Case report

Paraneoplastic opsoclonus-myoclonus syndrome as a presentation of high grade serous ovarian cancer

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ARTICLE INFO

Keywords:
Opsoclonus-myoclonus syndrome
Paraneoplastic syndrome
High grade serous ovarian cancer
BRCA2
Recurrence

ABSTRACT

Opsoclonus-myoclonus syndrome (OMS) is a rare paraneoplastic disorder that is most often seen in association with pediatric neuroblastoma, breast cancer, small cell lung cancer, and prostate cancer. There are only three previously documented cases relating paraneoplastic OMS to ovarian cancer. We present a unique case of OMS related to a stage IIC high grade serous ovarian carcinoma in a patient with germline BRCA2 mutation, with ten years of clinical follow up. This case report is presented to document the rare association of OMS with epithelial ovarian cancer. Additionally, in this case, OMS and epithelial cancer were successfully treated with medical therapy alone. This is the first report to our knowledge to document ten years of clinical follow up in this context, and to report that the association may not be evident at the time of ovarian cancer recurrence.

1. Background

Opsoclonus-myoclonus syndrome (OMS) is rare paraneoplastic syndrome typically related to pediatric neuroblastoma, breast cancer, small cell lung cancer, and prostate cancer. OMS is characterized by opsoclonus, truncal ataxia, encephalopathy, myoclonus, and pleocytosis, specifically, plasma B cells, in the spinal fluid cytology (Anderson et al., 1988). Similar to other paraneoplastic syndromes, it is thought to be immune mediated. Previous cases have shown associations with anti-ri, anti-ko, and anti-hu antibodies (Jongen et al., 1998). OMS has rarely been documented in relation to gynecologic neoplasms. Few case reports relate OMS to mature and immature ovarian teratomas (Fitzpatrick et al., 2008; Lou et al., 2010; Na et al., 2016), and only two prior case reports in the English literature and one in Spanish relate to an epithelial ovarian carcinoma, only one of which was a case of serous cystadenocarcinoma (Rubio Nazabal et al., 2003). OMS occurs prior to the diagnosis of malignancy in the majority of cases, with occasional presentation post malignancy diagnosis (Anderson et al., 1988; Lou et al., 2010; Bataller et al., 2001; Rubio Nazabal et al., 2003). A relapsing and remitting course of paraneoplastic OMS has been previously documented in a population of patients primarily with small cell lung cancer (Anderson et al., 1988). In terms of symptom progression during malignancy recurrences, one patient with ovarian cancer and a patient with small cell lung cancer demonstrated initial occurrence of paraneoplastic OMS at the same time as the relapse of their malignancies (Rubio Nazabal et al., 2003; Nadal et al., 2011). This finding is not consistent in all types of cancers. Moreover, there is paucity of reports on the long-term follow up of patients with the history of OMS and malignancies.

2. Case presentation

In November 2008, a 54-year-old woman with a history of hypertension and previous ocular transient ischemic attack presented to the hospital with progressive neurological deterioration including generalized shakiness, inability to ambulate and abnormal eye movements. On examination, she was agitated with vocalization, nystagmus with periodic saccadic intrusions and opsoclonus. Myotonic twitches were seen in face and arms, with symmetric reﬂexes, normal strength, and downward plantar responses. Her ECOG performance status was 4. Opsoclonus-myoclonus syndrome was diagnosed based on her exam findings. Brain MRI showed nonspeciﬁc punctate white matter signal changes consistent with chronic small-vessel ischemic changes, and no findings suspicious of metastatic disease or cerebellar degeneration. Her other symptoms included profound fatigue, decreased appetite, 60 lbs of unintended weight loss over six months, reflux, and right sided abdominal pain. She had no history of cancer in her ﬁrst-degree relatives. Abdominal-pelvic CT scan showed a complex multi-septated right adnexal cyst measuring 7.4x4cm from what was suspected to be the right ovary, as well as peritoneal thickening and extensive ascites.

