ANDALAS OBSTETRICS AND GYNECOLOGY JOURNAL
Address for Correspondence:
Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127

eISSN : 2579-8324 pISSN : 2579-8323

Website:
http://jurnalobgin.fk.unand.ac.id/index.php/JOE

CASE REPORT

Choriocarcinoma with Pulmonary and Spinal Metastases : A Case Report

Syafar, Fardani Putra1, Muhammad, Syamel2, Antonius, Puja Agung2

1. Obstetrics and Gynecology Department, Faculty of Medicine, Andalas University, Dr. M. Djamil Central General Hospital Padang, West Sumatera, Indonesia

2. Division of Oncolgy Gynecology, Department of Obstetrics and Gynecology, RSUP Dr M. Djamil, Unversitas Andalas, Padang, Indonesia

Corespondence: *Fardani Putra Syafar, email : fardaniputras@gmail.com*

Abstract

Background : Choriocarcinoma is extremely malignant tumor contains of anaplastic trophoblast and prominent hemorrhage, necrosis, and vascular invasion. Choriocarcinoma is a rare, aggressive neoplastic type of trophoblastic disease. This condition grow rapidly and can metastasize to the lung and liver. There are few cases of choriocarcinoma metastases to the spine that have been reported.
Case Report : A 28-year-old woman with complaints of haemoptoe and shortness of breath. Previously the patient complained of not feeling the sensation for defecation and micturition. The patient had been diagnosed with choriocarcinoma since 3 years ago, refused to have a hysterectomy and had received chemotherapy 12 times in the first year with choriocarcinoma, but dropped out of chemotherapy in the second year, then came with a worsening condition a year later. The results of the chest x-ray and lumbar MRI showed suspicion of metastases to the lungs and spine. The patient was continued with chemotherapy with paclitaxel and carboplatin and was monitored with periodic beta HCG evaluation. Choriocarcinoma a have different prognoses depending on stage and onset. In these patients, based on FIGO staging, she has reached stage IV and also suspected chemotherapy-resistant Gestational Trophoblastic Neoplasia (GTN), worsened by disobedience to previous treatment. Many patients with GTN require multiple regimens with or without surgery to achieve complete remission.

Keywords: *Choriocarcinoma, lung metastases, spine metastases, gestational trophoblastic neoplasia*

ANDALAS OBSTETRICS AND GYNECOLOGY JOURNAL
Address for Correspondence:
Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127
eISSN : 2579-8324 pISSN : 2579-8323
Website:
http://jurnalobgin.fk.unand.ac.id/index.php/JOE

INTRODUCTION

Based on literature choriocarcinoma is a highly malignant tumor composed of syncytiotrophoblastic, intermediate trophoblastic and cytotrophoblastic cells arranged in a bilaminar configuration, which chorionic villi are almost always absent, and distant lung, brain, or liver metastases may be present.[1] Quoted from Cunningham based on Soper research mentioned this is the most common trophoblastic neoplasm to follow a term pregnancy or a miscarriage, and only a fourth of cases follow a molar gestation.[2] In Europe and North America, about 1 in 40,000 pregnant patients and 1 in 40 patients with hydatidiform moles will develop choriocarcinoma.[3] Another source state that its incidence is only 1 in 20,000 to 40,000 pregnancies, but is more common in women of Asian or African ethnicity.[4] A previous hydatidiform mole is a strong risk factor and subsequentpregnancies have a 1% risk of being a choriocarcinoma.[1] Gestational choriocarcinoma should be considered in any reproductive-aged women found to have metastases from an unknown primary cancer.[4]

Patients with choriocarcinoma typically present with symptoms of abnormal vaginal bleeding, pelvic pain and pressure. However, additional symptoms may be present such as hemoptysis, dyspnea, chest pain or melena if metastatic disease has occurred. [5]

Choriocarcinoma was the first cancer to be reportedly cured by the chemotherapeutic agent methotrexate in 1958.[1] Later decades, the advent of combination chemotherapy and aggressive surgical removal of lung and cerebral metastasis, survival and cure rates approached 90% for such patients. [6] Randomised controlled trials in GTN are scarce owing to the low prevalence of this disease and its highly chemosensitive nature. As chemotherapeutic agents may be associated with substantial side effects, the ideal treatment should achieve maximum efficacy with minimal side effects. [7]

From literature mentioned that invasive moles and choriocarcinomas are highly chemosensitive tumours and chemotherapy (with or without surgery) will cure virtually all low-risk lesions and 80% to 90% of high-risk lesions. However, approximately 25% of these tumours will be resistant to primary treatment or relapse after cure and will require salvage chemotherapy.[8] Because it is a rare case the author raises the topic of choriocarcinoma that metastasizes to the lungs, spine and relapses after chemotherapy.

