Case Report

Complete remission of nonmetastatic persistent gestational trophoblastic tumour by Methotrexate and Actinomycin D: A case report

Shah Basant[1], Dangal Ganesh[2], Karki Aruna[2], Pradhan Hema[2], Shrestha Ranjana[2], Bhattachan Kabin[2]

[1]Department of Obstetrics and Gynecology, Paropakar Maternity and Women's Hospital, Kathmandu
[2]Department of Obstetrics and Gynecology, Kathmandu Model Hospital, Kathmandu
Corresponding Author: Dr Basant Kumar Shah
Email: Shahbasant@gmail.comPhone: +977-9804917114

ABSTRACT

Locally invasive non-metastatic persistent gestational trophoblastic tumours (PGTT) usually falls in low-risk group in WHO scoring system based on prognostic factors. We report a case of non-metastatic PGTT which followed a molar pregnancy. Complete remission of the tumour was achieved by 3 cycles of single agent chemotherapy (Methotrexate with leukovorin rescue) and 5 cycles of single agent (Actinomycin D).

Keywords: Persistent gestational trophoblastic tumour, molar pregnancy , Methotrexate, Actinomycin D

INTRODUCTION

Gestational trophoblastic disease (GTD) comprises a spectrum of interrelated conditions originating from the placenta[1]. Histologically distinct disease entities encompassed by this general terminology include complete and partial hydatidiform moles, invasive moles, gestational choriocarcinomas, and placental site trophoblastic tumors[1]. Gestational trophoblastic neoplasia (GTN) are characterized by aggressive invasion of the endometrium and myometrium of the uterus by trophoblastic cells[2]. Persistent gestational trophoblastic neoplasia is evidenced by the persistence of trophoblastic activity following evacuation of molar pregnancy or following previous abortion or ectopic pregnancy or even normal pregnancy. Gestational trophoblastic neoplasia follows hydatidiform mole (60%), previous spontaneous abortion/abortion (30%), and normal pregnancy or ectopic gestation (10%) [3,4].

GTN usually presents with continued vaginal bleeding, persistently soft and enlarged uterus and persistently raised beta hCG (human chorionic gonadotrophin) level following initial evacuation of a molar pregnancy [2].

Patient Information

Mrs Rai, 33 years resident of Kathmandu, Nepal.

A 33 years, mother of 9 years child presented to gyanaecology opd of Kathmandu Model Hospital, Kathmandu on 2020 December with complaint of per vaginal spotting for one and half months .

She gave history of medicine taken for medical abortion (MA) from local medical shop after her urine pregnancy test positive. She also gave history of passage of blood clots after taking medicine. Her menstrual cycle was irregular since 2 years. She did not give history of pain abdomen. Her bowel and bladder habits were normal and regular. For these complaints she visited at our gyanaecology opd after one and half months of MA taken. There were no significant medical and surgical history. Couple had not used any form of contraception. The patient was not on any medications.

On examination vitals were stable with pulse rate of 88 bpm, blood pressure of 110/70mmHg, R/R of 18 bpm and temperature of 98.F. Systemic examinations were within normal limit.On per abdomen examination abdomen was soft, non-tender. On per speculum examination cervical os closed, minimal bleeding was present with blood clots. Urine pregnancy test (UPT) done was positive.

Article Information
Received: 12 December 2024 Accepted: 28 May2025 Published online: 7 June 2025

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IMAGING

USG abdomen and pelvis

It showed highly vascular hypoechioc area measuring (17 *8 mm) in anterior myometrium, d/d invasive mole, AV malformation.Repeat USG after four weeks of first visit showed impression of heterochoic area measuring (29*20 mm) with high vascularity in anterior wall of uterus.

