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Research Article

Prognosis of Gestational Trophoblastic Neoplasia in Women at 40 Years Old and Above: A Multicentre Retrospective Study

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ABSTRACT

Purpose: To investigate the outcome of different treatment strategies in patients with gestational trophoblastic neoplasia (GTN) in women at 40 years old and above.

Patients and Methods: We analysed a historical cohort from 5 referral centres from 5 countries, including all women with GTN treated between 2012 and 2017, who were 40 years old and older. Baseline characteristics and outcome of different treatment strategies were recorded and evaluated. The patients were categorized into low-risk non-metastatic, low-risk metastatic and high-risk, based on the FIGO classification.

Results: A total of 112 cases were identified. Mean age was 45.4 years ± 4.2SD. Of 80 patients with LR non-metastatic GTN, 46 women received single agent chemotherapy and 34 a hysterectomy with or without (n = 4) chemotherapy. Higher remission rate and shorter treatment duration (P=0.001) was seen in the group that underwent hysterectomy. Seven of the 14 patients with low-risk, metastatic GTN were cured with methotrexate. Two of the 18 high risk patients died before treatment, four were treated with polychemotherapy; two of them needed second line chemotherapy for incomplete response. Two cases received induction with methotrexate followed by EMA/CO. Ten high-risk patients were treated with hysterectomy and chemotherapy, of these six achieved complete remission, three needed second line chemotherapy, and one patient died during chemotherapy treatment.

Conclusion: In this cohort of women with GTN at 40 years old or above, we found high proportions of metastatic and high-risk cases, of methotrexate resistance, and of need for multiple treatment lines. In all groups, hysterectomy was performed, but its role remains controversial in metastatic low-risk and high-risk disease.

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I Low risk cases – non metastatic (n = 80)

A Single-agent chemotherapy (n = 32)

i Complete response (n = 18)

a Uneventful follow up (FU) (n = 16)

i. Case 5, received 3 courses of Methotrexate (MTX), FU 20 months.
ii. Case 44, received 3 courses of MTX, FU 22 months.
iii. Case 43, received 4 courses of MTX, FU 25 months.
iv. Case 67, received 4 courses of MTX, FU 47 months.
v. Case 81, received 4 courses of MTX, FU 12 months.
vi. Case 4, received 5 courses of MTX, FU 23 months.
vii. Case 101, received 5 courses of MTX, FU 24 months.
viii. Case 71, received 6 courses of MTX, FU 12 months.
ix. Case 50, received 6 courses of MTX, FU 20 months.
x. Case 59, received 7 courses of MTX, FU 24 months.
xi. Case 69, received 7 courses of MTX, FU 24 months.
xii. Case 58, received 8 courses of MTX, FU 15 months.
xiii. Case 86, received 8 courses of MTX, FU 12 months.
xiv. Case 57, received 9 courses of MTX, FU 29 months.
xv. Case 47, received 9 courses of MTX, FU 45 months.
xvi. Case 52, received 13 courses of MTX, FU 17 months.

b Relapse (n = 1)

i. Case 25, received 5 courses of MTX, complete response. Relapse, treated with 4 courses of EMA/CO, FU 16 months.

c Lost to FU (n = 1)

i. Case 36, received 4 courses of MTX, FU 6 months.

ii Incomplete response (n = 14)

a 2nd line polychemotherapy (n = 12)

Complete response to 2nd line chemotherapy, further FU (n = 12)

i. Case 110, failed to 2 MTX, received 3 EMA/CO, FU 36 months.
ii. Case 74, failed to 5 MTX, received 3 EMA/CO, FU 20 months.
iii. Case 72, failed to 15 courses of MTX, received 5 courses of EMA/CO, FU 15 months.
iv. Case 34, failed to MTX, received 1 course of 2nd line chemo, FU 72 months.
v. Case 22, failed to MTX, received 2 courses of EMA/CO, FU 12 months.
vi. Case 35, failed to MTX, received 2 courses of 2nd line chemo, FU 60 months.
vii. Case 65, failed to MTX, received 2 courses of EMA/CO, FU 27 months.
viii. Case 29, failed to MTX, received 3 courses of EMA/CO, FU 20 months.
ix. Case 70, failed to MTX, received 3 courses of EMA/CO, FU 12 months.
x. Case 9, failed to MTX, received 4 courses of EMA/CO, FU 24 months.
xi. Case 33, failed to MTX, received 6 courses of EMA, FU 48 months.
xii. Case 26, failed to MTX, received 8 courses of EMA/CO, FU 17 months.

b Further hysterectomy (n = 2)

i. Case 40, failed to MTX, 2nd line hysterectomy. Pathology; choriocarcinoma, FU 17 months.
ii. Case 41, failed to MTX, 2nd line hysterectomy. Pathology; complete mole, FU 13 months.

