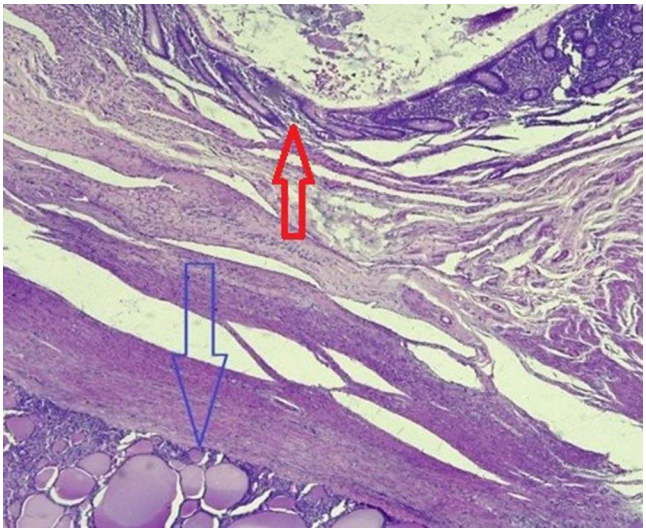

Figure 7 Inset view of the appendix (red arrow) and the periphery of the tumor deposit (blue arrow).

variant of papillary thyroid carcinoma (FVPTC) with secondary deposits on the appendix. The histopathology of the contralateral ovary, uterus and cervix was all unremarkable.

After the pathology report was signed out the patient was called. Thyroid function test and baseline thyroglobulin test were done to be found all in the normal range. She was then linked to the surgical side for complete thyroidectomy. She is now in a good post-operative condition. Other IHC markers could not be done since the patient could not afford them. She was discharged with an appointment to come back after six months. We planned to start her on hormonal therapy after discussion with the patient.

Discussion

Struma ovarii is an uncommon type of mature cystic teratoma accounting for only 3% of ovarian teratomas. They have an age distribution that is the same as that of the mature cystic teratoma. They most frequently occur in patients of child-bearing age with the average age at diagnosis being 43 years.[11,12] Most of these tumors behave in a benign manner with rare transformation to thyroid carcinoma in about 2% of cases with only 200 cases reported so far. Malignancies from the struma ovarii have been reported from all of the man-inhabited continents except for Africa.[11,13] To the best of our knowledge, this is the first report from the continent.

Since these tumors do not have characteristic clinical or radiologic features they are usually confused with other ovarian tumors. The most common symptom is abdominal swelling along with other non-specific gynecologic symptoms but as many as 40% of cases were asymptomatic only to be found incidentally which is the most common cause of advanced stage at diagnosis.[11] But the misdiagnosis of MSO is not solely due to the vague clinical and radiologic features. One study showed 17.8% of cases were misdiagnosed as mature cystic teratoma or as primary ovarian tumors with pathologic misdiagnosis as the most frequent reason.[11]

Most cases of struma ovarii are unilateral affecting the left ovary.[14,15] Struma ovarii has a non-specific clinical presentation that resembles that of other ovarian cancers. Pelvic mass, lower abdomen pain, irregular menstrual periods, vaginal bleeding, ascites, and deep vein thrombosis are the most common symptoms.[3,15,16] Up to 17% of cases have been documented to have ascites, and Meigs' syndrome can occasionally happen.[3,14,17] Regarding thyroid dysfunction, subclinical MSO patients predominate. In 5–8% of instances, clinical hyperthyroidism symptoms are observed.[1,14,16,18]

Imaging can be helpful in the diagnosis of struma ovarii even though it is frequently challenging to distinguish it from ovarian cancer.[19] Malignant struma ovarii is shown as a mixed solid and cystic mass on ultrasound, with color Doppler imaging showing abundant and low resistance flow within the core solid component.[20] A multiloculated cystic mass with a solid component that typically exhibits strong gadolinium enhancement and fluid with varying signal intensity (giving it a "stained glass appearance") is seen on MRI.[21] On a CT scan, calcifications may be seen along with a multiloculated cystic mass with fluid of varying density between the locules. On the basis of the aforementioned imaging features, it is not always simple to diagnose struma ovarii preoperatively; instead, a definitive diagnosis is made by postoperative pathological examination.[17,19,22]

With a much higher level of specificity for the tumor marker in the postmenopausal group, 51.16% of the cases tested positive for CA125 (>35 U/mL). However, it is important to remember that this marker is raised in all malignant ovarian tumors.[10] Our patient's CA125 level was high. (61 IU/mL) All thyroid cancers that develop from follicular cells have been documented, although papillary thyroid carcinoma is the most prevalent, accounting for 50% of cases, followed by follicular thyroid carcinoma with 27% of cases. With 18% of instances ascribed to it,[11,23] the follicular variant of papillary thyroid cancer comes in third. About 30% of malignant struma ovarii are in pure form, whereas the remaining 70% are impure that contain teratomatous components.[23]