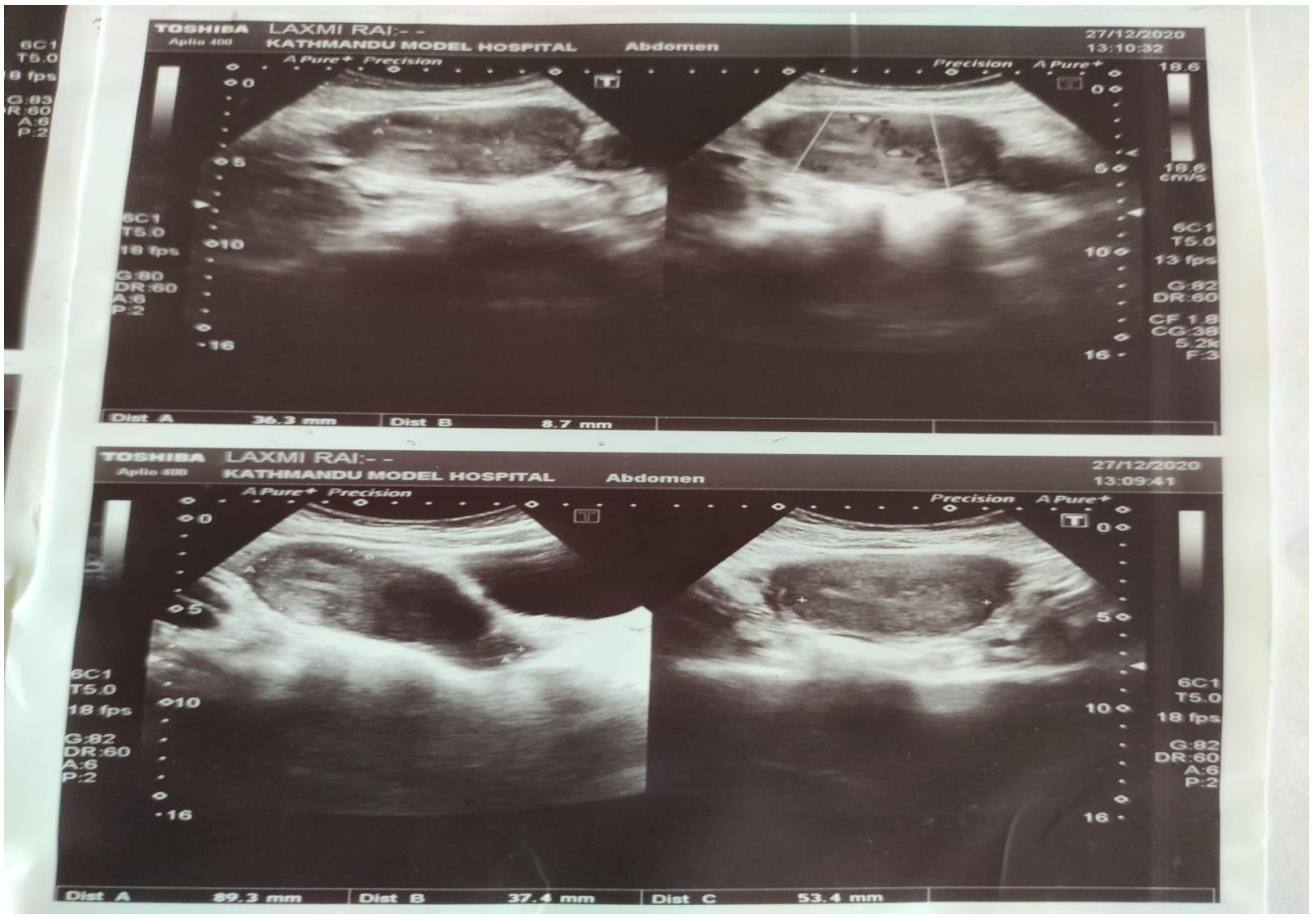


Fig.1: Ultrasound guided scan shows highly vascular hypoechoic area measuring 17*8 mm in size noted in anterior myometrium

