Annals of Clinical and Medical Case Reports

Case Report ISSN 2639-8109 Volume 6

Malignant Metastatic Struma Ovarii: A Case Report with Tyrosine Kinase Inhibitor Treatment and Long Follow Up

Taha T[1], Abu-sini H[1] and Billan S[1,2*]

[1]Oncology Institute, Technion Faculty of Medicine, Rambam Health Care Campus, Israel

[2]Holy Family Hospital, 6004 Street, 16234, Nazareth, Israel

***Corresponding author:**

Salem Billan,
Oncology Institute, Technion Faculty of Medicine, Rambam Health Care Campus, 8 HaAliyah HaShniyah Street, Rambam Health Care Campus 8 HaAliya HaShniya St., Haifa,, Israel 3109601,
Tel: +972-4-777-3016,
Fax: +972-4-777-2929, E-mail: s_billan@rmc.gov.il

Received: 22 May 2021
Accepted: 11 May 2021
Published: 16 Jun 2021

Citation:

Billan S, Malignant Metastatic Struma Ovarii: A Case Report with Tyrosine Kinase Inhibitor Treatment and Long Follow Up. Ann Clin Med Case Rep. 2021; V6(18): 1-5

Keywords:

Case report; Struma ovarii; Radioactive iodine; Thyroid cancer; Tyrosine kinase inhibitor

1. Abstract

Metastatic malignant struma ovarii (MMSO) is a very rare disease (incidence of less than one case in 10 million females annually in the United States). Its rarity results in paucity of data regarding diagnosis, treatment, and follow up. Herein, we describe a case of a 14-year old female who presented with malignant struma ovarii that later metastasized, and was followed up for over 10 years. The patient underwent right oophorectomy surgery and was then treated with a combination of radioactive iodine treatment followed by iodine scans to detect the absorption of radioiodine in the metastatic sites and radiation therapy to treat skeletal lesions. She subsequently received tyrosine kinase inhibitors (TKIs) including sorafenib in the first line and lenvatinib in the second line, and achieved a long-term stable disease. Thus, this case report adds to the limited data available on the treatment of MMSO and suggests that a combination of radioactive iodine treatment, radiation therapy, and TKIs can result in good responses and long overall survival.

2. Introduction

Struma ovarii (SO) is a monodermal teratoma representing a rare type of ovarian tumor. SO comprises 3% of ovarian teratomas and 0.5-1% of ovarian tumors [1,2]. To be qualified as SO, thyroid tissue must comprise at least 50% of the overall tissue in the tumor [3]. SO cases are mostly benign, but malignant transformations are described in approximately 5% of cases. Of these 5%, a minority (5-6%) could even metastasize [4,5]. Due to the rarity of SO, no clinical trials have been conducted and there is a paucity of data in the medical literature regarding diagnosis, treatment, and follow-up of this tumor. Treatment recommendations are based on reports of single cases or case series. The need for surgical resection of the primary tumor is considered a consensus, although the question surrounding whether to perform a radical or conservative surgery is debated. In contrast, there is no consensus regarding adjuvant treatment or the treatment paradigm in metastatic disease [6-8]. Herein, we present a rare case of malignant SO with rapid progression as metastatic disease with a good clinical response to tyrosine kinase inhibitors (TKIs) and more than 10 years follow-up.

3. Case Presentation

A 14-year old healthy female with normal childhood development and without any comorbidities presented in May 2009 with urinary incontinence and flank pain. She underwent ultrasonography (US)

of the kidney, which revealed bilateral hydronephrosis. She then underwent abdominal magnetic resonance imaging (MRI), which demonstrated a large right ovarian lump. Subsequently, a right oophorectomy surgery was performed and the pathological diagnosis revealed SO/monodermal teratoma.

Three months later, in August 2009, the patient felt a lump in her scalp. Brain computed tomography (CT) and MRI showed a soft tissue mass that involved the skull bone. She then underwent craniotomy with removal of the tumor. Pathological diagnosis was SO metastasis, follicular cell carcinoma of the thyroid gland.