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https://doi.org/10.1016/j.gore.2019.100511
Received 6 August 2019; Received in revised form 9 October 2019; Accepted 13 October 2019
Available online 21 November 2019
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throughout the pelvis (Fig. 1). Subsequent pelvic ultrasound demonstrated a thick walled cystic structure in the right adnexal region 6.6 × 5.7 × 4.3 cm, as well as ascites. Ca125 was 675, Ca15-3 was 317 and Ca19-9 was 1149. ANA titre was > 1280 mmol/L (normal < 80), and beta-hydroxyl butyric was 4.29 mmol/L (normal < 0.40). Anti-ri antibody was positive; however anti-hu and anti-yo were negative. Paracentesis cytology showed malignant non-small cell carcinoma cells, positive for CK7 but negative for CK20, calretinin, ER and TTF-1.

A detailed multi-disciplinary review was conducted including review of molecular pathology/cytological findings, imaging, and tumour markers, and a diagnosis was proposed of OMS secondary to an advanced stage epithelial ovarian carcinoma. Given her poor functional
status, neoadjuvant chemotherapy was recommended. Subsequently, she received primary chemotherapy with IV carboplatin and paclitaxel without primary surgical debulking. Pending her neurological status, interval debulking surgery was not scheduled. Her OMS was initially treated with prednisone 1 mg/kg and transitioned to oral dexamethasone 4 mg twice daily, thiamine supplementation, and clonazepam as needed. CT scan post 6 cycles of systemic chemotherapy showed no residual disease and the tumour markers normalized. She was discussed at multi-disciplinary rounds for consideration of delayed debulking. With no radiological or biochemically evidence of disease, in the setting of her somewhat improving OMS symptoms and recent diagnosis of bilateral pulmonary emboli, she was a high-risk surgical candidate and surgery was not recommended. Her OMS symptoms improved drastically and she was able to wean off the oral dexamethasone and clonazepam with only mild residual ataxia. Her neurological symptoms completely resolved within one year after initial diagnosis. By December 2009 she had no ongoing neurological symptoms, and no evidence of disease biochemically or radiographically. Further discussion at this point concluded that progression free survival would not be altered by a surgical procedure, and therefore was not recommended. She was placed on regular surveillance.

In May 2018, after a nine-year interval with no recurrence of neurological symptoms or disease, she developed increased urinary frequency, nocturia, and bladder pressure. The patient noted an increase in “shakiness”, similar to her initial presentation, however no eye or other neurological symptomatology. Her performance status was much higher with ECOG of 1. Investigations showed a CA125 of 27, which had increased modestly from her previous screening CA125 values (range 6–11). Abdominal-pelvic CT demonstrated a multi-loculated solid-cystic pelvic mass involving both adnexa, no ascites, peritoneal metastases were evident at the time of ovarian cancer recurrence. Furthermore, at the time of recurrence, she had some subjective symptoms of shakiness, however, no recurrence of OMS symptoms emerged. Given the lengthy disease-free interval, BRCA 2 carrier status, and absent OMS symptomatology in the 2018 malignancy diagnosis, we speculate that the recurrent tumour could, perhaps, have been a new primary diagnosis. The recurrent tumour may not have been associated with anti-ri antibodies and therefore did not cause recurrent OMS symptoms. Unfortunately, anti-ri titres were not evaluated during disease recurrence.

4. Conclusion

This case report is presented to document the rare association of OMS with epithelial ovarian cancer. Additionally, OMS and epithelial cancer in this case were successfully treated with medical therapy alone. This is the first report to our knowledge to document ten years of clinical follow up in this context, and to report that the association may not be evident at the time of ovarian cancer recurrence.

5. Declarations

Written informed consent was obtained from the patient for publication of this case report and accompanying images by Dr S Lee. Ethics approval was not required.

6. Disclosures

All authors have approved the final article. No funding sources.

Declaration of Competing Interest

The authors declare no conflict of interest related to this case report.

Acknowledgements

Thank you Dr Natasha Simula for assistance in Spanish language document translation. Dr Lien Hoang for providing pathology slides.

Author contributions

Manuscript was prepared by Kimberly Stewart, Shaina Lee, and Gavin Stewart. Dr Lee obtained written consent from the patient.

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