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(CASE REPORT)

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Unusual discovery of metastatic GTT causing death in a young woman

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Abstract

Gestational trophoblastic disease corresponds to cystic degeneration of the trophoblast villi with excessive secretion of choriogonatrophinic hormone (HCG), groups together lesions :

- Benign lesions known as hydatidiform moles (partial or complete)
- Malignant lesions known as gestational trophoblastic tumors (GTT), comprising :
  - Choriocarcinomas
  - Invasive moles
  - Trophoblastic tumors of the implantation site (TTSI)

Diagnosis is based on questioning and clinical examination, while paraclinical tests, especially ultrasound and Beta HCG, establish the diagnosis of hydatidiform mole. However, TTG may require other tests, and histology confirms the diagnosis.

Management is based on a protocol codified according to pre-established guidelines.

We report a rare case of an unusual presentation of metastatic GTT causing death in a 32 year old woman just one month post partum.

Keywords: Hydatidiform mole; GTT; Pregnancy; Post abortum; Death

1. Introduction

Gestational trophoblastic disease is a group of diseases derived from trophoblastic tissue with excessive secretion of choriogonatrophin hormone (HCG), comprising 2 subgroups:

- Benign trophoblastic diseases: partial or complete hydatidiform mole.
- Malignant trophoblastic diseases, known as gestational trophoblastic tumours (GTT), comprising :
  - Choriocarcinomas
  - Invasive moles
  - Trophoblastic tumours of the implantation site (TTSI)
  - Epithelioid trophoblastic tumours (ETT)

These malignant tumours most often follow a partial or complete mole, but also abortion or even a normal pregnancy.

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We report a rare case of an unusual presentation of metastatic GTT causing death in a 32 year old woman after just one month post partum and who had a history of complete hydatidiform mole in 2019 which was followed up, negatived and declared cured.

2. Clinical case

Patient aged 32, married, G2P2 (2 live children/ vaginal delivery), with a history of Hodgkin's lymphoma since 2009 having received 8 courses of CMT declared in remission in 2012, then on 08/ 2019 the patient underwent an aspiration on suspicion of a hydatidiform mole, for which the pathology test came back in favour of a complete hydatidiform mole, followed by post-molar surveillance, after a lung X-ray and liver ultrasound came back without any particularities:

- Clinical: uterine involution and absence of bleeding,
- Radiological at 10 days with absence of a retention image and achievement of the uterinevacuity line,
- Biological in the same laboratory with weekly monitoring until negativation (three negative weekly assays) obtained after 11 weeks post aspiration then monthly monitoring for 01 year with always negativation of the assessment, last check date 19/11/2020.

The patient became pregnant 9 months later, with the pregnancy being monitored by a private doctor and progressing normally until the vaginal delivery.

Everything was going well until 30 days post partum when the patient presented with left sciatica-like pain with heaviness in the 2 lower limbs making it impossible to walk without assistance, with the notion of a cough associated with sputum streake d with blood without chest pain, The whole evolving in a context of dyspnea and rapid alteration of general condition motivating her consultation to a neurologist where she benefited from a Magnetic Reasoning Image MRI objectifying secondary vertebral lesions, then a Thoraco abdomen pelvic CT TAP objectifying vertebral lesions and multiple nodules and pulmonary parenchymatous micronodules realizing a secondary Balloon Release aspect.

The patient was then referred to the Pneumology Department at the Hassan II University Hospital in Fez, where she underwent a CT biopsy of the right upper lobe lung lesions. Anapath analysis was inconclusive: necrotic and inflammatory remodelling with no specific lesions.

Staffed in thoracic Pluridisciplinary Concert Meeting: beta HCG assay back to 190,000 then referred to gynaecology department for further management to the gynaecology department for further management.

Patient underwent pelvic ultrasound: uterus normal size, endometrium thin, myometrium homogeneous thin endometrium, homogeneous myometrium, ovaries seen without any particularities and no effusion.