In light of these findings, a comprehensive evaluation was conducted. Thyroid US was normal, and positron emission tomography computed tomography (PET-CT) suggested metastatic disease as it showed pathological uptake in the bones (left scapula, left clavicle, and right acetabulum), spleen, lymph nodes (cervical, supraclavicular, mediastinal, axillary, retroperitoneal, pelvis, and inguinal), as well as subcutaneous findings in the neck. In a multidisciplinary discussion, it was decided to perform a thyroidectomy and radioactive iodine therapy. The case until this point was previously published [9]. In November 2009, the patient underwent thyroidectomy and the pathological report showed normal thyroid tissue. During the 4 weeks without levothyroxine after the surgery, while waiting for thyroid-stimulating hormone level to rise, which is mandatory for radioactive iodine treatment, the patient received palliative radiotherapy of 40 Gy to the right acetabulum and the left scapula with marked clinical improvement. In December 2009, the patient received 150 millicuries of radioactive iodine. Post-treatment radio-iodine scan which was carried out 10 days after treatment, showed increased absorption only in the skeleton (left scapula, right clavicula, right humerus, and right acetabulum). The patient remained under clinical follow-up, and 3 months later, a PET-CT was performed, which demonstrated improvement in the lymph nodes and skeleton alongside a new pathological finding in the pelvis. This finding led to another radioactive iodine treatment in May 2010 with 150 millicuries. A subsequent iodine mapping showed a mixed response, with stable skeletal findings and absorption in the ileum bone. Due to the mixed response and the differences between findings seen in PET-CT vs radio-iodine scan, which suggested that some of the lesions were non-iodine avid, the patient started receiving sorafenib (400 mg once a day) in August 2010. PET-CT scan in December 2010 showed improvement in previous findings alongside a new pathological finding in the paraaortic lymph node in the L3 vertebrae level. The patient continued her sorafenib treatment, and in January 2011 was treated again with 200 millicuries of radioactive iodine. A subsequent iodine post-treatment scan showed stable findings in scapula, clavicle, and ileum. Notably, the patient did not receive sorafenib for long periods of time due to poor compliance and because sorafenib was not available long-term (sorafenib is not approved for this indication, and therefore was not covered under the Israeli National Health Insurance Law). In July 2011, the patient had another PET-CT scan, which demonstrated new findings in the small lymph nodes in the base of the left neck, and exacerbation with new skeletal metastases (Figure 1). The patient reinitiated sorafenib treatment and in December 2011 received another treatment with radioactive iodine (100 millicuries). Subsequent iodine mapping showed similar results to the previous PET-CT scan, and a PET-CT scan performed in October 2012 suggested improvement in the lymph nodes, and a stable disease in all other sites. After this PET-CT scan, the patient decided, on her own, to discontinue the sorafenib treatment and declined further follow up. The patient was not monitored until October 2014, at which point she had a PET-CT scan which demonstrated exacerbation in the lymph nodes and skeletal findings. The medical treatment team recommended sorafenib reinitiation, but the patient refused. A PET-CT scan performed in April 2015 demonstrated a stable disease and another one performed in May 2016 showed new lymph node metastases in the lungs, above and below the diaphragm, and new finding in S2. The medical treatment team recommended starting a new line of treatment, and the patient started receiving lenvatinib (24 mg, once daily). Since then, the patient underwent several PET-CT scans in October 2016, February 2017, April 2018 (Figure 2), December 2019 and the last one in January 2021, all of which showed partial responses with improvement in metastatic dissemination. At the time of writing this report, the patient is still receiving lenvatinib treatment, although with moderate compliance, is in a good clinical state without any noted complaints, and with no significant adverse events.

