Case Report

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Choriocarcinoma with spinal metastasis: A case report

¹Casather DM, ²Kaluarachchi DP, ³Jayawickrama M, ⁴Garusinghe S & ⁵Atapattu H^{1,2}Obstetrics and Gynaecology Unit, Colombo North Teaching Hospital, Ragama, Sri Lanka³National Hospital of Sri Lanka, Colombo, Sri Lanka⁴Neuro-surgical unit, National Hospital of Sri Lanka, Colombo, Sri Lanka⁵De Soysa maternity Hospital for Women, Colombo, Sri Lanka

Correspondence: D.M.Casather

Acting Obstetrician and Gynaecologist.

Obstetrics and Gynaecology Unit, Colombo

North Teaching Hospital, Ragama, Sri Lanka.

Email: dilanmalinda7@yahoo.com <https://orcid.org/0000-0003-1704-0001>

Abstract

Choriocarcinoma is a highly malignant trophoblastic neoplasia, arising following any type of pregnancy. Even though choriocarcinoma has an early haematogenous metastasis to multiple organs, spinal metastasis is extremely rare. A 28-year-old woman presented with a two-week history of progressive numbness and weakness of the lower limbs and difficulty in walking. In magnetic resonance imaging of the spine, soft tissue components were noted adjacent to the spinal cord. She underwent laminectomy to remove the extramedullary located tumour mass, which was compressing the spinal cord. Although there was a significant improvement in tactile stimulation in the lower limb following six courses of multi-agent chemotherapy, she continued to have leg weakness. Despite improvements in treatment modality and the use of combined modality treatment with chemotherapy, surgery, and radiation, the prognosis for this choriocarcinoma with spinal metastasis is unfavourable. Earlier diagnosis and multimodality treatment is crucial for a significant reduction in mortality and morbidity.

Keywords: *Gestational Trophoblastic Diseases, Choriocarcinoma, Spinal metastasis, Thoracic vertebrae, Multiagent chemotherapy*

INTRODUCTION

Choriocarcinoma is a highly malignant trophoblastic neoplasia, arising following any type of pregnancy, more commonly seen among the patients following hydatidiform mole [1, 2]. Hyperplastic and anaplastic differentiation of cytotrophoblastic and syncytiotrophoblastic cell lines with the absence of chorionic villi are the histopathological features of choriocarcinoma [3]. Since there is a proliferation of syncytiotrophoblast

the tumour marker, β human chorionic gonadotropins (β HCG) typically elevated [4]. In addition to the fetal trophoblastic tissues, choriocarcinoma rarely arises from germ cells in the ovary, testis, or as differentiation of other carcinomas [5]. Choriocarcinoma has early haematogenous metastasis to multiple organs. Vulvo- vaginal and pulmonary metastasis commonly seen and metastasis less commonly

found in the liver and brain. Metastasis to the gastrointestinal tract, kidney, and breast are rare, however, spinal metastasis is extremely rare in choriocarcinoma [6]. Choriocarcinoma and other gestational trophoblastic neoplasias are typically highly sensitive to chemotherapy. Here we report a case of a patient who primarily presents with symptoms of spinal cord compression with multiple metastases to the lungs, breast, and thoracic spine.

CASE PRESENTATION

A 28-year-old woman was referred from a local hospital with a two-week history of progressive numbness and the weakness of the lower limb and difficulty in walking. There was no history of trauma to the spine, recent onset of significant headache, or fever. She had urinary incontinence for two days before admission. On initial examination, she was conscious, rational, afebrile, and the Glasgow coma scale was 15. She was normotensive and her respiratory system examination was normal. Fundal examination and

cranial nerves examinations were satisfactory. She was a paraplegic and impaired sensation was noted below the level of the twelfth thoracic level. On further examination, the limb power was grade III and grade II at the ankle and knee respectively. The knee reflexes were normal and she was negative for Babinski sign. Initial haematological and biochemical investigations were all normal.

Since she had a positive pregnancy test for urine she was referred to the obstetrician for further assessment. Her last menstrual period was 25 days ago and that period was the same as her previous periods and there was no period of amenorrhoea before that. Her abdominal and pelvic examinations were unremarkable. On pelvic ultrasound scan, there was a normal-sized anteverted uterus and there were no features of intrauterine or extrauterine pregnancy or retained products of conception within the uterine cavity. However, there was prominent Doppler activity in the myometrium, which was more prominent towards the endometrial cavity (figure 1). There were no adnexal masses or free fluid in the pelvis.

Figure 1: Transvaginal ultrasound scan shows anteverted normal sized uterus with prominent vasculature within the myometrium.

