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CASE REPORT

Papillary carcinoma in struma ovarii: an unusual presentation

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ABSTRACT

Struma ovarii is the presence of thyroid tissue as the major cellular component in an ovarian tumour. Papillary carcinoma in struma ovarii is exceptionally rare. We report a case of papillary carcinoma in struma ovarii in a postmenopausal 51-year-old female who initially presented clinically with hyperthyroidism. Serology, however, did not confirm hyperthyroidism. During a re-admission to our hospital later that year she appeared to have had periods of postmenopausal vaginal haemorrhage. An abdominal mass was located by radiography and pathological investigation revealed a papillary carcinoma in struma ovarii. Some striking features of this unusual presentation of importance to the internal medicine physician are discussed.

KEYWORDS

Papillary carcinoma, review, struma ovarii

INTRODUCTION

Struma ovarii is defined as a teratoma of the ovary, totally or predominantly composed of thyroid tissue.[1] Approximately 2.5% of cystic teratomas are struma ovarii.[1] Teratomas, by definition, may contain endodermal and mesodermal tissue, which can also involve endocrine tissue. Generally this endocrine tissue does not secrete significant amounts of thyroxine. However, in 5 to 10% of cases patients may present with manifest hyperthyroidism due to a thyroid adenoma in the struma.[2] Functional struma ovarii should be considered as a possible cause of thyrotoxicosis in a woman with hyperthyroidism who has no goitre.[3] As with cervical thyroid tissue, ectopic thyroid tissue can undergo carcinomatous changes. Thyroid carcinoma in struma ovarii is extremely rare.[4] The patient we report here presents with rare complications of struma ovarii. In addition, the atypical presentation misled us when making our diagnosis.

CASE REPORT

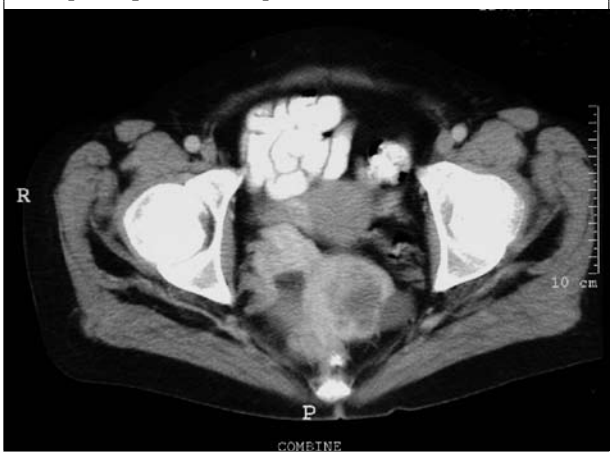
A 51-year-old female first came to our attention with the clinical suspicion of hyperthyroidism, diabetes mellitus type 2 *de novo* and postmenopausal vaginal haemorrhage. At that time she was admitted to our hospital because of respiratory failure following pneumococcal pneumonia. Her medical history revealed chronic obstructive pulmonary disease (COPD) and premature menopause at 38 years of age. Four years later she had undergone curettage because of postmenopausal vaginal haemorrhage.

There was suspicion of hyperthyroidism since she had unwillingly lost over 10 kg in a three-month period, suffering from fatigue, generalised anxiety and depression. Clinical examination of the thyroid showed no abnormalities. Laboratory findings showed normal haematology, liver and kidney function testing. Biochemically there was no evidence of hyperthyroidism with free thyroxine (fT4) 11 pmol/l (normal 10 to 25 pmol/l); triiodothyronine (T3) 1.3 nmol/l (normal 1.3 to 3.0 nmol/l) and antithyroid peroxidase antibody (anti-TPO) <10 U/ml (normal 0 to 35 U/ml). The thyroid-stimulating hormone (TSH), however, was surprisingly low at 0.01 mU/l (normal 0.2 to 4.2 mU/l). The hyperglycaemia proved to be steroid related and was treated with glimepiride 2 mg once daily. The postmenopausal vaginal haemorrhage was regarded secondary to discontinuing tibolone, which she had been using for several years since the menopause. Digital pelvic

examination, speculum examination and transvaginal ultrasound were unremarkable. CA-125 was 15.7 kU/l (normal <20 kU/l) and the carcinoembryonic antigen was 3.3 µg/l (normal <5 µg/l). Tibolone was restarted.