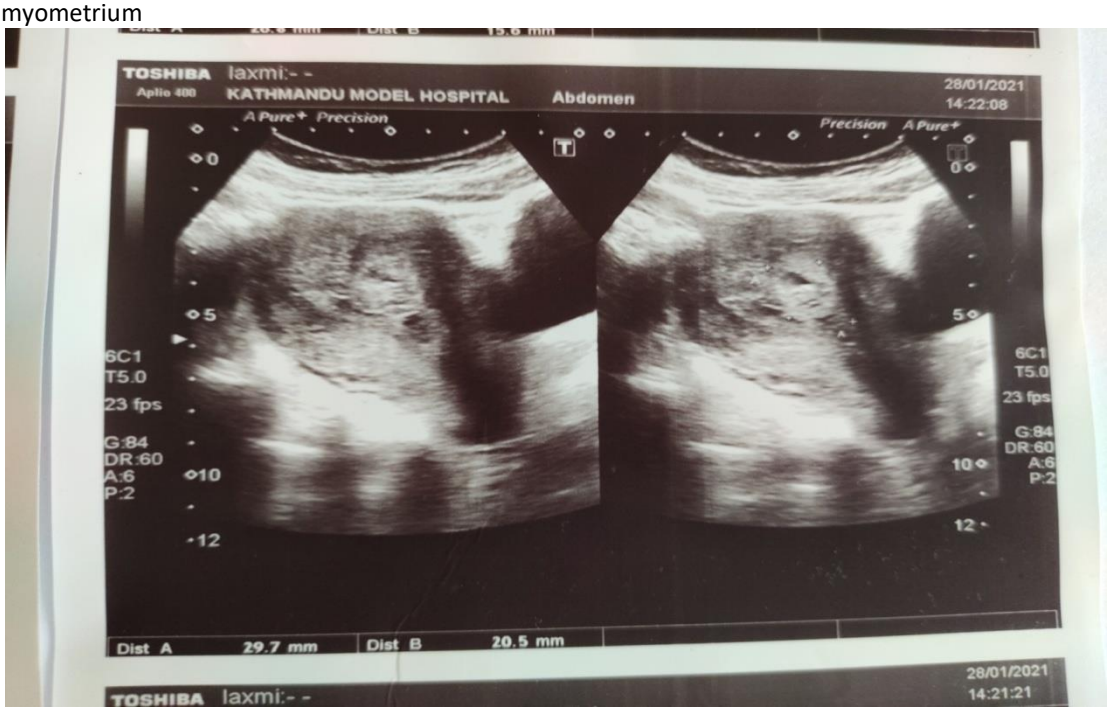


Fig.2: Ultrasound guided scan shows highly vascular hypoechoic area measuring 29*20 mm in size noted in anterior myometrium