CASE REPORT

At May 2022, a 28-year-old woman come to emergency department of M Djamil Hospital with complaints of haemoptoe and shortness of breath. At the beginning of 2019, the patient was pregnant for the first time with bleeding and after curettage, histopathological results of moles were found. Several months after curettage the patient still complained of vaginal bleeding, then then do a Beta hCG test. The patient was diagnosed with choriocarcinoma and recommended hysterectomy and chemotherapy but the patient refused hysterectomy. The patient was then given chemotherapy 12

ANDALAS OBSTETRICS AND GYNECOLOGY JOURNAL
Address for Correspondence:
Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127
eISSN : 2579-8324 pISSN : 2579-8323
Website:
http://jurnalobgin.fk.unand.ac.id/index.php/JOE

times with a beta HCG value that never reached zero. In 2020, because she felt asymptomatic, the patient did not go to the hospital for control. Then the patient was re-admitted to the hospital at 2021 with worsening condition, coughing up blood and shortness of breath. A chest X-ray examination revealed metastases to the lungs, and it was decided to give chemotherapy but drop out of chemotherapy for 5 weeks. Since the beginning is known of choriocarcinoma until the drop out of chemotherapy, the patient has received EM/CO (etoposide, methotrexate, cyclophosphamide, and vincristine) chemotherapy regimen.

Fig 1. Thorax X Ray with lung metastase at May, 2022

In several months the patient was complained of not feeling the sensation for defecation and micturition. Urine catheter inserted and consult to neurologist was performed, has been given amitriptilyn and B compex, and also suggested a lumbar MRI examination of the patient and suspected spinal choriocarcinoma metastases.

ANDALAS OBSTETRICS AND GYNECOLOGY JOURNAL
Address for Correspondence:
Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127
eISSN : 2579-8324 pISSN : 2579-8323
Website:
http://jurnalobgin.fk.unand.ac.id/index.php/JOE

Fig 3. Lumbal MRI with metastase to spine at August, 2022

Beta HCG check on June 3, 2022 is 85,809.73 mIU/mL. The patient was continued with chemotherapy with a regimen of Carboplatin and Paclitaxel. Four mounths later thorax X ray seen the remission metastase and beta HCG check in September 2022 is still 3241 mIU/mL.

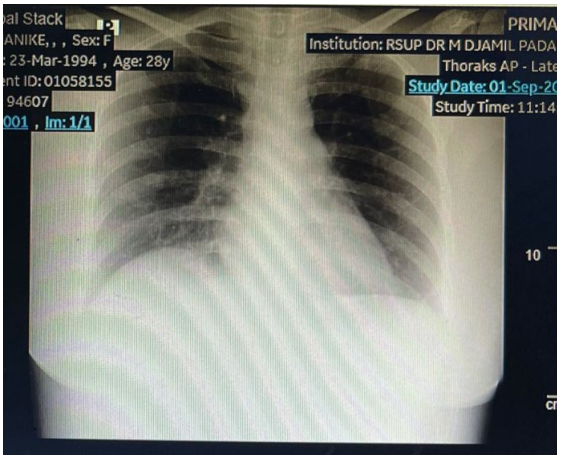

Fig 3. Thorax X Ray with remission lung metastase at September, 2022

ANDALAS OBSTETRICS AND GYNECOLOGY JOURNAL
eISSN : 2579-8324 pISSN : 2579-8323
Address for Correspondence:
Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127
Website:
http://jurnalobgin.fk.unand.ac.id/index.php/JOE