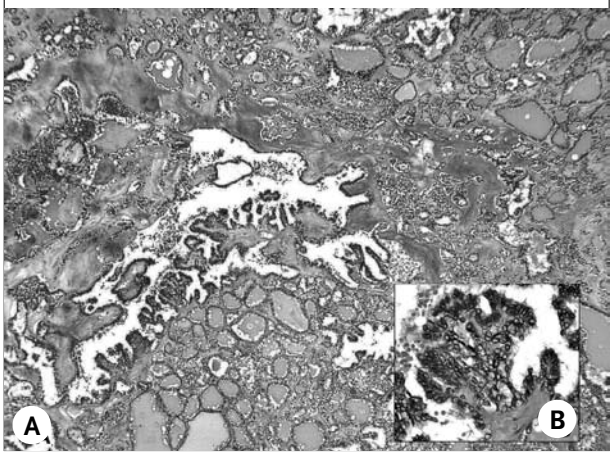
One year later she was readmitted to our hospital suffering from an exacerbation of chronic obstructive pulmonary disease. A short episode of postmenopausal vaginal haemorrhage reoccurred during her admission. Transvaginal ultrasound revealed a large mass in the left lower posterior abdomen originating from the left adnexum. Some ascites was detected. A computed tomography (CT) scan of the abdomen showed a large, lobed, multicystic, nodular pelvic mass with contrast enhancement in the small pelvis, associated with either the left or the right adnexum, or both. The tumour may have been connected to the sigmoid colon. Locally as well as para-aortally small nonpathological lymph nodes were seen (*figure 1*). No other abnormalities were found. Ultrasound of the thyroid showed normal thyroid dimensions and an irregular aspect of the left thyroid lobe. Scintigraphy revealed some 'cold' areas in the right and left lobe.

Figure 1. *CT scan of the abdomen showing a large multilobed mass with contrast enhancement in the small pelvis, associated with either the left or the right adnexum, or both, with diffuse lymphadenopathy locally and para-aortally*



During laparotomy exploration of the uterus and left adnexum showed no abnormalities. The right adnexum was enlarged at 10 x 8 x 6 cm and right adnexal torsion was found. Curettage of the uterus showed no abnormalities but the vagina canal was atrophic and bleed easily. Frozen section analysis of the right adnexum was performed. On pathological macroscopic examination the right ovary appeared to be enlarged (diameter 10 cm) with a nodular surface. On the cut surface it had a brown-red spongy, partly cystic appearance. Frozen section analysis showed struma ovarii. There was no indication of malignancy at that time. Further analysis (postoperatively), however, showed struma ovarii with a focus of papillary carcinoma (*figure 2*). Furthermore, a benign Brenner tumour was found in both adnexa. The partially resected omentum showed no evidence for malignancy.

Figure 2. *Low power photomicrograph demonstrates the papillary character of the carcinoma with normal colloid follicles in the right upper corner; H&E 5 x (A) and high power photomicrograph shows nuclear overlapping, the typical groundglass appearance of the nuclei, nuclear grooves and pseudoinclusions; H&E 40 x (B)*



When the final diagnosis was reached the patient was informed about the diagnosis of malignant struma ovarii, the necessary re-staging procedure, and the prognosis of her disease. Taking her clinical condition with low pulmonary reserve into account and in accordance with the patient's wishes no further surgical intervention or chemotherapy was performed.

In the follow-up period she did not have any vaginal haemorrhage or signs of hyperthyroidism. Levels of TSH, T3 and T4 normalised swiftly (*table 1*). Four years later she died of respiratory failure due to severe chronic obstructive pulmonary disease and persistent smoking. High-resolution CT scanning of the lungs and repeated X-rays of the thorax in the past four years had still not shown evidence of malignancy.

DISCUSSION

This case showed an unusual presentation of malignant struma ovarii with postmenopausal haemorrhage. To our knowledge this has only been described once before.[4]

Although there was some suspicion clinically for hyperthyroidism at an earlier stage this could not be confirmed by biochemical testing. At first presentation subnormal plasma TSH levels were repetitively measured.