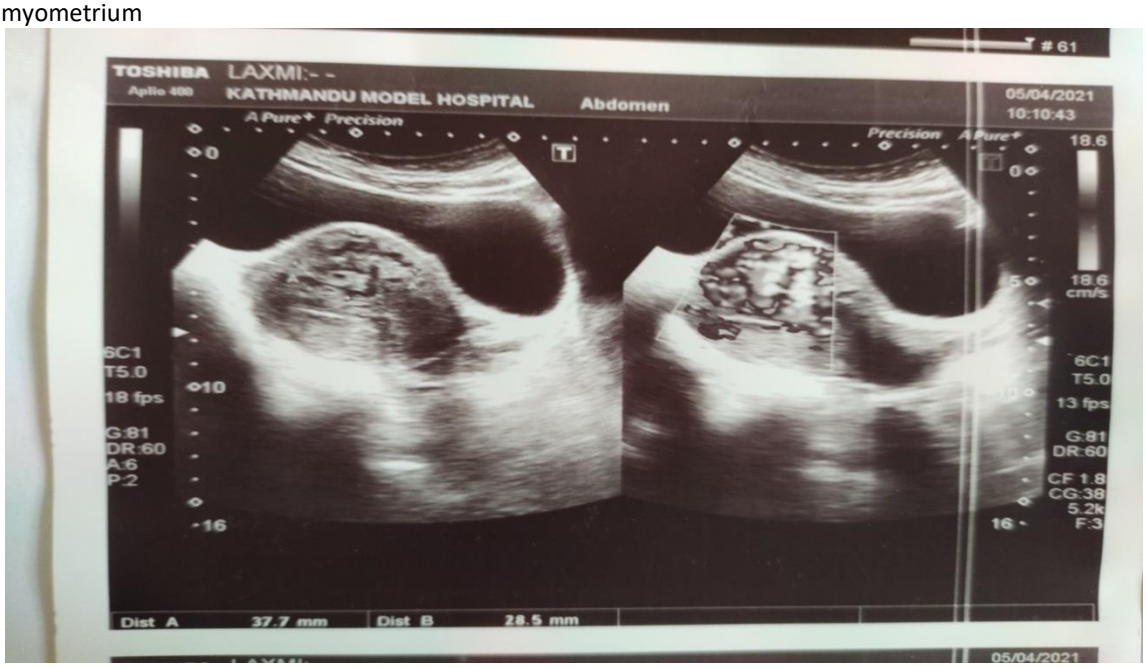


Fig.3: Ultrasound guided scan shows highly vascular hypoechoic area measuring 37*28 mm in size noted in anterior myometrium.

Haematology

Her serum beta hCG value was 1777.5 IU/L. Her blood investigations were as follows: haemoglobin 9.3 gm/dl, platelets 129,000/cumm, total count 14700/cumm, neutrophils 78%; liver fuction test, renal function test within normal limits

β-hCG measurements

Serial serum beta hCG monitoring was done after 3 days,7 days, 14 days and 28 days whichshowed values of 1576.4 IU/L, 5910.4 IU/L, 7135.9 IU/L, 14184 IU/L respectively.

Diagnostic Assessment

Her rising β-hCG follow up showed rise > 10% over three values in > 2 weeks and her USG abdomen and pelvis scan also supported diagnosis of invasive mole which were applied to justify GTN diagnosis(FIGO/WHO 2021 criteria).

Interventions

Manual Vacuum Aspiration (MVA) was done under intavenous anesthesia, with the intra-operative findings of about 50 milligrams of tissues and/or clots. Specimen was sent for histopathological examination (HPE).

Follow up

The patient was discharged the following day of MVA with oral antibiotic for 7 days and was advised to follow up in the gyanaecology OPD after 1 week with beta hCG and HPE report. After 1 week her betahCG level was 18160 IU/L. HPE report showed histo-morphological features compatible with decidualized tissue, however chorionic villi and trophoblastic cells (features of product of conception) not seen.

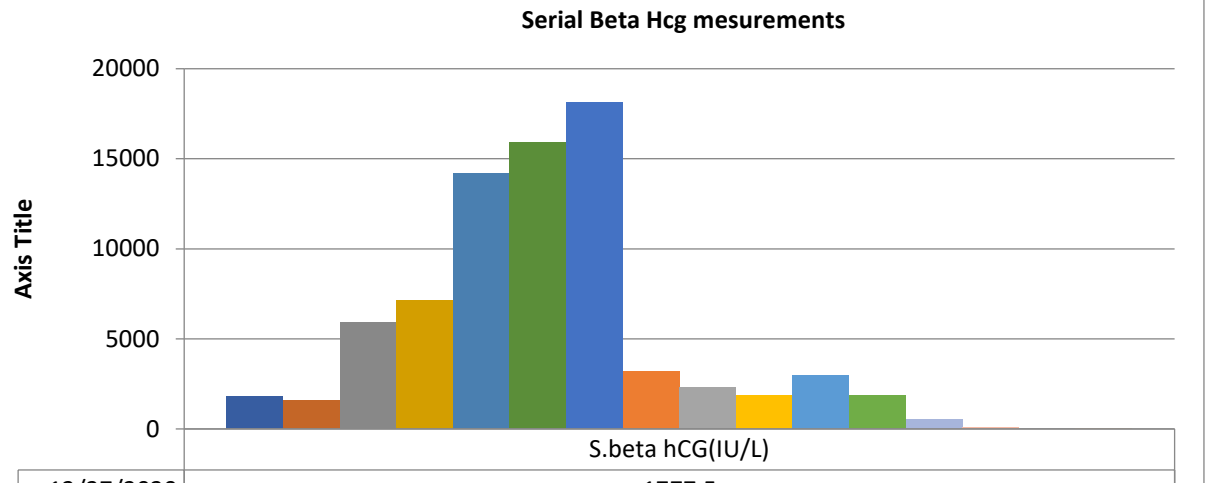
Before starting first line chemotherapy, complete blood count (CBC), liver function test(LFT) and renal function test(RFT) and chest x-ray were performed. Hemoglobin was 12 g/dl and all the other investigations were within normal limits. And, chest X-ray was normal. WHO Prognostic scoring was 2 (pre-treatment beta hCG level in the range of 1,000-10,000 ;18160-Score of 2). So, single agent chemotherapy with Methotrexate (with Leukovorin rescue) was started. She was treated on opd basis for 8 days course of Methotrexate 50 mg IM and Folinic acid 5 mg IM on alternate days.