B Curettage and chemotherapy (n=14)

i Complete response (n = 11)

a Uneventful FU (n = 9)

i. Case 96, received 1 course of MTX, FU 56 months.
ii. Case 98, received 1 course of MTX, FU 12 months.
iii. Case 105, received 1 course of MTX, FU 23 months.
iv. Case 106, received 1 course of MTX, FU 12 months.
v. Case 107, received 1 course of MTX, FU 12 months.
vi. Case 2, received 2 courses of MTX, FU 20 months.
vii. Case 7, received 2 courses of MTX, FU 12 months.
viii. Case 8, received 4 courses of MTX, FU 12 months.
ix. Case 24, received 4 courses of MTX, FU 12 months.

b Lost to FU (n = 2)

i. Case 103, received 1 course of MTX, FU 1 month.
ii. Case 90, received 3 courses of MTX, no FU.

ii Incomplete response (n = 3)

a Complete response to 2nd line polychemotherapy, further FU (n = 2)

i. Case 3, failed to MTX, received 4 courses of EMA/CO, FU 20 months.
ii. Case 6, failed to MTX, received 5 courses of EMA/CO, FU 12 months.

b Complete response to 2nd line polychemotherapy, lost to FU (n = 1)

i. Case 91, failed to MTX, received 3 courses of EMA/CO, FU 6 months.

C Hysterectomy (n = 4)

i Complete response, further FU (n = 4)

i. Case 38, pathology; invasive mole, FU 12 months.

ii. Case 46, pathology; invasive mole, FU 18 months.
iii. Case 84, pathology; invasive mole, FU 14 months.
iv. Case 104, pathology; invasive mole, FU 12 months.

D Hysterectomy and chemotherapy* (n = 30)

* One case (case 10) EMA/CO, all others MTX

i Complete response (n = 29)

a Complete response, uneventful FU (n = 28)

i. Case 19, pathology; invasive mole, received 1 course of MTX, FU 12 months.
ii. Case 23, pathology; invasive mole, received 1 course of MTX, FU 12 months.
iii. Case 94, pathology; choriocarcinoma, received 1 course of MTX, FU 12 months.
iv. Case 111, pathology; complete mole, received 1 course of MTX, FU 12 months.
v. Case 10, pathology; choriocarcinoma, received 2 courses of EMA/CO, FU 36 months.
vi. Case 13, pathology; invasive mole, received 2 courses of MTX, FU 18 months.
vii. Case 14, pathology; invasive mole, received 2 courses of MTX, FU 42 months.
viii. Case 15, pathology; invasive mole, received 2 courses of MTX, FU 36 months.
ix. Case 16, pathology; invasive mole, received 2 courses of MTX, FU 30 months.
x. Case 17, pathology; choriocarcinoma, received 2 courses of MTX, FU 14 months.
xi. Case 21, pathology; invasive mole, received 2 courses of MTX, FU 12 months.
xii. Case 32, pathology; invasive mole, received 2 courses of MTX, FU 48 months.
xiii. Case 12, pathology; invasive mole, received 3 courses of MTX, FU 18 months.
xiv. Case 18, pathology; invasive mole, received 3 courses of MTX, FU 23 months.
xv. Case 63, pathology; invasive mole, received 3 courses of MTX, FU 19 months.
xvi. Case 76, pathology; invasive mole, received 3 courses of MTX, FU 12 months.
xvii. Case 85, pathology; invasive mole, received 3 courses of MTX, FU 12 months.
xviii. Case 20, pathology; invasive mole, received 4 courses of MTX, FU 14 months.
xix. Case 75, pathology; invasive mole, received 4 courses of MTX, FU 58 months.
xx. Case 77, pathology; choriocarcinoma, received 4 courses of MTX, FU 31 months.
xxi. Case 61, pathology; choriocarcinoma, received 5 courses of MTX, FU 60 months.
xxii. Case 73, pathology; invasive mole, received 5 courses of MTX, FU 12 months.
xxiii. Case 83, pathology; invasive mole, received 6 courses of MTX, FU 25 months.
xxiv. Case 28, pathology; complete mole, received 6 courses of MTX, FU 14 months.
xxv. Case 31, pathology; invasive mole, received 6 courses of MTX, FU 24 months.
xxvi. Case 88, pathology; invasive mole, received 7courses of MTX, FU 12 months.
xxvii. Case 60, pathology; invasive mole, received 8 courses of MTX, FU 24 months.
xxviii. Case 48, pathology; complete mole, received 12 courses of MTX, FU 16 months.

b Complete response, lost FU (n=1)

i. Case 95, pathology; invasive mole, received 1 course of MTX, FU 6 months.

ii Incomplete response (n =1)

2nd line chemotherapy after hysterectomy (n = 1)

i. Case 54, Pathology invasive mole, failed to MTX (7 courses), 2nd line 3 courses of etoposide, FU 17 months.

