1. Background

Primary non-gestational mediastinal choriocarcinoma is a rare germ cell malignancy that is diagnosed in the absence of a primary tumor in the gonads or metastatic disease in the retroperitoneal lymph nodes. It represents 1–4% of all mediastinal tumors and < 5% of all germ cell malignancies (Tanaka et al., 2017). Non-gestational choriocarcinoma can be differentiated from gestational choriocarcinoma as the latter is a type of gestational trophoblastic neoplasia associated with a prior molar or normal pregnancy. It is important to make a distinction between the two forms of choriocarcinoma as non-gestational is very rare and carries a poorer prognosis. Demographically, primary non-gestational mediastinal choriocarcinoma is noted to be more prevalent in men than in women and is a clinically aggressive disease despite treatment. Symptoms at the time of presentation frequently include dyspnea, chest pain, cough, or other common features of metastatic disease. Elevated human chorionic gonadotropin (hCG) levels typically aid in the diagnosis. We present a case of primary mediastinal choriocarcinoma in a female patient with a brief review of the literature.

2. Case presentation

53 year old Gravida 3 Para 3 woman presented to our clinic as a referral for further evaluation and treatment of metastatic choriocarcinoma. Prior pregnancy records were unavailable though she had three prior term deliveries, one of which was via cesarean section. At the time of presentation, documentation noted three living adult children. She had initially presented with week-long complaints of diplopia and subsequent difficulty balancing in addition to cough, fatigue, and a one month history of dyspnea on exertion.

She then presented to the Emergency Department ten days later after multiple falls at home with injury to her head and chest. A computed tomography (CT) of her head was performed and demonstrated three hyper-dense intra-axial masses concerning for metastatic disease. Subsequent head magnetic resonance imaging (MRI) identified four metastatic intracranial lesions. Further imaging was obtained including CT of the chest, abdomen and pelvis which revealed a mediastinal mass consistent with a 7 × 9 cm coalescent malignant adenopathy. The CT also demonstrated a 1.4 cm rounded left axillary lymph node, concern for splenic metastasis, and suspicious lesions in the iliac bones.

Mediastinoscopy and biopsy of the large mass identified high-grade carcinoma, morphologically and immunophenotypically consistent with choriocarcinoma. Tumor markers including hCG, alpha fetoprotein (AFP), and lactate dehydrogenase (LDH) were negative. Immunohistochemistry was performed including CK pool, CK5/6, CK-7, CK-20, Hepatocyte, p63, melan A, S100, CD117, TTF-1, WT-1, PLAP, GATA-3, AFP, OCT4, CD30 and hCG. The tumor cells stained strongly positive with CK pool, CK-7, PLAP and GATA-3. There was focal positivity with CK5/6 and hCG. The tumor cells were negative for CK20, Hepatocyte, p63, melan A, CD5, CD117, TTF-1, WT-1, CD30, AFP, and OCT4. The immunophenotypic pattern with positive staining for CK pool, PLAP, GATA-3 and focal positivity with hCG supported the diagnosis of choriocarcinoma.

Tissue pathology was consistent with the immunohistochemistry findings of choriocarcinoma. Histologic analysis was suggestive of pleomorphic malignant neoplasm with cellular findings of abundant pink cytoplasm, indistinct cell borders, scattered multinucleated giant cells, focal somewhat lacy cytoplasm and abundant necrosis (Fig. 1).

Array comparative genomic hybridization (aCGH) was obtained to evaluate for tumor genome imbalances. Gain of the chromosomal region from 2p16 to 2p terminal, and losses of or from 6p, 6q12–q22,
Primary non-gestational mediastinal choriocarcinoma: a summary of the literature.

Table 1

| Authors (reference) | Cases reviewed | Sex ratio | Age range | Chemotherapy regimens | Range of survival |
|---------------------|----------------|-----------|-----------|-----------------------|------------------|
| Fine et al. (1962)  | 19 possible, 9 proven | Male | 19-60 | NA | NA |
| British Medical Journal, (Br Med) (1969) | 20 | 19 Male | 20-30 | NA | 4 weeks – 6 months after symptoms |
| Cohen and Needle (1975) | 1 | 9 Male | 50% in 30s | Methotrexate, chlorambucil, actinomycin D | < 5 years |
| Forest et al. (1977) | 2 | 2 Male | 26-45 | Actinomycin D alone; actinomycin D, cyclophosphamide, vincristine | 10 days to 2 months |
| Lam et al. (2011) | 1 | Male | 25 | Variable; case report with etoposide, cisplatin | 2 weeks |
| Zhang et al. (2014a) | 6 | Male | NA | Available; patient in report received EMA-CO | 6 weeks to 1 year |
| Zhang et al. (2014b) | 44 | 40 Male | NA | Actinomycin D alone; actinomycin D, cyclophosphamide, vincristine | NA |
| Kuno et al. (2016) | 1 | Female | 58 | Etoposide, MTX, actinomycin, cyclophosphamide, vincristine | 41 days |
| Zhang et al. (2016) | 1 | Male | 25 | Chemoradiation with etoposide, cisplatin, bleomycin | Survival > 16 months at time of publication |
| Francischetti et al. (2017) | 1 | Male | 41 | VIP (etoposide phosphate, ifosfamide, cisplatin) | NA |

In summary, our case of non-gestational mediastinal choriocarcinoma was notable for its absence of hCG production and typical gain of 12p material, requiring histologic diagnosis. The genomic markers found in our case add to the existing body of literature regarding markers associated with this rare form of malignancy. Due to its rarity, there currently exists no consensus regarding treatment protocols. This malignancy unfortunately carries a poor prognosis. Thus, case reports such as ours contribute to the scant literature to assist in the diagnosis of these aggressive tumors.
Conflict of interest statement

The authors whose names are listed certify that they have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

Author contribution

Samantha Batman is the primary author who wrote the majority of the manuscript and performed the literature review. Terry Morgan is a pathologist who performed the immunohistochemical stains. Marta Brunetti, Rønnaug A.U. Strandabø, and Francesca Micci are experts in cytogenetics who consulted on the array comparative genomic hybridization. Melissa Moffitt is a gynecologic oncologist who was the patient’s primary oncologist and determined her treatment plan. Tanja Pejovic is a gynecologic oncologist who oversaw this collaboration and also contributed to the writing of the manuscript.

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