Then, second cycle of chemotherapy was completed on OPD basis. Serum beta hCG level following completion of second cycle of chemotherapy was 3196.3 IU/L. The third cycle of chemotherapy was also completed in OPD basis. Serum beta hCG level after third cycle of chemotherapy was 2308 IU/ L .

Second line chemotherapy was initiated switching to Actinomycin-D due to lack of > 15% decline in β-hCG after two cycles of Methotrexate and Folinic acid therapy citing FIGO/WHO guidelines on low-risk GTN management.

Before starting second line chemotherapy, CBC, LFT, RFT and chest x-ray were performed. Hemoglobin was 11.1 gm/dl and platelets 135,000/cumm and all the other investigations were within normal limits. And, chest x-ray was normal. The fourth cycle of chemotherapy was started with Actinomycin D 0.5 mg intravenous od for 5 days with pre-treatment level of beta hCG 2308 IU/L. The fifth cycle, sixth cycle and seventh cycle of single agent chemotherapy was started with Actinomycin D with beta hCG level of 1859 IU/L ,526 IU/L and 81 IU/L respectively.

She had been advised with serum beta hCG, CBC, LFT, RFT reports after 1 week .After 1 week of follow up her serum beta hCG level was 32.1 IU/L and her CBC, LFT, RFT were within normal limits. Her eight cycle of single agent chemotherapy was started at beta hCG level of 32.1 IU/L on OPD basis. After receiving eighth cycle of Actinomycin D, her s.betahCG level was 4.8 IU/L(normal).Two more cycles were given. She was advised for follow up every 2weeks for 3 months, monthly for 3months, 3monthly for 2years and then yearly for 5 years.



	S.beta hCG(IU/L)
12/27/2020	1777.5
12/30/2020	1576.4
1/7/2021	5910.4
1/14/2021	7135.9
1/28/2021	14184
2/5/2021	15897
2/11/2021	18160
3/16/2021	3196.3
4/1/2021	2308
4/19/2021	1878.8
5/31/2021	2988
6/13/2021	1859
6/25/2021	526.7
7/11/2021	81.5
7/25/2021	32.1
8/9/2021	4.8

Fig.4: Changes in β hCG levels (IU/L) during the treatment period.

OUTCOME

Following last two cycles of chemotherapy her USG abdomen & pelvis scan showed complete disappearance of the mass. No serious side effects of the chemotherapy were noticed during the treatment. Finally she achieved complete remission of nonmetastatic persistent gestational trophoblastic tumour.

DISCUSSION

Gestational Trophoblastic Neoplasms (GTN) are proliferative as well as degenerative disorders of placental elements and include complete or partial hydatidiform mole (90%), invasive mole (5-8%), villous or a villous choriocarcinoma (1-2%), and placental site tumour (1-2%)[5]. The incidence of GTN varies in different regions from 0.6 – 1.1 per 1,000 pregnancies in Europe and North America to 2 per 1000 pregnancies in Japan and 1 in 160 pregnancies in India and Middle East[6,7].

PGTT may be non-metastatic or metastatic. Nonmetastatic locally invasive disease known as invasive mole develops in 20% of patient after complete molarpregnancy and 2-4% after a partial molar pregnancyand very rarely after normal delivery or abortion[8].