The serum β hCG was 6000 IU/ml and magnetic resonance imaging of the spine revealed, a low-intensity lesion on T1W1 and a high signal intensity lesion on T2W1, compressing the adjacent spinal cord and a lytic lesion involving the spinous processes, bilateral pedicles, and entire body of the fifth thoracic vertebrae (figure 2 and 3). She underwent a laminectomy to remove the extramedullary located tumour mass, which was compressing the spinal cord. The cerebrospinal fluid β hCG was 456 IU/ml. In the histopathological examination of the mass, there were several hemorrhagic foci and multiple cellular infiltrations

through the vertebral bones. There was a biphasic pattern cellular arrangement at high magnification. In one cell arrangement, there were polygonal-shaped clear cytoplasm and large irregular-shaped vesicular nuclei with prominent nucleoli and these features are compatible with cytotrophoblast. In another cell line, there was eosinophilic cytoplasm with cytoplasmic vacuoles and they were identified as syncytiotrophoblasts. In the immune histochemistry study, β hCG was positive for the cytoplasm of the syncytiotrophoblast (figures 4 and 5).

Figure 2: Magnetic resonance images of sagittal section of the spine. Pre-operative images of the spine show low signal intensity on T1W1, and a lesion affecting the entire T5 vertebral body. Arrow indicates the lesion.

Figure 3: Magnetic resonance images of axial spine. Pre-operative images of the spine show low signal intensity on T1W1, and a lesion affecting the entire T5 vertebral body. Arrow indicates the lesion.

Figure 4: Cellular infiltration throughout the vertebrae. Infiltrated tumour is composed of two cell lines. Arrow indicates the vertebral bone. Hematoxylin and eosin, X 100)

Figure 5: hCG was positively stained in the cytoplasm of syncytiotrophoblasts but not cytotrophoblasts (hCG stain, X 200)

On contrast-enhanced computed tomography, there were bilateral multiple small (2mm to 5 mm) irregular soft tissue nodules of varying sizes with contrast enhancement involving all three zones of both lungs (figure 6). In addition, there were bilateral multiple nodules in breasts to suggest breast metastasis of choriocarcinoma. There were no lesions in the abdomen. With the metastatic lesions, the patient was diagnosed with having a stage IV disease. Then she was referred for chemotherapy, and she received six courses of multiagent chemotherapy with etoposide, methotrexate, cyclophosphamide, actinomycin, and vincristine. Following six weeks after initiation

of the chemotherapy β hCG levels returned to normal (<1 IU/ml). In a followed-up computed tomography scan at 8 weeks, there were no significant metastatic pulmonary and breast lesions. There was a significant improvement in tactile stimulation in the lower limb following chemotherapy. However, she continued to have leg weakness. In lower limb neurological assessment in the motor component, there was no notable improvement. She was referred to the regional rehabilitation center for lower limb physiotherapy.

Figure 6: Contrast enhance Ct Shows multiple nodules, suggestive of metastatic lesions.

DISCUSSION

Gestational trophoblastic diseases (GTDs) consist of a heterogeneous group of neoplastic disorders that arise from trophoblastic tissues and they are characterized by producing a distinct tumour marker, β Human Chorionic Gonadotropins [4]. GTDs are usually classified into several distinct groups based on their histopathological and cytogenetic features. They are complete and partial hydatidiform mole, invasive mole, choriocarcinoma, placental site trophoblastic tumour, and epithelioid trophoblastic tumour. Choriocarcinoma is a rare, highly malignant neoplasm [7]. Although the choriocarcinoma can follow any type of pregnancy, it most often occurs following a hydatidiform mole (50%), following a miscarriage (25%), less frequently following an ectopic pregnancy (3%). It can occur even following a normal term pregnancy (10%), and rarely, it originates from germ cells of the ovary [8]. In men, it may arise from germ cells in the testis. In our case, the patient was diagnosed with choriocarcinoma following a normal term pregnancy. The latent period may be long as in our

case where the disease was diagnosed 18 months after term delivery.

Choriocarcinoma has a marked tendency of early dissemination. Because of the affinity of trophoblasts for blood vessels and its innate capacity to invade and erode the vessel wall, dissemination generally haematogenous[9]. The most common metastatic sites are the lungs (70-95%), vagina (40- 50%), vulva (10-15%), brain (28%), liver (15%), kidney and spleen (<5%). Metastasis to the musculoskeletal system, such as the spine, is extremely rare [10].

The disease often presents with symptoms related to metastatic spread, as the primary tumour may remain very small. Symptoms and clinical signs vary depending on the site of the lesion [11]. The patient may present with either headache, visual field defect, or muscle weakness when there is central nervous system involvement or with dyspnea in case of involvement of the respiratory system. In our case, the presentation was weakness in the lower extremities, and difficulty in walking due to metastatic deposits in the spine.