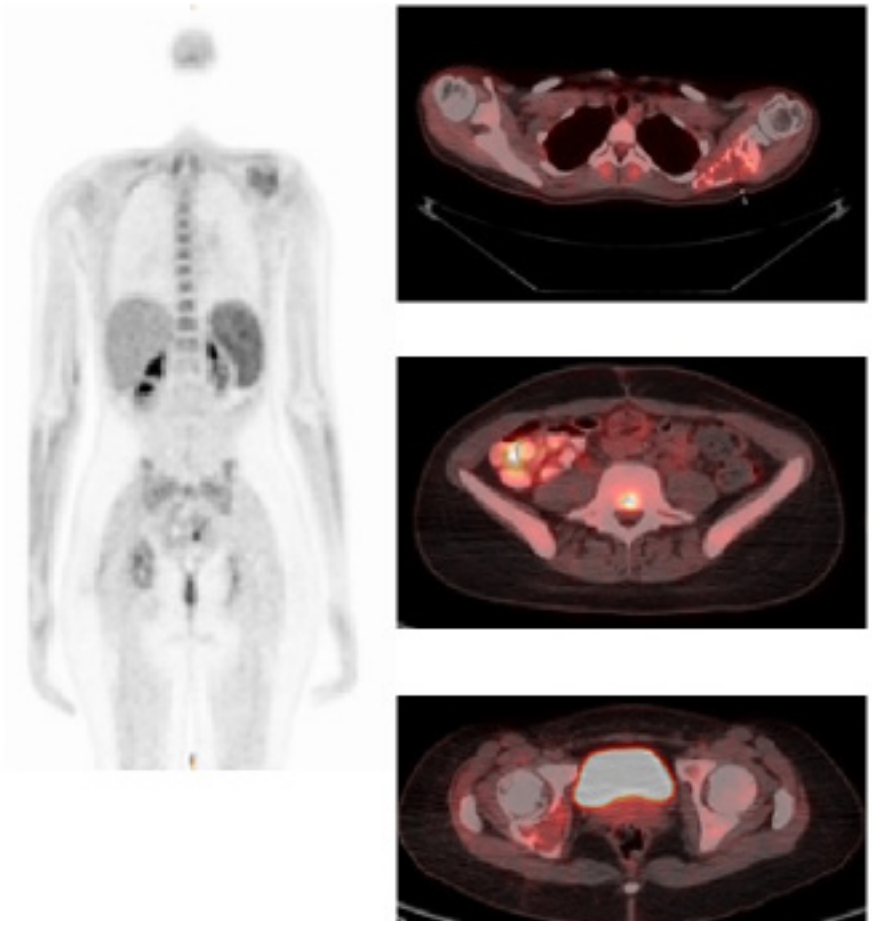

Figure 1: PET-CT scan (2011)

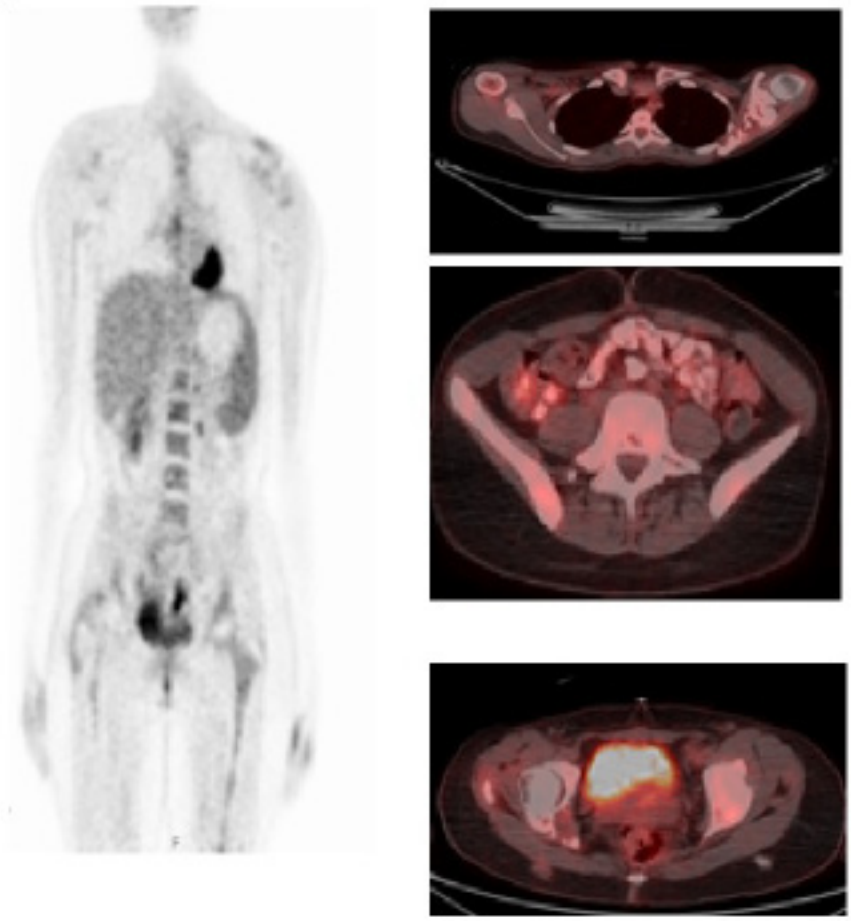

Figure 2: PET-CT scan (April 2018)

4. Discussion

SOs are rarely malignant (5-6%), and some data suggest a discrepancy between biological and histological malignant SO [10]. Metastatic malignant SO (MMSO) is a very rare entity, and its rarity results in paucity of data regarding diagnosis, treatment, and follow up.