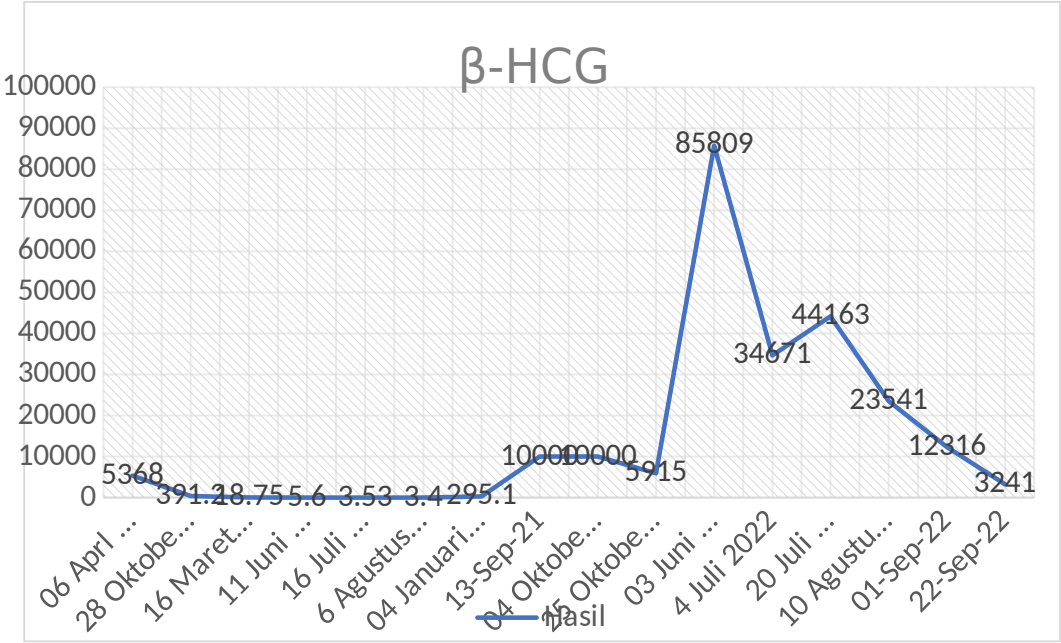

Fig 4. Graphic Beta HCG

DISCUSSION

The patient in the case we presented was preceded by a molar pregnancy, where this condition can be an early development of gestational trophoblastic disease, according to the literature that choriocarcinoma (CC) is a highly malignant tumor originating in the trophoblastic tissue, which majority of cases of CC arise due to malignant transformation of a complete molar pregnancy, although it has been reported following term pregnancy, spontaneous abortion, few cases follow a molar gestation and even after ectopic pregnancy.[2,9]

The patient in this case started with a molar pregnancy and was then cured, and rebleeding several months after the curettage. According the Journal of the National Comprehensive Cancer Network (JNCN) the presentation of GTN can vary depending on the antecedent pregnancy event and disease type and extent. Postmolar GTN, including invasive mole or choriocarcinoma, can be associated with irregular bleeding after initial treatment of molar pregnancy, an enlarged and irregular uterus, and bilateral ovarian enlargement. [10]

The patient was refused histerectomy and treated with multi-drug chemotherapy but had dropped out of chemotherapy, then never achieved remission. Repeat dilation and curettage or hysterectomy can be considered for persistent postmolar GTN.[10]

ANDALAS OBSTETRICS AND GYNECOLOGY JOURNAL
eISSN : 2579-8324 pISSN : 2579-8323
Address for Correspondence:
Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127
Website:
http://jurnalobgin.fk.unand.ac.id/index.php/JOE

All patients with post molar GTN and those with choriocarcinoma have their clinical, imaging and hCG data utilised to complete the FIGO scoring system to enable accurate selection of single verses multi-agent chemotherapy.[8] All other distant metastatic such lung and spinal in our case categorized into stage IV according to the FIGO criteria such in our case. The occurrence of choriocarcinoma with spinal metastasis is extremely rare, at 2014 Atjimakul et al presented a rare case of a patient who primarily presented with symptoms of spinal compression caused by lumbar spinal metastasis of choriocarcinoma, then was then successfully treated with a surgery followed by multiagent.[11]

A high proportion of all high-risk patients will fail first-line therapy or will relapse after remission. Although high-risk GTN is less frequent than low risk GTN, drug resistance and relapse in high-risk GTN is inherently much more difficult to treat.[7] To date, there is no standard guideline to define the criteria for resistance to chemotherapy even though some physicians determine this condition by a plateau or rise in serum human chorionic gonadotropin (hCG) and/or development of new metastases.[12]

According to the literature, our patient started with EM/CO as a chemotherapeutic agent, but seemed to have resistance and refractory GTN. However, up to 30% of patients develop either resistance or recurrence. Although EMA/CO resistant GTN is a relatively rare disease, it can be challenging to manage. The cure rate to such a condition is highly dependent on the availability of an effective multiagent chemotherapy regimen with reasonable toxicity profile. Close monitoring of high-risk patients, early diagnosis and recognition is key for a successful outcome. Despite the primary role of chemotherapy in EMA-CO resistant disease, surgical interventions have been shown to improve survival and cure rate. A variety of multiagent chemotherapy regimens have shown efficacy in EMA-CO resistant disease. Unfortunately, to date, there is no strong evidence to suggest which regimen is the standard second-line therapy. Many patients require multiple regimens with or without surgery to achieve complete remission. [12]

