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Case report

Malignant struma ovarii with insular carcinoma: A case report and literature review

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1. Introduction

Mature teratomas account for approximately 20% of ovarian tumors (Hinshaw et al., 2012). When thyroid tissue is present in greater than 50% of the tumor histology, the tumor is defined as struma ovarii (Devaney et al., 1993). Struma ovarii are rare and occur in 2–3% of mature ovarian teratomas (Hinshaw et al., 2012; Goffredo et al., 2015). Malignant transformation of these tumors is even more rare and occurs in 0.5–5% of all cases (Hinshaw et al., 2012). When malignant transformation occurs, the most common histologies identified are papillary and follicular carcinoma (Roth et al., 2008). Additionally, there is only one case report found in the literature of a poorly differentiated or insular carcinoma subtype which has been shown to be associated with a poorer prognosis (Olinici & Mera, 1988). Patients typically present with a pelvic mass or abdominal pain (Devaney et al., 1993; DeSimone et al., 2003). Hyperthyroidism has been reported to be present in 5–8% of cases (DeSimone et al., 2003).

We present a second case of insular carcinoma (poorly differentiated carcinoma) with adjacent papillary thyroid carcinoma arising out of a mature cystic teratoma composed predominantly of struma ovarii.

2. Case report

The patient is a 61 year old female who originally presented with abdominal pain and was found to have a 22 cm pelvic mass. Her medical history was complicated by morbid obesity, chronic obstructive pulmonary disease, atrial fibrillation, deep venous thrombosis, pulmonary embolism, and major depressive disorder. Secondary to severe depression, the patient refused to ambulate and was bed-ridden for approximately two years giving her a Karnofsky score of 20 (GOG performance status of 4). Physical exam in clinic was extremely limited due to the patient's body habitus and discomfort. Laboratory values were significant for an elevated CA-125 of 340 U/mL. Computed tomography of the abdomen and pelvis revealed a large pelvic mass lesion measuring 19.8 cm × 17.5 cm × 14.2 cm that was likely arising from the left adnexa with central hypodensity concerning for necrosis (Image 1). A homogenous right pelvic lesion was seen and thought to represent the right ovary with possible tumor involvement. A small to moderate amount of ascites was present.

The patient was not a surgical candidate secondary to her multiple medical comorbidities and poor performance status. She underwent ultrasound guided biopsy of the pelvic mass to guide potential neoadjuvant therapy. The pathology revealed struma ovarii. She had no clinical signs of hyperthyroidism and her thyroid function testing was normal with a TSH of 2.14 μIU/mL. The patient took initiative to lose weight herself and received antidepressive medication and counseling to help with her depression. These two factors greatly helped optimize her medical conditions in preparation for surgery. She had been cleared for surgery when she developed a pulmonary embolism which further delayed surgical intervention. Approximately 1.5 years after initial presentation her performance status had improved to a Karnofsky score of 60 (GOG performance status of 2) and she received clearance to undergo surgery.

She underwent an exploratory laparotomy, total abdominal hysterectomy, bilateral salpingo-oophorectomy with abdominopelvic mass removal, rectosigmoid resection with reanastomosis, and omentectomy. Intraoperative findings revealed a 25 cm, friable abdominopelvic mass arising from the left adnexa which was removed intact. The mass was densely adherent to the omentum, small bowel, colonic mesentery, sigmoid colon, rectum, and uterus. The right ovary was grossly normal

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with no additional intra-abdominal disease. Rectosigmoid resection was performed as the mass was densely adherent to the rectum and unable to be separated without removing part of the rectosigmoid colon (Image 1). The patient's postoperative course was complicated by an episode of atrial fibrillation and delayed return of bowel function. She was discharged on postoperative day eight.

