Health & Medical Informatics

Maeda, J Health Med Informat 2014, 5:2
http://dx.doi.org/10.4172/2157-7420.1000e113

Editorial Open Access

Prophylactic MTX Therapy to Prevent Choriocarcinoma

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Choriocarcinoma is the very malignant tumor in gynecology characterized tumor metastases to whole organs and tissues, where the patientdied mainlydue to the brain metastasis. It developed after the evacuation of total hydatidi form mole, where no fetus was present, but the uterus was filled with cystic molar tissue, which was covered by abnormal trophoblasts, and its presence was confirmed by human chorionic gonadotraopine (HCG) in the blood and urine, and recently by ultrasonic image. A uterine choriocarcinoma is diagnosed by hemorrhage, enlarged uterus, ultrasound and the high HCG (usually beta HCG) in the blood and urine, and confirmed by histologic examination that the tumor was composed purely by trophoblasts but no molar villus pattern. In old times before 1960, the treatment was hysterectomy, which was followed by a pulmonary metastasis after one year and hematologically spread to whole body. The disease was frequent in East Asia old times. Maeda studied the trophoblastic diseases including choriocarcinoma, which was not a local malignancy but a systemic disease, and treated the metastases by Methotrexate (MTX), which was the most sensitive by choriocarcinoma, and achieved the disappearance of metastasis. Afterwards, the systemic MTX was administered before the hysterectomy (primary chemotherapy), where not only the metastasis but also primary uterine focus disappeared, if the drug was administered until the HCG disappeared in the blood and urine. The primary chemotherapy was effective to maintain the fertility of the patient; actually a case was normally pregnant after the primary chemotherapy. That was the first success of drug therapy of malignant neoplasia preserving fertility.

We intended to prevent the postmolar development of choriocarcinoma by prophylactic chemotherapy with MTX, after confirmation of the primary chemotherapy with MTX in 1960s at the Department of Obstetrics and Gynecology, Kyushu University, Fukuoka Japan [1].

The prophylactic chemotherapy was started as early as after the evacuation of total hydatidi form mole in 108 cases. The MTX was orally administered for 10mg a day for 7 days, 70 mg in total in typical cases. Two prolonged positive pregnancy test cases after molar evacuation were given 230 and 340 mg MTX in total until the urinary HCG was negative by the biological Friedman's rabbit's ovulation tests. The control were 81 cases composed of 42 cases of no chemotherapy and 39 cases received chemotherapy other than MTX.

Toxic signs	No. of the sign
Vomiting or nausea	29
Anorexia	16
Lip erosion	12
Stomatitis	34
Pharyngeal pain	27
Stomach pain	11
Diarrhea	5
Gingiva hemorrhage	5
Leukopenia <4,000	22
Headache	4
Skin rash	3
No toxicity in 23 cases	

Table 1: Systemic toxicity of MTX in the prophylactic chemotherapy.

No choriocarcinoma developed in 108 MTX treated cases, while 6 choriocarcinoma (7.4%) developed in 81 control cases. Significant difference (p=0.004) was noted between MTX and control groups in the development of choriocarcinoma.

The invasive mole was found in 2 (1.9%) in 108 MTX group and 2 (2.5%) in the control, where insignificant difference (p=0.77) was noted between two groups. It is natural, because molar tissue invaded the myometrium before the molar evacuation, and the outcome of invasive mole is benign after the hysterectomy.

Therefore, the prevention of malignant choriocarcinoma was successful by the MTX treatment in postmolar state. As the result, the development of choriocarcinoma is rare in Japan after the establishment of postmolar prophylactic chemotherapy. Another reasonwill be the early detection and removal of hydatidi form mole before trophoblastic invasion to the endometriumby the ultrasound imaging of early pregnancy in the first trimester.

Side effects of prophylactic MTX administration were shown, where no life threatening heavy toxicity was found (Table 1).

References

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Received October 22, 2013; **Accepted** October 23, 2013; **Published** October 28, 2013

Citation: Maeda K (2014) Prophylactic MTX Therapy to Prevent Choriocarcinoma. J Health Med Informat 5: e113. doi:10.4172/2157-7420.1000e113