The patient's general condition deteriorated and her SaO2 was 60%,She was transferred to Mother and Child Intensive Care Unit for treatment.

The patient was referred to the Gynaecological Pluridisciplinary Consultation Meeting and, in view of the very high beta HCG levels checked on 2 occasions, the diagnosis of high-risk GTT was accepted. the diagnosis of high-risk GTT was adopted with the decision to use polychemotherapy after stabilisation of the patient.

The patient died after 10 days in intensive care.

3. Main questions are being asked

- Is it a post-pregnancy molar GTT that the patient had when the follow-up was correct with negativation of the work-up withou t any disturbed evolution (absence of the Federation internationale des gynecologues et obstetriciens (FIGO) diagnostic criteria)
- Is it a post partum GTT with this very rapid metastatic progression? (delivery 30 days ago)?
- Recurrence or progression of her lymphoma which had started in 2009, but the patient was declared cured in 2012, and her beta HCG level was very high, whereas in lymphoma this level is very moderate.

4. Discussion

GTTs are rare tumours which occur in

- - 15% after complete mole, 3% after partial mole,
- - 1/160,000 normal pregnancies, 1/15,000 abortions, 1/5000 EctopicP regnancy EPs.

4.1. Diagnosis

The diagnosis is essentially based on the FIGO 2002 diagnostic criteria, especially if post-molar:[1].

- A rise in HCG of 10% or more on at least 3 consecutive weekly tests for at least two weeks (D0, D7, D14)
- HCG stagnation (defined as a variation of less than 10% in the level at one-week intervals) on at least 4 consecutive weekly tests for at least three weeks (D0, D7, D14, D21)
- Persistence of an abnormal hCG level for more than 6 months after evacuation of the hydatidiform mole, a very rare occurrence.
- The situation of a proven histology of choriocarcinoma on a sample (uterine or distant) in the aftermath of a hydatidiform mole.

4.1.1. If it is a post-partum or post-abortal GTT

The diagnosis cannot be made on the basis of FIGO criteria, as hCG monitoring is not carried out in these situations. It is therefore evoked different specific circumstances few :

- Persistent metrorrhagia following a miscarriage or abortion or in the post-partum period
- The discovery of metastases (pulmonary, vaginal, hepatic, cerebral or other) in a woman during genital activity at a more or less distant stage from childbirth or abortion.
- Severe respiratory distress or hyperthyroidism.
- Haemorrhage from a metastatic site.
- Elevated BHCG level (after ruling out a new pregnancy)
- Histological diagnosis of choriocarcinoma.

Our patient was not included in the FIGO diagnostic criteria after her molar pregnancy of more than 02 years, which had a very good clinical and biological evolution for more than a year, bearing in mind that in most cases the diagnosis of GTT is made when the HCG is not yet negative and that the average delay for the occurrence of GTT is around 2 to 4 months in a patient who has presented with a hydatidiform mole[3].

In our case, the discovery of metastases and the unexpected beta HCG level after an unremarkable pelvic ultrasound led to the diagnosis of TTG, but after just one month post partum, this development and the deterioration in general condition leading to death came as a real surprise.

4.2. Assessment of extension

Essential before any therapeutic decision, which will be based on the calculation of the FIGO score

4.2.1. Regional extension assessment

- Clinical examination

The clinical examination looks for vaginal metastases. These are raised vaginal orvulvar lesions with a hyper-vascular, framboised appearance, of all sizes. Biopsies of such lesions are strongly discouraged because of the serious risk of haemorrhage.

- Endovaginal ultrasound with colour Doppler and pelvic MRI

Assess whether the TTG is located in the uterus, its size and extension into the thickness of the myometrium. Infiltration as far as the serosa may cause cataclysmic haemoperitoneum with a life-threatening outcome.

In our patient, this locoregional clinical and ultrasound work-up was unremarkable.