On gross pathologic examination, the tumor weighed 4990 g and measured 23.0 × 18.5 × 15.4 cm. There was no grossly normal ovarian tissue identified, and no growth of tumor on the external surface. Microscopic pathologic evaluation revealed 90% insular carcinoma (poorly differentiated carcinoma) with adjacent papillary thyroid carcinoma (Fig. 1) arising out of and overgrowing a mature cystic teratoma composed predominately of struma ovarii (Fig. 2). Carcinoma involved the uterine serosa in an area of adhesion, and the cervix contained a focus of metastatic thyroid-type carcinoma in the deep aspect of the cervical stroma. Both the insular carcinoma and adjacent areas of papillary thyroid carcinoma were positive for Thyroid Transcription Factor 1 (TTF-1) and negative for chromogranin and synaptophysin (Fig. 3). The right ovary contained a benign fibroma. The omentum and rectum were free of carcinoma.

Following recovery, she underwent a baseline PET-CT scan and was without evidence of metastatic disease. Her case was presented at our multidisciplinary tumor conference, which included surgical oncology, medical endocrinology, and nuclear medicine. She was recommended to undergo total thyroidectomy, which showed benign thyroid adenomatoid nodules, followed by radioactive iodine ablation therapy, which she has not yet started. Three months out from her initial surgery, she continues to recover and remains free of disease. The patient has elected not to follow up for additional therapy or observation. The reason for this is unknown.

3. Discussion

Due to the rarity of malignant struma ovarii, most of the knowledge regarding treatment and surveillance has been obtained from case reports and small case series. A review of the literature finds that most authors recommend surgical treatment with total abdominal hysterectomy, bilateral salpingo-oophorectomy and complete surgical staging (Hinshaw et al., 2012; DeSimone et al., 2003; Dardik et al., 1999). If the patient desires fertility preservation, unilateral oophorectomy is an option if there is no evidence of metastasis at the time of surgery (Dardik et al., 1999). Following surgery, all cases with pathological confirmed malignant struma ovarii should undergo postoperative total-body scintiscanning with I^{131} to evaluate for residual disease (DeSimone et al., 2003; Dardik et al., 1999). The overall incidence of metastasis has been reported to be 5–27% (DeSimone et al., 2003). DeSimone et al. found that 4 patients treated with I^{131} did not have disease recurrence and 7 patients with recurrence then treated with I^{131} initially had a complete response to therapy (DeSimone et al., 2003). Given these findings, they recommend adjunct thyroidectomy with I^{131} therapy to be considered first line management following surgery (DeSimone et al., 2003). This is a reasonable approach since I^{131} therapy is used in primary thyroid cancer to decrease recurrence. Thyroidectomy does come with the risk of iatrogenic parathyroidectomy, recurrent laryngeal nerve damage and the need for thyroxine replacement, however, DeSimone et al. point out that metastatic lesions may not be evident with nuclear medicine imaging until the normal thyroid tissue is removed (DeSimone et al., 2003). Regardless of treatment course, a multidisciplinary approach with gynecology oncology, endocrinology, surgical oncology and/or otolaryngology is recommended to achieve the best outcome.

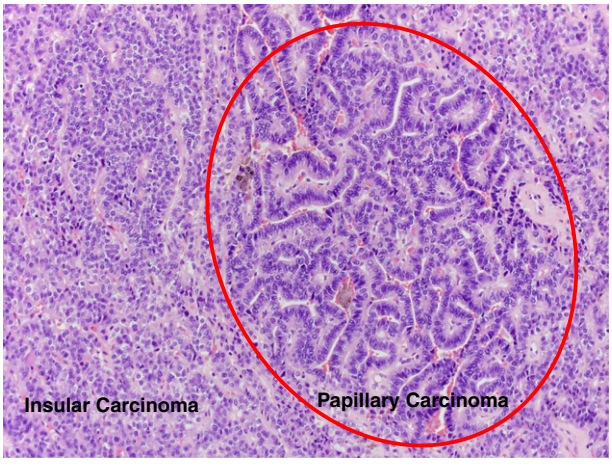

Fig. 1. Photomicrograph of primary insular carcinoma with associated papillary carcinoma (red circle), 200× magnification.

