Two interesting cases of gestational trophoblastic disease with methotrexate failure

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ABSTRACT

Gestational trophoblastic disease is group tumours that are more sensitive and respond well to a wide variety of chemotherapeutic regimes. Presented here are two interesting cases one with life threatening bleeding requiring hysterectomy and other with persistent disease post evacuation. Both being low risk were treated with single agent methotrexate, but failed to respond. They responded to alternative chemotherapy. Methotrexate resistant is seen even in low risk group.

Keywords: Choriocarcinoma, Uterine perforation, Methotrexate

INTRODUCTION

Gestational trophoblastic disease (GTD) is a group of unique benign and malignant tumours derived from the human placenta. These groups of tumours are more sensitive and respond well to a wide variety of chemotherapeutic regimes. Single dose methotrexate has often been used with success in patient with low risk disease. We present two interesting cases one presenting with perforating uterine choriocarcinoma and other with persistent disease after evacuation which turned to be resistant to methotrexate therapy.

CASE REPORT

Case 1

A 30 yrs female G8P4L4A3 presented with bleeding per vaginum on and off for the last six months and pain in abdomen for one day. Six months back she had amenorrhea for one and half month with positive urine pregnancy test for which she took pills to medically terminate the pregnancy. After that she had irregular bleeding and underwent dilatation and evacuation twice in private hospital. However her bleeding still continued. She then reported to us. On admission she was pale, pulse 112/min, BP 90/60 mm Hg. Per abdomen soft distension was present with guarding and mild tenderness. Per speculum examination revealed minimal bleeding through cervix. On per vaginal examination uterus was retroverted, 8 weeks in size with cervical motion tenderness and fullness in the pouch of Douglas.

Her haemoglobin was 6.3gm/dl and the rest of her blood investigations were normal. Urine pregnancy was still positive with beta-hCG 2,11,000 mIU/ml. Chest X-ray was normal. Ultrasound revealed bulky uterus with lesion measuring 25 x 23 mm on posterior wall with increased vascularity. Bilateral adnexa were normal with free fluid present in POD.

Patient was planned for emergency laparotomy after arranging three unit packed red cells. Injection methotrexate 50mg IM was given before surgery. Per operative 1200cc of haemoperitoneum was present, uterus was 8 weeks in size with 3cm polypoidal mass perforating and protruding through fundus . Fig1, 2

Bilateral tubes and ovaries were normal. Rest of the abdomen was normal. Hysterectomy was done due to excessive bleeding and friability of the tissues. Tissue was sent for histopathology. Histopathological examination...
revealed feature suggestive of choriocarcinoma. Postoperative period was uneventful. Her beta-hCG was 46,054 mIU/ml 48 hours after surgery.

She was given single agent chemotherapy with methotrexate. After completion of first cycle of chemotherapy her beta-hCG was 18,299 mIU/ml. Her beta-hCG after completion of second cycle of chemotherapy increased to 1,01,067 mIU/ml instead of falling.

As there was more than 10% rise of beta-hCG after second cycle patient was diagnosed to be resistant to methotrexate. She was then given multiagent chemotherapy, EMACO. Patient received five cycle of chemotherapy in total. She is currently under follow up.

Case 2

28 year old female, P1L1A2 was admitted with irregular vaginal bleeding post dilation and evacuation done two months ago. She had past history of hydatidiform mole two and half years ago. This time also histopathology revealed partial hydatidiform mole. Her general physical examination was normal except for slight bleeding per vaginum. All the blood investigations were within normal limits. Ultrasound showed irregular mass invading the myometrium. MRI had done revealed persistent trophoblastic disease with lesion extending in to full thickness of posterior myometrium wall. Pre evacuation her serum beta-hCG was more than 5 lakhs mIU/ml. One month after evacuation it fell to 14,321 mIU/ml. But then even after four weeks the value still remained 13,325 mIU/ml and instead showed a rising trend to 21,690 mIU/ml. She was low risk by WHO prognostic score. In view of the rising beta-hCG values and MRI showing persistent disease she was given single agent chemotherapy with methotrexate.

**DISCUSSION**

Gestational Trophoblastic disease (GTD) is a group of unique benign and malignant tumours derived from the human placenta. Choriocarcinoma is a rare malignancy with an incidence of 1 in 40,000 pregnancies. It is characterized by abnormal trophoblastic hyperplasia and anaplasia. There is absence of villi and presence of areas of hemorrhage and necrosis. In 50 % of the cases it is preceded by hydatidiform mole and in the rest by normal pregnancy, abortion and ectopic pregnancy.

Surgery is done for complications like perforation and haemorrhage which can be life threatening or when family is complete for large mass or PSTT. The main stay of treatment is chemotherapy as these groups of tumours are more sensitive and respond well to a wide variety of chemotherapeutic regimes. However resistance is seen even to this and need to give alternate therapy at times.

In our first case the patient presented to us with haemorrhagic shock with the tumor perforating the uterus. The diagnosis of GTD was missed earlier by others who performed repeated dilatation and evacuation for it. Here we would like to reiterates the need of high index of suspicion to diagnose this condition as reported by few authors. Choriocarcinoma should be suspected when there is abnormal uterine bleeding following an abortion or hydatidiform mole. Hysterectomy was necessary to control uterine hemorrhage and to resect resistant disease. Our second case was case of persistent disease post evacuation.

Single-dose methotrexate regimen has been used in the treatment of low-risk gestational trophoblastic neoplasia with success rate of 77.5%. Failure has been reported with methotrexate and various factors like FIGO scoring...
and high pre-treatment beta-hCG have been attributed to it.\textsuperscript{5,6} Salvage chemotherapy in these patients has complete remission rate.\textsuperscript{7} Both our case failed to respond to single agent chemotherapy and required multidrug regime or alternate drug with favourable results.\textsuperscript{5}

In conclusion patients with low risk GTD though respond well to single agent methotrexate may develop resistance to this first-line chemotherapy. Alternative chemotherapy leads to complete remission in these patients.

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\section*{REFERENCES}

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