Metastatic disease develops in about 4% of patient after a complete hydatidiform mole but develops more commonly after a non molar pregnancy[9]. For the

management and prognosis purpose a patient is considered to have high risk group if the WHO prognostic score is more than 7, middle risk group if score is 5-7 and low risk if the score is 4 or less[10]. Patients with non metastatic disease very rarely fall into high risk group but those with metastatic disease invariably have high risk score[11].

In our case, the patient was presented to gyanaecology OPD with symptom of per vaginal spotting since one and half months after taking medicine for MA from local shop. She was diagnosed to be molar pregnancy by USG. Her β hCG level was high. The patient underwent Manual Vacuum Aspiration but her β hCG level was still higher after one week of follow up. The patient was started on chemotherapy with single agent (Methotrexate) first two cycles and then second line single agent (Actinomycin D) chemotherapy because of variable rise and fall in β hCGlevel.After five cycles of Actinomycin D, she achieved complete remission. This explains the high chemosensetive behaviour of the tumour to Actinomycin D. The report is presented here because of the challenges faced during the course of the treatment process.

CONCLUSION

Persistent GTT are life-threatening conditions, complete remission can be obtained with appropriate chemotherapy. Delayed diagnosis and treatment can worsen prognosis by putting even non-metastatic disease into a high-risk category. Even single agent chemotherapy can achieve complete remission of low risk non metastatic tumor without requiring full EMA-CO regimen.

Patient Perspective & Informed Consent

Before commencing with the interventions and treatments, written informed consent was taken from her. She was well explained about nature of disease, treatment protocols, complications, prognosis and failure of treatment. All preparations and precautions were undertaken as per the standard hospital protocol regarding safety measures and the management of possible complications. Informed consent was also taken for publication of the case after completion of treatment. Her identity and personal information were kept confidential throughout the case study.

Author Contributions:

1. Aruna Karki and Hema Pradhan reviewed the literature; Ganesh Dangal conceptualized and designed the research; Basant Shah did data collection, data analysis, data Interpretation.
2. Ranjana Shrestha and Kabin Bhattachand drafted the manuscript.
3. All authors reviewed the manuscript and approved the final version of the manuscript ready for submission.
4. All authors agreed to be accountable for all aspects of the research work.

Acknowledgements: I would like to express my sincere gratitude to my guide, my teacher and my mentor Prof. Dr. Ganesh Dangal for his constant guidance, support and valuable suggestions throughout the study period and case report writing. I'm really grateful for the patience and belief he had on me and the continuous support and encouragement he had given me. I would also like to express my gratitude towards my seniors Dr. Kenusha Tiwari, Dr. Sonu Bharti for her constant help in statistical analysis, data collection during my study period. I'm very much obliged to my teachers Dr. Aruna Karki, Dr. Hema Pradhan, Dr. Ranjana Shrestha, Dr. Kabin Bhattachan for their guidance during my study period. Lastly I'm very grateful to my parents, wife for their immense help, care, love and encouragement during my study period.

Consent/Assent: Informed written consent was obtained for data collection and publication of the case report

Data Availability Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Conflicts of Interest: There is no financial or non-financial conflict of interest any of the authors.

Source of Funding: The authors received no external fund for this research

Layman summary:

Locally invasive non-metastatic persistent gestational trophoblastic tumours (PGTT) usually falls in low-risk group in WHO scoring system based on prognostic factors. We reported a case of non-metastatic PGTT which followed a molar pregnancy. Persistent GTT are life-threatening conditions, complete remission can be obtained with appropriate chemotherapy. Delayed diagnosis and treatment can worsen prognosis by putting even non-metastatic disease into a high-risk category. Complete remission of the tumour was possible by single agent chemotherapy (Actinomycin D) in our case which showed the high chemosensetive behaviour of the tumour to Actinomycin D. Even single agent chemotherapy can achieve complete remission of low risk non metastatic tumor without requiring full EMA-CO regimen.

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