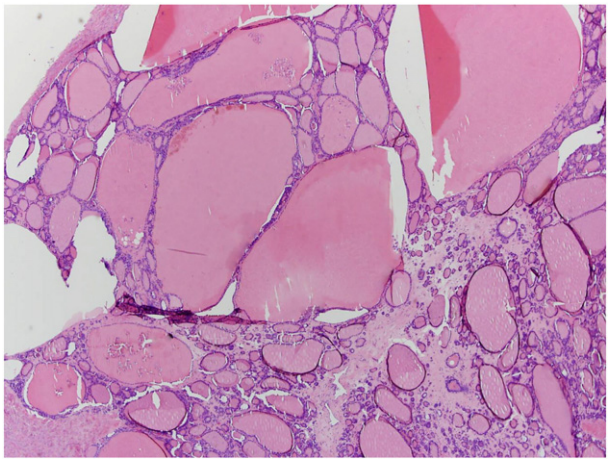

Fig. 2. Photomicrograph of struma ovarii component of mature cystic teratoma, 40× magnification.

Patients opting to forgo thyroidectomy and ablation should be closely followed as recurrences have occurred more than a decade following initial diagnosis (Hinshaw et al., 2012). Estimated time to recurrence is 4–7 years, therefore surveillance measuring thyroglobulin levels for at least 10 years has been recommended (Dardik et al., 1999; Rose et al., 1998). A case series review by Robboy et al. demonstrated survival for malignant struma ovarii to be 81% at 10 years and 60% at 25 years (Robboy et al., 2009). Median survival when metastasis was documented at initial laparotomy was found to be 9 years (Robboy et al., 2009). Overall, the risk of recurrence has been estimated to be between 15 and 38% (Hinshaw et al., 2012).

The most common histologic subtypes are papillary carcinoma and follicular carcinoma (DeSimone et al., 2003). Specific histologic features have not been shown to reliably predict malignant behavior, but factors associated with adverse outcome (increased incidence of recurrence or metastasis) include adhesions to other organs, large size (>5 cm), and the presence of ascites (>1 L) (Roth et al., 2008). Insular carcinoma, also known as poorly differentiated carcinoma, had previously only been reported in struma ovarii in one case report making the treatment and surveillance plan for our patient even more challenging (Olinici & Mera, 1988). The current standard of care for insular carcinoma of the thyroid gland consists of total thyroidectomy and neck dissection followed by I^{131} remnant ablation (Hod et al., 2013). In the thyroid gland, insular carcinoma is typically seen in older patients, is more common in women, and follows a more aggressive clinical course (Hod et al., 2013). Surveillance consists of neck US, I^{131} scanning and measurement of serum thyroglobulin levels (Hod et al., 2013).

Based upon our current literature review, we agree with a multidisciplinary approach to treatment, surgical intervention and staging followed total thyroidectomy and I^{131} ablation especially when the