The clinical characteristics of SO are diverse and non-specific, mostly consisting of pelvic mass causing lower abdominal/pelvic/flank pain, urinary incontinence, abnormal vaginal bleeding, and hyperthyroidism [2]. Still, 40-50% of SO patients present with other symptoms [2].

SO treatment, although still controversial, generally includes a surgery in benign and malignant localized disease [11]. The surgery could be a unilateral salpingo-oophorectomy that can be done in a fertility-preserving manner, or a hysterectomy with bilateral salpingo-oophorectomy in bulky disease or postmenopausal patients. Adjuvant treatment is not standardized either. The adjuvant treatments, as reported in the literature, include radioactive iodine, radiation therapy, and different chemotherapy protocols (e.g., cisplatin, cyclophosphamide, etoposide and tegafur-uracil, carboplatin, and paclitaxel) [12,13]. Due to the small number of cases, no clear treatment guidelines exist. It is accepted though (still, with no consensus) that adjuvant therapy should be given in advanced stage or highly aggressive disease (e.g., >2 cm, extra ovarian extension, aggressive histological features) [14-16].

MMSO occurs usually in differentiated thyroid tumors (for example, papillary or follicular carcinomas) [12]. The metastatic spread in MMSO cases is wide with described cases having metastases in the lymph nodes, bones, liver, lungs, omentum, peritoneum, and even the brain [6, 17-21]. The treatment of MMSO is based on the treatment of thyroid cancer. It consists of thyroidectomy and, radioactive iodine treatment followed by iodine scans to detect the absorption of radioiodine in the metastatic sites. Poor radioiodine absorption indicates poor response and is generally followed by external beam radiation therapy. The medical literature barely suggests any additional lines of therapy for progressing MMSO.

In this case, TKIs were added in a relatively early phase of the treatment plan, concomitantly with radioactive iodine treatments for several reasons: *i)* The patient had a mixed disease, which was partly iodine avid and partly non-iodine avid; *ii)* the patient had several bulky metastases which were not expected to respond to the radioactive iodine treatment; and *iii)* the combination was administered to gain an indirect advantage, namely, augmenting the radioactive iodine uptake thereby increasing the treatment effect [22]. Our patient was treated first with sorafenib which was administered inconsistently (due to insufficient compliance and unavailability of the drug) and resulted in a stable disease for almost 48 months, and then upon disease progression the patient received lenvatinib, which resulted in a stable disease for additional 72 months and counting (at the time of writing this case report, the patient had stable disease).

Since the molecular pathogenesis of SO is similar to that of thyroid cancer, we suggest applying the approach used for iodine-refractory thyroid cancer to MMSO. Our case suggests that TKIs can produce a good and durable response in MMSO. Furthermore, as thyroid cancer is characterized by a high rate of targetable gene alterations (RET, BRAF, PTEN, KRAS/NRAS/HRAS, and PI3KCA [23]), we suggest performing next-generation sequencing tests in cases of MMSO in order to allow personalized treatment with targeted therapies.

5. Conclusion

MMSO still constitutes a challenging tumor to treat, especially due to the absence of clinical trials and the lack of significant data in the literature. Nonetheless, it seems that the combination of radioactive iodine treatment and TKIs can result in good responses and long overall survival [13].