We continued with other agent such Foncopac and Cisplatin and then Carboplatin and Paclitaxel to this patient, however until now the patient's condition is still under monitoring. Mirji et al mentioned that despite the high chemo sensitivity, resistance to first line chemotherapy is sometimes encountered, requiring second or third line salvage chemotherapy. In some cases, surgical excision of isolated chemoresistant disease may be required.[13]

CONCLUSION

In conclusion, we have reported an uncommon case of metastasic choriocarcinoma to the lumbar spine and lung (stage IV according FIGO staging) which was suggested resistance first line chemotherapy agents due to patient inobedient to treatment. The neurology symptoms such not feeling the sensation for defecation and micturition. In our case, the diagnosis was made

ANDALAS OBSTETRICS AND GYNECOLOGY JOURNAL
Address for Correspondence:
Editorial Room Andalas Obstetrics and Gynecology Journal, 3rd floor of KSM of Obstetrics and Gynecology, RSUP DR. M. Djamil Padang, Jl. Perintis Kemerdekaan Padang, Sumatera Barat 25127
eISSN : 2579-8324 pISSN : 2579-8323
Website:
http://jurnalobgin.fk.unand.ac.id/index.php/JOE

by clinical history, imaging, and beta hCG levels. Subsequently, the patient was given multi-agent chemotherapy with clinical monitoring and beta HCG results.

REFERENCES

1. Berek, J. S. & Hacker, N. F. Berek & Hacker's gynecologic oncology.
2. Cunningham, F., Leveno, K., Dashe, J. & et al. *Williams Obstetric Edisi 26*. (Mc Grow Hill, 2022).
3. Zhang, W., Liu, B., Wu, J. & Sun, B. Hemoptysis as primary manifestation in three women with choriocarcinoma with pulmonary metastasis: a case series. *J Med Case Rep* **11**, (2017).
4. Callahan, T. L. *Blue Prints Obgyn*. vol. 148 (Wolters Kluwer, 2018).
5. Dugan, P. *Management of gestational trophoblastic disease*. (2020).
6. Goto, S. *et al.* Survival rates of patients with choriocarcinoma treated with chemotherapy without hysterectomy: Effects of anticancer agents on subsequent births. *Gynecol Oncol* **93**, 529–535 (2004).
7. Alazzam, M. *et al.* Chemotherapy for resistant or recurrent gestational trophoblastic neoplasia. *Cochrane Database of Systematic Reviews* vol. 2016 Preprint at https://doi.org/10.1002/14651858.CD008891.pub3 (2016).
8. Clark, J. J., Slater, S. & Seckl, M. J. Treatment of gestational trophoblastic disease in the 2020s. *Current Opinion in Obstetrics and Gynecology* vol. 33 7–12 Preprint at https://doi.org/10.1097/GCO.0000000000000674 (2021).
9. Mangla, M., Singla, D., Kaur, H. & Sharma, S. Unusual clinical presentations of choriocarcinoma: A systematic review of case reports. *Taiwanese Journal of Obstetrics and Gynecology* vol. 56 1–8 Preprint at https://doi.org/10.1016/j.tjog.2015.05.011 (2017).
10. Abu-Rustum, N. R. *et al.* Gestational trophoblastic neoplasia, version 2.2019. *JNCCN Journal of the National Comprehensive Cancer Network* vol. 17 1374–1391 Preprint at https://doi.org/10.6004/jnccn.2019.0053 (2019).
11. Atjimakul, T., Hanprasertpong, J. & Saeaib, N. *Choriocarcinoma with Spinal Metastasis: A Case Report and Literature Review*. *JSM Clin Oncol Res* vol. 2 (2014).
12. Babaier, A., Jim, B. & Ghatage, P. Management of EMA-CO resistant/refractory gestational trophoblastic neoplasia. *Cancer Rep Rev* **3**, (2018).
13. R. Mirji, S. *et al.* Chemo-resistant gestational trophoblastic neoplasia: a review of cases at a tertiary cancer centre. *Int J Reprod Contracept Obstet Gynecol* **8**, 1620 (2019).