A hospital-based multicentric study results on gestational trophoblastic disease management status in a developing country

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Summary

Objective: To determine the clinical management of gestational trophoblastic disease in Turkey.

Material and Methods: An inquiry form was sent to 55 health centers including unversity hospitals, maternity hospitals with residency programs and maternity hospitals without residency programs in 1997. The inquiry consisted of questions about the type of classification systems in use, distribution of cases according to those classifications, use of prophylactic chemotherapy and its indications, and drug preference for single-agent or combined chemotherapies.

Results: The overall response rate to the conducted inquiry was 47.1%. A clinical classification system was identified in 60% of the hospitals in Turkey. Generally, methotrexate was the most used single-agent chemotherapy. With regard to first-line combined chemotherapy, MAC (methotrexate, antinomycin-D, cyclophosphamide) was the preferred combination. EMA-CO (etoposide, methotrexate, actinomycin-D, cyclophosphamide, vincristine) was the most common used second-line chemotherapeutic regimen.

Conclusion: Due to insufficient data acquisition from all the medical centers and a lack of national population-based studies, it is difficult to draw a conclusion with respect to the interpretation of the data about the management protocols of gestational trophoblastic disease.

Key words: Gestational trophoblastic disease; Management; Hospital-based study.

Introduction

Gestational trophoblastic disease (GTD) comprises a spectrum of disorders of placental development from hydatiform mole to malignant choriocarcinoma [1]. To determine the prognosis and guide the therapy several clinical, anatomical and prognostic classifications have been proposed [2-4].

We conducted an inquiry covering a one-year period to assess the clinical approaches of different hospitals in Turkey.

Materials and Methods

An inquiry of one years duration was conducted by the Osmangazi University School of Medicine, Gynecologic Oncology Unit in Eski ehir, Turkey. Thirty-three university hospitals, 13 maternity hospitals with residency programs and eight maternity hospitals without residency programs were initially planned to be enrolled in the study. Inquiry forms were mailed to the chiefs of obstetrics and gynecology departments of each hospital. They were requested to respond to the questions regarding the following information: classification system in use (according to clinical, WHO, FIGO and others), case distributions according to those classifications, prophylactic chemotherapy use and agents used for single and combined chemotherapy.

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Results

Of 55 hospitals, the overall response rate to this study was 47.1% (26/55). This figure varied among the types of hospitals; 57.6% (19/33) for university hospitals, 30.8% (4/13) and 33.3% (3/9) for maternity hospitals with and without residency programs, respectively. Total number of GTD was 257 during a one-year period, 57.2% of which were reported form university hospitals. The classification systems in use are shown in Table 1. The majority of classifications were clinical only (60%) followed by more than one system combined in 28% of hospitals in different regions of Turkey. The distribution of GTD according to hospitals in regard to the clinical or WHO scoring system are shown in Table 2.

In the clinical classification, most of the cases were in a non-metastatic category. Furthermore, in cases classified according to the WHO score, a low-risk group (< score 4) comprised the majority. In 87% of reported GTD, methotrexate was the preferred single chemothera-

Table 1. — Distribution of centers in regard to preference of classification system

Classification system	Number of centers	%
A. Clinical	15	60
B. WHO score	3	12
C. FIGO score	_	_
D. Other/A+B+C,B+C (others)	7	28
Total	25	100

Table 2. — Clinical and WHO score distribution of cases

A. Clinical

71. Chinear				
Health centers	Non-metastatic	Low-risk metastatic	High-risk metastatic	
Universities	108	45	10	
Maternity hospitals				
with residency program	_	13	_	
Maternity hospitals				
without residency program	3	_		
Total	111	58	10	

B. Who Scoring System

Health centers	Low-risk	Medium-risk	High-risk
Universities	4	_	3
Maternity hospitals with residency program Maternity hospitals	32	6	4
without residency program	11	1	
Total	47	7	7

peutic agent. For combined chemotherapy, MAC was the predominant chemotherapeutic regimen followed by an EMA-CO protocol.

In this study 60% of centers were not currently using prophylactic chemotherapy. In 40% of the hospitals, prophylactic chemotherapy was preferred if risk factors were prevalent.

Discussion

Due to an inadequate response rate of the enrolled inquiry, it is difficult to extrapolate the results to all hospitals in Turkey. According to this study, although the participation percentage is low, the major classification in use was clinical, followed by a combination of more than one classification system.