Usually, the diagnosis is made by clinical history, imaging, serum β hCG levels, and tissue confirmation by the histopathological examination. In the case of spinal metastasis, imaging such as CT scans, MRI, or myelography, is useful in the diagnosis and planning the surgery [12]. The MRI in our case revealed a complete blockage at T4 –T5 vertebra, due to the intraspinal, extramedullary soft tissue lesion with severe cord compression. The macroscopic appearance of the choriocarcinoma is often purple or dark red colored and it bears resemblance to a friable segment of placental tissue [1]. Microscopically, it is characterized by the presence of multiple haemorrhagic and necrotic foci around the neoplastic cells and the absence of hydropic villi. The neoplastic cells are biphasic and mixed close to each other. The cytotrophoblastic cells are cuboidal in shape, and it has large pale cytoplasm and irregular shaped vesicular nucleus with large nucleoli. On the other hand, syncytiotrophoblastic cells have eosinophilic cytoplasm with cytoplasmic vacuoles. They have many pleomorphic and hyperchromatic nuclei with hazy border, appearing like multinucleated giant cells, and they may form syncytial knots. The immunohistochemical staining for β hCG is positive in the cytoplasm of syncytiotrophoblastic cells but not in cytotrophoblastic cells [13]. Other germ cell tumours such as dysgerminoma, teratoma, endodermal sinus tumour, embryonal carcinoma, polyembryoma, and mixed germ cell tumour can also show β hCG positive cells, but these tumours characteristically do not exhibit a biphasic pattern consisting of cytotrophoblasts and syncytiotrophoblasts, as in choriocarcinoma.

Choriocarcinoma is highly sensitive to chemotherapy. Gestational trophoblastic neoplasias (GTNs) are categorized into either high risk or low risk based on several factors, such as age, pretreatment serum β hCG, type of antecedent pregnancy, the time elapsed following antecedent pregnancy, tumour size, sites of metastasis, and size of metastasis [14]. The majority of high-risk GTNs respond extremely well to multiagent chemotherapy including, etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine (EMA-CO) with or without adjuvant surgery or radiotherapy [15]. However, up to 30% of patients develop either resistance or recurrence.

Since it is very rare, the best treatment for patients with spinal metastasis has not been established. There have been few reported cases of spine metastasis of choriocarcinoma treated with chemotherapy followed by radiation [6,17]. The surgery is usually indicated when there is a massive mass effect due to tumour mass or hematoma. Because choriocarcinoma is an exceptionally hemorrhagic tumour, the surgical procedures may exacerbate the metastatic potential of this tumour [11]. Thus, preoperative angiographic embolization or at least angiography of the tumour should be used to reduce perioperative haemorrhage and evaluate vascularity of the tumour site, respectively [16]. Our patient with multiple sites of metastasis classified as “high risk” and had 6 courses of multiagent chemotherapy following spinal surgery. Even though the patient did not gain complete neurological recovery, all the metastatic lesions were well responded to chemotherapy.

Naito et al. found that a patient who had spinal and lung metastasis of choriocarcinoma did not respond to 3 courses of methotrexate. However, the patient had complete recovery following, total en-bloc spondylectomy and, radiotherapy [14]. Vani et al. reported the case of a patient with spinal and lung metastasis who had a poor response to 12 courses of multiagent chemotherapy and after the treatment, that patient received palliative radiotherapy [17]. Manegaz et al. reported a case of choriocarcinoma with spinal metastasis treated with multiagent chemotherapy and radiotherapy, however, the patient had died during treatment due to sepsis caused by neutropenia [6]. Kuten et al. also reported a case of choriocarcinoma with lumbar epidural space involvement, successfully treated with decompression surgery, radiotherapy, and chemotherapy [18]. Lee et al. reported a case of metastatic choriocarcinoma with spinal involvement; was successfully treated with decompression surgery followed only by chemotherapy [1].

CONCLUSION

In conclusion, we have reported a rare case of metastatic choriocarcinoma to the thoracic spine and pulmonary metastasis, which was successfully treated with laminectomy and multiagent

chemotherapy. In our case, the diagnosis was made by clinical history, imaging, elevated β hCG level, and histology. The treatment involves multiagent chemotherapy with or without surgery or radiotherapy. Despite improvements in treatment modalities and the use of combined treatment with surgery, chemotherapy and radiotherapy, the prognosis of the choriocarcinoma with spinal metastasis is unfavourable. Earlier diagnosis and multimodality treatment is crucial for a significant reduction in morbidity and mortality from metastatic choriocarcinoma.

Abbreviations

Beta-HCG: Beta-human chorionic gonadotropin
 GTDs: Gestational trophoblastic diseases
 GTNs: Gestational trophoblastic neoplasias
 CT scan: Computer Tomography Scan
 MRI scan: Magnetic resonance Imaging scans
 EMA-CO: etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine

Author declaration

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Author Contributions

First author DMC did the conception, design, and writing/editing of the paper, and he is responsible for the principal work of this paper. Author DPK contributed in the conception and editing of the paper. Authors MJ, SG and HA involved in the clinical management of the patient. Authors personally accountable for the author's own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which the author was not personally involved, are appropriately investigated, resolved, and the resolution documented in the literature.

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Availability of data and materials

Complete informed written consents were obtained from the patient for the publication of this study and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Ethics approval and consent to participate

Specific ethical board approval was not required for this study as she is receiving routine, standard clinical care.

Competing interests

Author certifies 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.

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