INTRODUCTION

Choriocarcinoma is a malignant disease characterized by the secretion of human chorionic gonadotropin (hCG). It is highly malignant form of gestational trophoblastic neoplasia (GTN), arising in any type of pregnancy and is more common in patients with a history of hydatidiform mole [1,2]. Choriocarcinoma is composed of abnormal cytotrophoblast and syncytiotrophoblast with hyperplasia and anaplasia, and characterized by absence of chorionic villi, hemorrhage, and necrosis. The direct invasion into the myometrium and vascular invasion resulting in spread of choriocarcinoma into distant sites, most commonly to the lungs, vagina, brain and liver [1-3].

The occurrence of choriocarcinoma with spinal metastasis is extremely rare [4-8]. We present a rare case of a patient who primarily presented with symptoms of spinal compression caused by lumbar spinal metastasis of choriocarcinoma. The patient was then successfully treated with a surgery followed by multi-agent. We also present a review of the literature with particular emphasis on the diagnostic and therapeutic issues related to the choriocarcinoma.

CASE PRESENTATION

A 34-year-old woman came to the provincial hospital with a 2 month history of having difficulty in walking, progressive weakness and numbness in the bilateral lower extremities within a month after the onset of backache (3 months before admitted to the provincial hospital).

The patient was gravida 3, para 2. The first and second pregnancies were delivered spontaneously at term. In year 2010, the third pregnancy was found to be partial hydatidiform mole. Curettage was done at our institute, Songklanagarind hospital. Post surgery, she reported intermittent vaginal bleeding but she did not return back for the follow up.

Three years later she returned back to hospital with a history of having difficulty in walking, progressive weakness and numbness in bilateral lower extremities. At the provincial hospital, an initial examination revealed paraplegia, an impaired sensation below the level of thoracic 12 (T12). Urinary incontinence had resulted from loss of urinary bladder sphincter control. A myelography discovered complete thecal sac blockage at L1-L2 vertebra. Then, she underwent a laminectomy to remove the extradurally located tumor mass, which was causing compression of the spinal cord. Pathological examination revealed blackish brown colored tumor mass consisting of multinuclear syncytiotrophoblastic cells with large eosinophilic cytoplasm around the mononuclear cytotrophoblastic cells (Figure 1). These findings were consistent with choriocarcinoma. A computed tomography (CT) scan of the chest showed multiple variable size nodules, about 2-5 mm, in both lungs that were most likely metastases. The patient was then transferred to our institute. During surgery and six courses of adjuvant chemotherapy and physiotherapy, she was able to walk again. Ten months after diagnosis and treatment, she is now healthy without any evidence of disease.

Keywords

• Choriocarcinoma
• Spine metastasis

Conclusion: Choriocarcinoma with spinal metastasis is an unusual phenomenon. Spine surgery plus chemotherapy is highly effective for treatment of this condition.

admission, an evaluation with magnetic resonance imaging (MRI) revealed post L1-3 laminectomy with epidural hematomas at left lateral posterior aspect along the surgical defects. Extrudal and soft tissue masses were extending from T11 to L4 level with severe thecal sac encasement, conus medullaris and cauda equinum root compression (Figure 2 and 3). This extradural mass contained multiple flow voids and heterogeneous enhancement, which suggests hypervascularity. The patient then underwent multi-agent chemotherapy in the form of six courses of EMA-CO (etoposide, methotrexate, actinomycin D, cyclophosphamide, and vincristine). Her β-hCG level in serum was normal (< 1 mIU/mL) after a total of 3 courses of EMA-CO. At the end of chemotherapy, the marrow infiltration at L2 and L3 bodies were markedly decreased. The surrounding soft tissue and epidural soft tissue disappeared and could not seen on the subsequent MRI examination. She was sent for rehabilitation and physiotherapy. She showed improvement in her neurological status, and she was able to walk again. She is now in tumor remission 10 months after diagnosis.