The histopathologic diagnosis of PTC is fairly straightforward when both the cytological and architectural features of PTC that are seen in those that arise from the thyroid gland. That includes washed-out chromatin, nuclear enlargement, and crowding, nuclear membrane irregularity with nuclear grooving, and pseudo inclusions. In the presence of these cytopathologic features, if the tumor shows the papillary architecture conventional PTC is rendered as a histopathologic diagnosis. If the lesions show a follicular growth pattern with an absent or negligible papillary pattern (<1%), a diagnosis of follicular variant of PTC (FVPTC) is placed.[2,23] The follicular variant of papillary carcinoma is represented by lesions that share similar nuclear characteristics but lack papillary architecture.[17,24]

The diagnosis of follicular carcinoma in MSO is not as simple as it is in the thyroid gland. Even if it is recommended to see capsular invasion, these lesions are most of the time unencapsulated. One should see vascular invasion, infiltration of the adjacent ovarian stroma, or metastasis to differentiate benign from malignant follicular lesions. We should also be cautious not to misdiagnose a case of ruptured and spilled follicles to the peritoneum as malignant cases.[5,11] The thyroid nature of an ovarian lesion can be confirmed by thyroglobulin. Even if it cannot tell the nature of the tumor, it is highly important to follow for recurrence after tumor resection and thyroidectomy. Patients with any level of rise in its level should have an I-131 scan to detect recurrence.[8,11,25] The malignant nature of the lesion can be revealed by CK-19, galectin-3, and CD56 with a 100% sensitivity for malignancy when all three are positive.[24,26] The BRAF, KRAS, KIT, and NRAS genes, which are associated with PTC, were found to be mutated in five of the six patients who underwent genomic profiling with PTC and FVPTC, but no such mutations were detected in cases of follicular thyroid carcinoma.[11]

A study demonstrated that BRAF mutations are linked to the development of various papillary thyroid cancer histological types. They also noted that the follicular papillary thyroid cancer subtype carries BRAF K601E mutation, which is unique to this subtype of PTC.[27] The presence of BRAF mutations (V600E, K601E, and a deletion/substitution TV599-600M) is demonstrated, indicating the existence of a shared pathogenesis for all papillary thyroid tumors regardless of location.[16,28]

Malignant struma ovarii seldom metastasizes to distant sites; it happens in just 5% of patients. However, they occur more frequently, up to 23% of the time, in the abdominal cavity, which is considered a local metastasis via direct seeding.[16,29] Our patient has appendiceal metastasis which has never been reported so far. Since hematogenous metastasis to the appendix is very rare and the subserosal location of the deposits along with the adhesion of the mass to the appendix in the intraoperative finding tells us that the appendiceal mass is most likely due to direct seeding.

Due to the rarity of these tumors, the treatment option is still in debate, but the most widely accepted standard treatment is conservative treatment with total abdominal hysterectomy and bilateral salpectomy, with many centers opting for a more conservative therapy of unilateral salpingectomy for young patients who wish to maintain fertility.[17,28,30] In the case of our patient total abdominal hysterectomy, bilateral salpingo-oophorectomy, total omentectomy, and appendectomy was done since the patient completed her family size and there was adhesion of the mass to the surrounding structure. According to one study, patients who had tumors larger than 2 cm, extra-ovarian dissemination, or high grade histological traits have to be considered for thyroidectomy followed by I-131 ablation.[6] Another study suggested that MSO with a diameter ≥1 cm should be treated with I-131 ablation after thyroidectomy.[31] A different study recommended I-131 ablation for MSO following thyroidectomy if its diameter was greater than 1 cm.[31] Thyroglobulin is principally released by the thyroid gland; hence, thyroglobulin can only be considered a tumor marker of relapse after the patients' thyroid glands have been entirely removed.[27] Thyroglobulin, on the other hand, can eliminate the likelihood of cervical thyroid carcinoma metastases. Post-operative monitoring of MSO is very essential so that we can detect metastasis. Therefore, long-term with serum thyroglobulin level is critical.[6,32,33] One study advised assessment of this marker every six to twelve months.[32] Multiple studies showed the indolent nature of the tumors with since 97%, 94%, and 85% of patients survived at 5th, 10th and 20th years, respectively.[12,23] It is also suggested these cases should be followed for at least two decades since recurrence has been found with a median duration of 14 years.[32]

Conclusion

Malignant struma ovarii is a rare occurrence, choosing the best course of therapy and next steps might be challenging. There are currently no established histopathologic characteristics that may be utilized to direct clinicians when they encounter these types of disorders. The size of the tumor and whether or not it has metastasized are the two main factors utilized to determine the surgical treatment's scope. To learn more about prognostication and therapy options that take into account pathologic traits, large-scale investigations are essential.

Abbreviation

FVPTC, follicular variant of papillary thyroid carcinoma; IHC, immunohistochemistry; MSO, malignant struma ovarii; PTC, papillary thyroid carcinoma.

Data Sharing Statement

The authors of this manuscript are willing to provide information regarding the case report. All the data can be provided by the corresponding author.

Ethical Clearance

After being reviewed by an ethics board, this case report was found to be morally sound.

Consent

The patient's written informed consent to have the case details and accompanying images published was obtained before this manuscript was prepared. The chief editor of this journal can have access to a copy of the written consent.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest in this work.

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