Most of the reports in the literature emphasize that despite its complexity, the WHO scoring system has been found to be more predictive for prognosis than the revised FIGO anatomical staging [5]. In contrast, some centers claimed that FIGO anatomical staging is relatively simple to use and as reliable as WHO scoring [6]. However, some trophoblastic disease centers have indicated that they would no longer score the ABO blood group, one of the criteria of WHO scoring [7]. In recent years, a tendency towards combined WHO scoring and revised FIGO staging has emerged in order to reach a more realistic estimate of prognosis and treatment strategy [8].

Most women are reluctant to come to follow-up visits due to patient characteristics. Hence, a considerable percentage of centers (40%) in Turkey prefer to use prophylactic chemotherapy, mostly methotrexate, in the presence of risk factors.

As a single-agent chemotherapy for low-risk non-metastatic GTD, methotrexate was the most common agent reported in this study, since the majority of women with GTD have been cured by single-agent methotrexate and folinic acid chemotherapy [9]. In contrast to this study, where the MAC protocol was the most preferred chemotherapeutic regimen, most of the centers proposed the EMA- CO protocol as a first-line chemotherapy for persistent metastatic GTD [10]. As second-line agents, as well as for first-line use, methotrexate, etoposide, dactinomycin and etoposide, cisplatin or etoposide, dactinomycin chemotherapies have become established as the treatment of choice for gestational trophoblastic tumors which have relapsed or become refractory to EMA-CO chemotherapy [11, 12].

Conclusion

This study defines the clinical management options in GTD of some, but not all hospitals in Turkey. Therefore, it is mandatory to carry-out a study designed for wide participation by all health centers in Turkey in order to assess contemporary management plans for GTD among centers, and to determine objective and standardized criteria for evaluating and treating GTD. Finally, it is hoped that this report will constitute and provide a database for future cross-sectional analytic studies on GTD management strategies.

References

- [1] Semer D. A., Macfee M. S.: "Gestational trophoblastic disease: epidemiology". *Seminars in Oncology*, 1995, 22 (2), 109.
- [2] Hammond C. B., Borchert L. G., Tyreyl L. et al.: "Treatment of metastatic trophoblastic diseases: good and poor prognosis". Am. J. Obstet. Gynecol., 1973, 115, 454.
- [3] Berkowitz R. S., Goldstein D. P.: "Gestational trophoblastic disease". In: Berek J. S. (ed.): "Novak's Gynecology". Twelfth edition, Williams and Wilkins, Baltimore 1996, 1261.
- [4] Gestational trophoblastic disease: "WHO technical report series 692". WHO Geneva 1983.
- [5] Smith D. B., Newslands E. S., Holden L., Bagshawe K. D.: "Correlation between clinical staging and FIGO staging groups with gestational trophoblastic disease". Br. J. Obstet. Gynaecol., 1993, 100, 157.
- [6] Goldstein D. P., Zanten Przybysz I. V., Bernstein M. R., Berkowitz R. S.: "Revised FIGO staging system for gestational trophoblastic tumours; recommendations regarding therapy". *J. Reprod. Med.*, 1998, 43, 37.
- [7] Kohorn E. I.: "Assessing and staging of trophoblastic tumors". Trophoblastic Disease Update, 1998, 2, 3.
- [8] Hanconck B. W., Welch E. M., Gillespie A. M., Newslands E. S.: "A retrospective comparison of current and proposed staging and scoring systems for persistent gestational trophoblastic disease". *Int. J. Gynecol. Cancer*, 2000, 10, 318.
- [9] Gillespie A. M., Kumar S., Hancock B. W.: "Treatment of persistent trophoblastic disease later than 6 months after diagnosis of molar pregnancy". Br. J. Cancer, 2000, 82 (8), 1393.
- [10] Bagshawe K. D., Begent R. H. J., Rustin G. J. S., Brock C., Short D., Holden L. et al.: "EMA/CO for high-risk gestational trophoblastic tumors: results from a cohort of 272 patients". J. Clin. Oncol., 1997, 15, 2636.
- [11] Hancock B. W., Coleman R. E., Lorigan P. C., Dobson L. S.: "Persistent gestational trophoblastic disease: results of MEA (methotrexate, etoposide, dactinomycin) as first-line chemotherapy in highrisk disease and EA (etoposide and dactinomycin) as second-line therapy for low-risk disease". Br. J. Cancer, 2000, 82 (9), 1547.
- [12] Rustin G. J. S., Seckl M. J., Holden L., Mulholland P. J., New-slands E. S.: "Etoposide and cisplatin/etoposide, and actinomycin-D (EMA) chemotherapy for patients with high-risk gestational trophoblastic tumors refractory to EMA/CO chemotherapy and patients presenting with metastatic placental site trophoblastic tumors". J. Clin. Oncol., 2000, 18, 854.

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