References

1. Outwater EK, Siegelman ES, Hunt JL. Ovarian teratomas: Tumor types and imaging characteristics. Radiographics. 2001; 21(2): 475-490.
2. Yoo SC, Chang KH, Lyu MO, Chang SJ, Ryu HS, Kim HS. Clinical characteristics of struma ovarii. J Gynecol Oncol. 2008; 19(2): 135-138.
3. Willemse PH, Oosterhuis JW, Aalders JG, Piers DA, Sleijfer DT, Vermey A, et al. Malignant struma ovarii treated by ovariectomy, thyroidectomy, and 131I administration. Cancer. 1987; 60(2): 178-182.
4. Dardik RB, Dardik M, Westra W, Montz FJ. Malignant struma ovarii: Two case reports and a review of the literature. Gynecol Oncol. 1999; 73(3): 447-451.
5. Böcker W. WHO classification of breast tumors and tumors of the female genital organs: pathology and genetics. Verh Dtsch Ges Pathol. 2002; 86: 116-119.
6. DeSimone CP, Lele SM, Modesitt SC. Malignant struma ovarii: A case report and analysis of cases reported in the literature with focus on survival and I131 therapy. Gynecol Oncol. 2003; 89(3): 543-548.
7. Marti JL, Clark VE, Harper H, Chhieng DC, Sosa JA, Roman SA. Optimal surgical management of well-differentiated thyroid cancer arising in struma ovarii: A series of 4 patients and a review of 53 reported cases. Thyroid. 2012; 22(4): 400-406.
8. Michels A, Haugen B. Malignant struma ovarii. J Clin Endocrinol Metab. 2010; 95(4): 1505.
9. Billan S, Abdah-Bortnyak R, Cohen H, Bar-Shalom R, Guilburd J, Michael K, et al. Metastatic malignant struma ovarii. Isr Med Assoc J. 2011; 13(4): 247-248.
10. Robboy SJ, Shaco-Levy R, Peng RY, Snyder MJ, Donahue J, Bentley RC, et al. Malignant struma ovarii: An analysis of 88 cases, including 27 with extraovarian spread. Int J Gynecol Pathol. 2009; 28(5):

405-422.

11. Kunstmann L, Fénichel P. Struma ovarii, a rare form of ovarian tumor. Gynecol Obstet Fertil. 2007; 35(1): 49-54.
12. Wu M, Hu F, Huang X, Tan Z, Lei C, Duan D. Extensive peritoneal implant metastases of malignant struma ovarii treated by thyroidectomy and 131I therapy: A case report. Medicine (Baltimore). 2018; 97(51): e13867.
13. Ukita M, Nakai H, Kotani Y, Tobiume T, Koike E, Tsuji I, et al. Long-term survival in metastatic malignant struma ovarii treated with oral chemotherapy: A case report. Oncol Lett. 2014; 8(6): 2458-2462.
14. McGill JF, Sturgeon C, Angelos P. Metastatic struma ovarii treated with total thyroidectomy and radioiodine ablation. Endocr Pract. 2009; 15(2): 167-173.
15. Yassa L, Sadow P, Marqusee E. Malignant struma ovarii. Nat Clin Pract Endocrinol Metab. 2008; 4(8): 469-472.
16. Janszen EW, van Doorn HC, Ewing PC, de Krijger RR, de Wilt JH, Kam BL, et al. Malignant struma ovarii. Ned Tijdschr Geneeskd. 2008; 152(29): 1647.
17. Konez O, Hanelin LG, Jenison EL, Goyal M, Randolph W. Functioning liver metastases on an I-131 whole-body scan: A case of malignant struma ovarii. Clin Nucl Med. 2000; 25(6): 465-496.
18. McDougall IR, Krasne D, Hanbery JW, Collins JA. Metastatic malignant struma ovarii presenting as paraparesis from a spinal metastasis. J Nucl Med. 1989; 30(3): 407-411.
19. Steinman RA, De Castro IO, Shrayyef M, Chengazi V, Giampoli E, Van Der Sloot P, et al. Two cases of malignant struma ovarii with metastasis to pelvic bone. Gynecol Obstet Invest. 2013; 75(2): 139-144.
20. Checrallah A, Medlej R, Saadé C, Khayat G, Halaby G. Malignant struma ovarii: An unusual presentation. Thyroid. 2001; 11(9): 889-892.
21. Oudoux A, Leblanc E, Beaujot J, Gauthier-Kolesnikov H. Treatment and follow-up of malignant struma ovarii: Regarding two cases. Gynecol Oncol Rep. 2016; 17: 56-59.
22. Oh JM, Baek SH, Gangadaran P, Hong CM, Rajendran RL, Lee HW et al. A novel tyrosine kinase inhibitor can augment radioactive iodine uptake through endogenous sodium/iodide symporter expression in anaplastic thyroid cancer. Thyroid. 2020; 30(4): 501-518.
23. Tirrò E, Martorana F, Romano C, Vitale SR, Motta G, Di Gregorio S, et al. Molecular alterations in thyroid cancer: From bench to clinical practice. Genes (Basel). 2019; 10(9): 709.