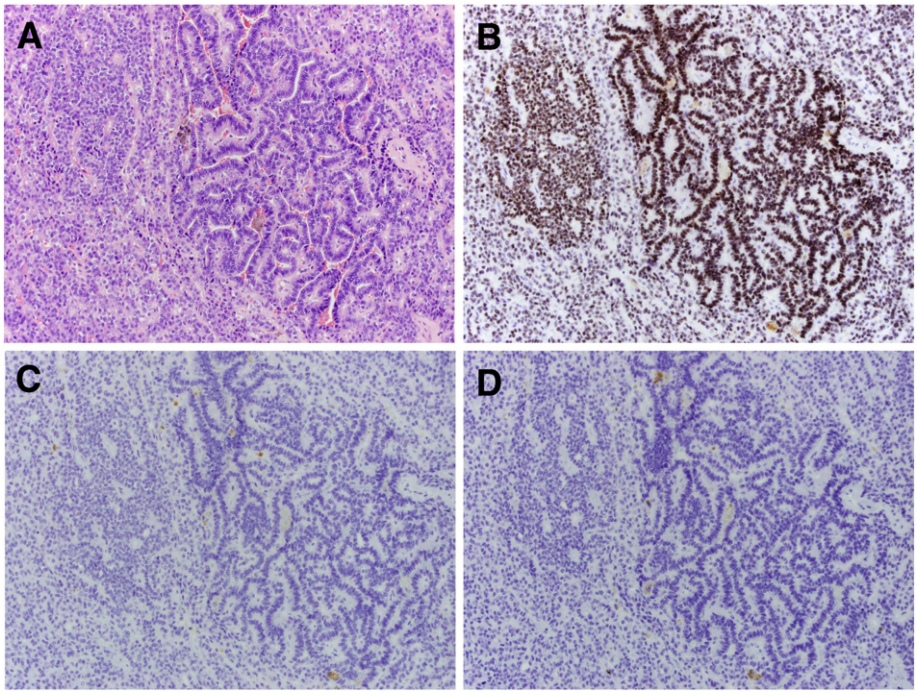

Fig. 3. Photomicrograph of A) primary insular carcinoma with papillary carcinoma as in Fig. 1 stained for H & E, B) Thyroid Transcription Factor 1 (TTF-1) positive nuclear staining in both the insular carcinoma and papillary thyroid carcinoma, C) Negative staining for Chromogranin and D) Synaptophysin, 100× magnification.

disease is considered to be more aggressive, as in this case. Given the large tumor burden within our case, the extensive overgrowth of the malignant component, the presence of insular carcinoma, adhesions to the uterine serosa, lymphovascular space invasion and metastasis to the cervical stroma, we feel our patient has multiple high-risk features for recurrence and these features highlight the aggressive nature of the insular carcinoma variant of malignant struma ovarii. As a result, we choose to recommend adjuvant treatment for our patient. This was decided because adjuvant therapy with thyroidectomy and I^{131} has been shown to decrease recurrences in malignant struma ovarii and a recent report on insular thyroid carcinoma involving 508 patients has demonstrated an improvement in overall survival in both univariate and multivariate analysis (DeSimone et al., 2003; Pezzi et al., 2016). Further study is warranted concerning this uncommon but aggressive histologic variant of thyroid carcinoma arising in struma ovarii.

Conflict of interest statement

None of the authors have any conflict of interest to report.

References

Dardik, R.B., et al., 1999. Malignant struma ovarii: two case reports and a review of the literature. Gynecol. Oncol. 73 (3), 447–451.

DeSimone, C.P., Lele, S.M., Modesitt, S.C., 2003. Malignant struma ovarii: a case report and analysis of cases reported in the literature with focus on survival and I131 therapy. Gynecol. Oncol. 89 (3), 543–548.

Devaney, K., et al., 1993. Proliferative and histologically malignant struma ovarii: a clinicopathologic study of 54 cases. Int. J. Gynecol. Pathol. 12 (4), 333–343.

Goffredo, P., et al., 2015. Malignant struma ovarii: a population-level analysis of a large series of 68 patients. Thyroid 25 (2), 211–215.

Hinshaw, H.D., et al., 2012. Malignant transformation of a mature cystic ovarian teratoma into thyroid carcinoma, mucinous adenocarcinoma, and strumal carcinoid: a case report and literature review. Case Rep Obstet Gynecol 2012, 269489.

Hod, R., et al., 2013. Insular thyroid carcinoma: a retrospective clinicopathologic study. Am. J. Otolaryngol. 34 (4), 292–295.

Olinici, C.D., Mera, M., 1988. Poorly differentiated ("insular") thyroid carcinoma of the ovary. Morphol Embryol (Bucur) 34 (2), 135–137.

Pezzi, T.A., et al., 2016. Treatment and survival of patients with insular thyroid carcinoma: 508 cases from the National Cancer Data Base. Head Neck 38 (6), 906–912.

Robboy, S.J., et al., 2009. Malignant struma ovarii: an analysis of 88 cases, including 27 with extraovarian spread. Int. J. Gynecol. Pathol. 28 (5), 405–422.

Rose, P.G., Arafah, B., Abdul-Karim, F.W., 1998. Malignant struma ovarii: recurrence and response to treatment monitored by thyroglobulin levels. Gynecol. Oncol. 70 (3), 425–427.

Roth, L.M., Miller 3rd, A.W., Talerman, A., 2008. Typical thyroid-type carcinoma arising in struma ovarii: a report of 4 cases and review of the literature. Int. J. Gynecol. Pathol. 27 (4), 496–506.