DISCUSSION

Approximately 30% of choriocarcinoma patients show metastasis at the time of diagnosis [9]. Early hematogenous and widespread metastasis is well documented [8]. The most common sites of metastasis are the lungs and the vagina whereas metastasis within the bony system, especially in the spine is extremely rare, as also evident from our case. To our knowledge, from the published literature, only five cases of spinal bone metastasis from choriocarcinoma have been reported [4-8].

In reported cases, the age at diagnosis has ranged from 21 to 45 years [4-8]. Two of them presented with back pain [4-5], similar to our case. In other cases, symptoms arising due to the spread of cancer to coexisting organ(s) were the presenting complaints, such as central nervous system symptoms of headache [7-8] or visual field defect or paraplegia [5,8], or rarely as pulmonary system symptom of dyspnea [7]. Our case presented with back pain, weakness in lower extremities, and difficulty in walking due to cancer in the spine and epidural sac. All of the cases included in this report showed radiologic evidence of pulmonary metastasis [4-8]. Only one of them has symptoms of dyspnea [7]. Other organs involved were brain and spinal cord [7,8].

Although choriocarcinoma can follow any type of pregnancy, approximately 50% of the cases of choriocarcinoma are preceded by a hydatidiform mole. The remaining 50% are equally distributed between normal antecedent term gestational and abortion or...
Choriocarcinoma is one of the malignant tumors that is most sensitive to chemotherapy [2,10]. A patient with spine metastasis, as our case, is classified as “high risk” and is improbable to respond to single chemotherapy. Naito found that a choriocarcinoma patient, like in our case, is classified as “high risk” and is improbable to respond to chemotherapy [2,10]. A patient with spine metastasis, levels ranged from 15,000 to more than 100,000 mIU/Ml (Table 1) [4-8].

There have been two reported cases of spine metastasis of choriocarcinoma treated with multiagent chemotherapy with radiation [4-5]. Vani reported a poor response to 12 courses of multiagent chemotherapy in a choriocarcinoma patient with spine and lung metastasis. After treatment the patients received palliative radiotherapy [4]. Manegaz reported a choriocarcinoma patient with spine and lung metastasis who responded well to 7 courses of EMA-CO and radiotherapy. However, the patient died from sepsis caused by febrile neutropenia [5].

Surgery for a case of spinal metastasis of choriocarcinoma was firstly reported by Naito et al. in 2009 [6]. Surgery is indicated when a massive mass effect is due to tumor mass or hematoma. In this situation, spine surgery such as spondylectomy or laminectomy is required to provide acute decompression or palliative radiotherapy. However, the patient was successfully treated by total en bloc spondylectomy and radiotherapy [6]. To date it is agreed that patients with high risk GTN should be treated initially with multiagent chemotherapy especially EMA-CO with or without adjuvant surgery or radiotherapy. Cure rates for high risk GTN of 80-90% are now achievable with intensive multimodality [2,10]. However, the best treatment for patients with spinal metastasis has not been established because of its rarity.

Table 1: Reported cases of Gestational choriocarcinoma with spine metastasis.