II Low risk cases – metastatic (n = 14)

A Hysterectomy and single agent chemotherapy* (n = 6)

* In all cases MTX

i Complete response: (n = 3)

i. Case 97, pathology; choriocarcinoma, received 1 course of MTX, FU 43 months.
ii. Case 79, pathology; invasive mole, received 3 courses of MTX, FU 19 months.
iii. Case 78, pathology; invasive mole, received 5 courses of MTX, FU 17 months.

ii Incomplete response (n = 3)

Polychemotherapy after hysterectomy and single-agent chemotherapy (n = 3)

i Complete response (n = 2)

i. Case 66, pathology; choriocarcinoma. Failed to MTX (5 courses). 2nd line 5 courses of polychemotherapy, FU 27 months.
ii. Case 68, pathology; invasive mole. Failed to MTX (6 courses). 2nd line 2 courses of polychemotherapy, FU 33 months.

ii Incomplete response (n = 1) 2nd and 3rd line chemotherapy, relapse and 4th line

i. Case 37, pathology; choriocarcinoma. Failed to MTX (4 courses), 2nd line failed (2 courses of carboplatin), 3rd line 3 courses of

EMA/CO. Complete response. Lung relapse after 7 months, treated with EMA/CO and cured, FU 17 months.

B Single-agent chemotherapy (n = 8)

i Complete response

a Uneventful FU (n = 4)

i. Case 62, received 3 courses of MTX, FU 24 months.
ii. Case 80, received 3 courses of MTX, FU 15 months.
iii. Case 109, received 5 courses of MTX, FU 12 months.
iv. Case 64, received 9 courses of MTX, FU 22 months.

ii Incomplete response (n = 4)

2nd line actinomycin D after MTX (n = 1)

i. Case 49, failed to MTX (4 courses), 2nd line received 4 courses of actinomycin D, FU 17 months.

2nd polychemotherapy after MTX (n= 1)

i. Case 27; failed to MTX (2 courses), 2nd line received 7 courses of EMA/CO, FU 12 months.

2nd line polychemotherapy and 3rd line surgery (n = 2)

a Uneventful after surgery

i. Case 82, failed to MTX (7 courses), 2nd line failed (2 courses of polychemotherapy), 3rd line hysterectomy. Pathology; invasive mole, FU 13 months.

b Relapse after surgery

i. Case 108, failed to MTX (1 course), 2nd line failed (7 courses of polychemotherapy), 3rd line excision of vaginal metastasis. Pathology: choriocarcinoma. Relapse after 2 years, treated with EMA/CO, FU 24 months.

III High risk patients (n = 18)

A Death prior to treatment start (n = 2)

i. Case 93, died before start of treatment.
ii. Case 112, died before start of treatment.

B Hysterectomy and chemotherapy (n= 10)

Died during treatment (n=1)

i. Case 100, pathology; choriocarcinoma, received 5 courses of EMA/CO, Died during treatment.

i Complete response (n = 7)

a Uneventful FU (n = 5)

i. Case 11, pathology; choriocarcinoma, received EMA/CO, FU 40 months.
ii. Case 45, pathology; choriocarcinoma, received 6 courses of EMA/CO, FU 63 months.
iii. Case 55, pathology; Invasive mole, received 1 course of EMA/CO, FU 18 months.
iv. Case 87, pathology; invasive mole, received 6 courses of EMA/CO, FU 15 months.
v. Case 102, pathology; invasive mole, received EMA/CO, FU 12 months.

b Lost to FU (n = 1)

i. Case 39. pathology; choriocarcinoma, received EMA/CO, FU 10 months.

c Relapse (n = 1)

i. Case 30, pathology; choriocarcinoma, received EMA/CO, complete response. Relapse (renal), treated with nephrectomy and 3 courses of EMA/CO, FU 36 months.

ii Incomplete response, further treatment polychemotherapy (n = 2)

2nd line polychemotherapy (n = 2)

a Complete response to 2nd line polychemotherapy, further FU (n = 1)

i. Case 42, failed to MTX (5 courses) 2nd line 2 courses of EMA/CO. FU 12 months. Complete response to 2nd line polychemotherapy, lost FU (n = 1)
ii. Case 99, hysterectomy; choriocarcinoma, failed to EMA/CO (5 courses), received 5 courses of 2nd line chemotherapy with complete response, FU 10 months.

C Induction monochemotherapy followed by polychemotherapy (n = 2)

(because of poor general condition)

i Complete response (n = 2)

a Uneventful FU (n =1)

i. Case 89, received 1 course of MTX followed by 5 courses of EMA/CO, FU 44 months.

b Relapse (n =1)

i. Case 92, received 1 course of MTX followed by 5 courses of EMA/CO. Relapse treated with EMA/CO, FU 43 months.

D Polychemotherapy (n = 4)

i Complete response (n = 2)

a Uneventful FU (n = 2)

i. Case 53, received 7 courses of EMA/CO, FU 17 months.
ii. Case 51, received 9 courses of EMA/CO, FU 27 months.

ii Incomplete response (n = 2)

2nd line polychemotherapy (n = 2)

b Complete response to 2nd line chemotherapy, further FU (n = 2)

i. Case 56, received 7 courses of EMA/CO, incomplete response, 2nd line 5 EMA/EP, FU 24 months.
ii. Case 113, received 5 courses of EMA/CO, incomplete response, 2nd line EMA/EP, FU 12 months.