Table 1. *Thyroid-stimulating hormone (TSH), free thyroxine (fT4), and triiodothyronine (T3) measurements and signs and symptoms of hyperthyroidism in our patient with malignant struma ovarii*

						Ovariectomy		
Date	**29-07-99**	**29-12-99**	**04-02-00**	**10-02-00**	**25-02-00**	**29-01-02**	**28-01-03**	**10-02-04**
T SH	0.03	0.04	0.01	0.33 (TRH test)	0.01	0.44	1.63	0.97
fT4	19	14	11		-	20	-	13
T3	-	-	1.3		-	-	-	-
Signs and symptoms	Weight loss, depression, anxiety							

A thyroid-releasing hormone (TRH) test appeared to be normal. This may have indicated ectopic thyroglobulin production which could not be detected in our immunoassay. Therefore T3 and fT4 might have appeared to be in the normal range. Discordant findings of serum thyroglobulin in patients with papillary thyroid carcinoma have been described before.[5] After bilateral ovariectomy the TSH, T3 and fT4 levels completely normalised (*table 1*).

Retrospectively, our patient had had a previous episode of vaginal haemorrhage five months before. Physical examination as well as transvaginal ultrasound at that time had shown no abnormalities. This suggests that the tumour, which was large at the time of surgery, had progressed rapidly.

Malignant struma ovarii is exceptionally rare. It generally occurs in the fifth decade of life and preferentially affects the left rather than the right ovary for unknown reasons.[2,6] Recently all reported cases, a total of 39 cases up till 2004, were reviewed.[6] The average age at presentation was 44. Patients predominately presented with a pelvic mass (45%), abdominal pain (40%), menstrual irregularities (9%) and hyperthyroidism (5%). Papillary carcinoma was the most common (44%) histopathological finding followed by follicular carcinoma (30%) and the follicular variant of papillary carcinoma (26%). Metastasis was seen in nine cases (23%), recurrence occurred in six cases (15%). The average time to detection of recurrence was four years.[6]

Owing to its rarity, there has been some controversy about the diagnosis and treatment of patients with malignant struma ovarii.[1,2] The preoperative diagnosis of struma ovarii may be possible through thyroglobulin measurement or scanning in patients affected by hyperthyroidism,[7] but the majority of patients are diagnosed postoperatively as was the case in our patient. The histological criteria for malignancy include increased cellularity and cellular atypia. Thyroid carcinoma metastasised to the ovary can be confused with true struma ovarii.[8] Struma ovarii may cause elevated CA-125 and ascites, as was the case in our patient, which is usually nonmalignant.[1]

Because of the rarity of such cases and the difficulties related to preoperative diagnosis, the management of malignant struma ovarii has not been clearly defined. Some authors have suggested a management as used for other germ cell tumours.[9] Others have proposed that malignant struma ovarii should be treated like its thyroid counterpart.[10] For women of childbearing age, conservative management could be warranted, although there are not enough data available.

After completion of childbearing, treatment should consist of total abdominal hysterectomy, bilateral salpingo-oophorectomy and staging in the usual fashion.[7] Our patient, however, suffered from severe COPD and was a persistent smoker. In 1999 she was admitted to the intensive care unit and needed mechanical ventilation due to respiratory insufficiency following pneumococcal pneumonia and sepsis. In the following four months she was readmitted to our hospital four times with an exacerbation of COPD and had developed steroid-induced diabetes. When the final diagnosis was reached the patient was informed about the diagnosis of malignant struma ovarii, the necessary re-staging procedure, and the prognosis of her disease. Taking her clinical condition with low pulmonary reserve into account and in accordance with the patient's wishes no further surgical intervention or chemotherapy was performed.

A variety of postoperative treatments can be considered;[11] however, most patients do not undergo adjuvant therapy following initial surgery.[11] Thyroidectomy and ablation with radioiodine (^{131}I) are necessary for treating advanced disease. Malignant struma ovarii appears to have a good prognosis. The metastatic potential is low.[11]

CONCLUSION

Malignant struma ovarii is a medical rarity. This is the second report of a presentation with postmenopausal vaginal haemorrhage. Although no biochemical evidence was found there was clinical suspicion for hyperthyroidism, due to ectopic thyroglobulin production by the struma ovarii. Radiographic follow-up suggests that the tumour had progressed very rapidly, which has not been described before. The postmenopausal vaginal haemorrhage may have been partially due to vaginal atrophy as was observed

during surgical exploration. More likely this presentation is caused by tumour progression in the small pelvis without overt uterus pathology.

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