<table>
<thead>
<tr>
<th>Author</th>
<th>Year</th>
<th>Age</th>
<th>Symptom(s)</th>
<th>Duration of symptom</th>
<th>Method of Diagnosis</th>
<th>Antecedent pregnancy interval</th>
<th>hCG level (mIU/ml)</th>
<th>Location of spine metastasis</th>
<th>Treatment</th>
<th>Status of last follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vani [4]</td>
<td>27</td>
<td>Back pain</td>
<td>1 week</td>
<td>CT and hCG</td>
<td>4 year after term</td>
<td>30,000</td>
<td>S5 vertebal body</td>
<td>Lung</td>
<td>MTX + ActD + Chlorambucil + VP-16 x 12 course</td>
<td>CR</td>
</tr>
<tr>
<td>Naito [6]</td>
<td>45</td>
<td>Pain, paraplegia, lower limb</td>
<td>4 month</td>
<td>MRI and hCG</td>
<td>2 year after mole</td>
<td>22,400</td>
<td>L3 vertebra body, L2-S1 epidural space</td>
<td>Lung</td>
<td>EMACO x 7 cycle</td>
<td>45 Gy 5 weeks</td>
</tr>
<tr>
<td>Vani [4]</td>
<td>38</td>
<td>Abnormal uterine bleeding, Persisted hCG level</td>
<td>6 month</td>
<td>PET/CT and history</td>
<td>6 month after term</td>
<td>15,793</td>
<td>L2 vertebra body, lumbar epidural space</td>
<td>Lung</td>
<td>Total en bloc spondylectomy</td>
<td>MTX 20mg/d 5 dx 3 courses</td>
</tr>
<tr>
<td>Lee [7]</td>
<td>33</td>
<td>Headache, dyspnea, hemoptysis</td>
<td>2 week</td>
<td>Histology and MRI</td>
<td>2 week after term</td>
<td>&gt; 100,000</td>
<td>L3 vertebra body, lumbar epidural space</td>
<td>Lung, brain</td>
<td>Embolization and laminectomy</td>
<td>EMA-CO</td>
</tr>
<tr>
<td>Ko [8]</td>
<td>21</td>
<td>Headache, nausea, visual field defect</td>
<td>Sudden</td>
<td>Histology and MRI</td>
<td>10 month after mole</td>
<td>&gt; 100,000</td>
<td>L2 vertebra body</td>
<td>Lung, thoracic spinal cord, brain</td>
<td>Craniotomy</td>
<td>Multi-agent chemotherapy</td>
</tr>
<tr>
<td>This case</td>
<td>34</td>
<td>Back pain, weakness in lower extremities, difficulty in walking</td>
<td>3 month</td>
<td>Myelography, Histology and MRI</td>
<td>3 year after partial mole</td>
<td>605,257</td>
<td>L1-L2 vertebra bodies T11-L4 epidural space</td>
<td>Lung</td>
<td>Laminectomy</td>
<td>EMACO x 6 cycle</td>
</tr>
</tbody>
</table>

Abbreviations: EMA-CO: Etoposide, Methotrexate, Actinomycin D, Cyclophosphamide, Vincristine; HCG: Human Chorionic Gonadotropin; MTX: Methotrexate; Actd: Actinomycin D; VP-16: Etoposide; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; PET/CT: Positron Emission Tomography/Computed Tomography; S: Surgery; C: Chemotherapy; R: Radiation
to control bleeding [6-7]. Because choriocarcinoma is extremely hemorrhagic, it is quite possible the surgical procedures may have exacerbated the invasive and metastatic potential of this tumor. Thus, preoperative angiographic embolization, or at least angiography of the tumor should be used to reducing perioperative hemorrhages and evaluate vascularity of the tumor site, respectively [6-7]. Lee reported a good course for choriocarcinoma with a patient with spine, epidural, lung and brain metastasis who was managed successfully by embolization of the lesion of the lumbar spine, followed by an injection of polymethymethacrylate in the L3 vertebral body, total laminectomy of L3, subtotal removal of the epidural mass, screw fixation of L2 and L4, and multiagent chemotherapy (EMA-CO) [7].

When central nervous system metastases are present, radiotherapy (whole brain irradiation) is usually given simultaneously with the initiation of systemic chemotherapy [2,10]. Radiotherapy was performed as adjuvant treatment in four previous cases of spine metastasis of choriocarcinoma [4-6,8]. This therapy can also be utilized when spine metastasis are present [5-6,8]. In our case, the patient was successfully treated by 6 courses of EMA-CO after laminectomy without radiotherapy.

Despite improvements in treatment modality and the use of combined modality treatment with chemotherapy, surgery and radiation, the prognosis for these choriocarcinoma cases with spinal metastasis is unfavorable. The longest reported survivor lived for 13 months after diagnosis [8]. Earlier diagnosis and multimodality treatment is crucial for significant reduction in mortality.

In conclusion, we have reported an uncommon case of metastatic choriocarcinoma to the lumbar spine and lung, which was successfully treated by laminectomy with multiagent chemotherapy. The neurological symptoms, history of a hydatidiform mole, and the possibility of metastatic GTN should always be considered especially in fertile females. In our case, the diagnosis was made by clinical history, imaging, and hCG levels. The treatment involved multiagent chemotherapy with or without surgery or radiotherapy.

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REFERENCES