4.3. Remote extension report

- Thoraco-abdominal scan + chest x-ray:
  - Lung metastases must be counted on chest x-ray if present to maintain a universal language
  - Search for hepatic metastases (poor prognosis), splenic metastases, etc.
- Cerebral MRI: more accurate early detection and description of brain tumours

The extension work-up enables GTT to be classified into 4 stages (Table 1), and scored as low or high risk (Table 2).

Table 1 FIGO 2000 classification [4]

stage I	GTT strictly limited to the uterine body
stage II	GTT extended to adnexa and vagina, but limited to genital structures
stage III	TTG extended to the lungs, with or without genital tract involvement
stage IV	any other metastatic site

Table 2 FIGO score [4]

Scores	0	1	2	4
Age	< 40	≥ 40	-	-
Antecedent pregnancy	Mole	Abortion	Term	-
Interval from index pregnanacy/months	<4	4-<7	7-<13	≥13
Pre-treatment serum hCG (IU/ml)	$< 10^3$	$10^3 < 10^4$	$10^4 < 10^5$	$\geq 10^5$
Largest tumor size(including uterus)	-	3-<5 cm	≥5 cm	
Site of metastases	Lung	Spleen,kidney	Gastro-intestinal	Liver,brain
Number of metastases	-	1-4	5-8	>8
Previous failed chmotherapy	-	-	Sigle drug	2 or more drugs

Low risk ≤ 6 ; High≥ 7

The experience of the Hassan II FES University Hospital in the follow-up of GTT, through a study of 29 cases over a period of 7 years [2] revealed that in 83% of cases the GTT was post-molar, and the staging of patients showed lung metastases in 67%, liver metastases in 19%, kidney metastases in 7% and brain metastases in 7% of cases: this classified the patients as 52% high-risk and 48% low-risk.

4.4. Support

- Pre-chemotherapy work-up: plasma ionogram with creatininemia, liver biology work up with bilirubinemia and CBC.
- The FIGO score will classify patients as low or high risk.

4.4.1. Low-risk patient (score less than or equal to 6) [1].

- Methotrexate as a single chemotherapy is the standard first-line treatment for low-risk GTT. The recommended protocol is: methotrexate 1 mg/kg intramuscularly on Days 1, 3, 5 and 7 and calcium folinate (folinic acid) 0.1 mg/kg IM or 10 mg per os on Days 2, 4, 6 and 8.
- Repeat the protocol every 14 days with a new pre-chemotherapy test until 3 negative results are obtained.
- Actinomycin D remains an alternative in cases of intolerance to methotrexate or renal failure.
- If this fails, switch to polychemotherapy.

4.4.2. High-risk patient (score greater than or equal to 7) [1].

Two types of protocols can be used in the first instance:

- (MTX)Methotrexate-based protocols (EMA-CO: etoposide, MTX, actinomycin D, cyclophosphamide, vincristine)
- Cisplatin-based protocols may be offered, particularly in cases where MTX is contraindicated.

In the case of brain metastases: high-dose EMA-CO (increase MTX dose) combined with intrathecal MTX.

The evolution of our patients was marked by a complete clinical and biological remission in 89.65% of patients after 12 weeks on average [3], a study by SEKHARAN et al [5] found a complete response rate of 93% in a series of 321 patients in the low-risk group, but in the high-risk group several retrospective series have demonstrated cure rates of around 80% [6].

Our patient is classified as high-risk and was a candidate for polychemotherapy, but unfortunately died on day 10 of her admission to intensive care.

5. Conclusion

GTT is a rare and difficult disease with a heavy psychosocial impact that affects the young woman who has not only suffered a pregnancy loss but may also be faced with a potentially fatal illness.

A better understanding of risk factors and carcinogenesis is needed to optimise patient management.

Larger studies are still needed.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed.

Statement of ethical approval

The present research work does not contain any studies performed on animals/humans subjects by any of the authors'.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

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