OBJECTIVE(S): To study the current status of gestational trophoblastic neoplasms (GTN).

METHOD(S): The records of cases of GTN managed over a period of 10 years from 1994 to 2003 were analyzed retrospectively.

RESULT(S): During the study period there were 99 histopathologically proved cases of GTN, constituting 0.27% of the obstetric admissions and 0.29% of births; 88 (88.88%) were cases of hydatidiform mole, eight (8.7%) of invasive mole, and three (3.03%) of choriocarcinoma. Case fatality was 2.02%. Most of the cases who were given chemotherapy responded well to methotrexate alone, but in cases of persistent disease (2.2%) etoposide and actinomycin were added and a good response was obtained. Of the 11 cases in whom chemotherapy was given only two (18.18%) needed multidrug therapy.

CONCLUSION(S): If recognized in time and treated appropriately GTN is amenable to treatment with good cure rates. However there are inherent problems and high risk factors which lead to fatality.

Key words: gestational trophoblastic neoplasia, hydatidiform mole, invasive mole, choriocarcinoma, methotrexate

Introduction

Gestational trophoblastic neoplasms (GTN) are proliferative as well as degenerative disorders of placental elements and include complete or partial hydatidiform mole (90%), invasive mole (5-8%) which could also be metastatic, villous or avillous choriocarcinoma (1-2%), and placental site tumor (1-2%) 1. Seckl et al 2 (2004) report the incidence of a complete hydatidiform mole as 1:1000 pregnancies and state that 15% of complete hydatidiform moles are likely to be transformed into malignant GTN (invasive mole, choriocarcinoma, and placental site trophoblastic tumor), which if undiagnosed can be rapidly fatal. However the incidence of GTN varies in different regions from 0.6 – 1.1 per 1000 pregnancies in Europe and North America to 2 per 1000 pregnancies in Japan 3. A ratio of 1 in 695 live births and of 1 in 836 pregnancies has been reported from New Mexico 4. Wolfberg et al 5 report that complete hydatidiform mole occurs in around 1 per 1000 conceptions. In Asia, Indonesia has the highest incidence 6 (1 in 77 pregnancies and 1 in 57 deliveries). In Malaysia it has been reported to be 2.8 per 1000 deliveries 4. In India and Middle East the incidence is believed to be 1 in 160 pregnancies. Others report that 15 % of complete and 4% of partial hydatidiform mole might become invasive 8 and 4% of hydatidiform mole might grow into choriocarcinoma 3. Even in the presence of disseminated disease, most of the cases are amenable to treatment with almost 100% survival.

Methods

Ninety-nine cases of GTN managed over a period of 10 years from 1994 to 2003 were analyzed retrospectively to
find out the incidence of GTN in relation with variables like age, gravidity, and presentation, and the outcome with special reference to invasive mole.

Results

During the study period there were 36486 obstetric admissions and 33940 births took place while 99 cases of GTN were diagnosed and treated giving an incidence of 0.27% of obstetric admissions and 0.29% of births. Of these 99 cases, 86 (86.86%) were from rural areas and 13 (13.13%) from urban areas. Rural incidence was statistically significantly higher when compared to overall incidence of 65% rural obstetric cases (P < 0.001). Twenty-eight women (28.28%) were less than 20 years of age, statistically significantly more than overall 5% teenage births (P < 0.01). Twenty-four (24.24%) women were more than 25 years of age and 47 (47.47%) were between 20 and 25 years. There were 21 (21.21%) primigravidas, statistically significantly less than the overall 40.45% during the same period (P < 0.001). Seventy-eight (78.78%) women were multigravidas, (51 second gravidas, 23 third gravidas and four fourth gravidas). Of the 51 second gravidas 18 had previous abortions, of the 23 third gravidas, 10 had two previous abortions, and the two fourth gravidas had two previous abortions. (Table 1).

Seven (7.07%) women presented with amenorrhea of less than 8 weeks, 26 (26.26%) with 8-12 weeks amenorrhea, and 66 (66.66%) with more than 3 months amenorrhoea (Table 1). Overall 82 (82.82%) women had presented with vaginal bleeding while 17 (17.17%) were asymptomatic in whom diagnosis of GTN was made on ultrasonography (USG) done for mismatch between weeks of gestation and size of uterus. Theca lutein cysts were revealed only in 20 (20.20%) cases.

Out of 99 women 88 (88.88%) had hydatidiform mole, eight (8.08%) had invasive mole (three teenage primigravidas, three second gravidas, and two third gravidas) and three had choriocarcinoma. All the three (3.03%) women with choriocarcinoma were second gravidas between 20 and 25 years of age and two had abortions in the past.

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hCG levels were elevated in all the cases and 63 (63.63%) had levels more than 100000 IU / dL at admission, 12 (12.12%) had high levels after 3 weeks (seven initially diagnosed as hydatidiform mole, three as invasive mole, and two as choriocarcinoma). Only two (2.28%) women out of 89 with hydatidiform mole had persistently elevated \( \Delta \)hCG and were given methotrexate. Of the seven cases of invasive mole who had received methotrexate, six responded well to the drug but one had persistent disease after six courses of methotrexate. So etoposide and actinomycin were given. On last follow up at the end of 1 year she was doing well. One woman with an invasive mole died within hours of evacuation. Out of the three cases of choriocarcinoma, one responded well to chemotherapy, one had to undergo abdominal hysterectomy because of heavy bleeding, and the third woman died before she could be given any definitive therapy.

Overall there was 2.02% (2/99) case fatality. One woman had an invasive mole, had presented with heavy vaginal bleeding and severe anemia, and died within hours after evacuation with the diagnosis of hydatidiform mole. She was found to be having metastatic invasive mole with extensive deposits in the lungs. Another fatality was the above mentioned case of choriocarcinoma. She was admitted with 6 months amenorrhoea followed by continuous vaginal bleeding with dyspnea, severe anemia, anasarca, and vaginal metastasis. She had severe bout of hemoptysis within few hours of admission, went into cardiorespiratory arrest, and could not be revived.

Table 1. Gravidity and gestation period.

<table>
<thead>
<tr>
<th>Primigravidas</th>
<th>Second gravidas</th>
<th>Third gravidas</th>
<th>Fourth gravidas</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestation (weeks)</td>
<td>TOTAL</td>
<td>Gestation (weeks)</td>
<td>Total</td>
</tr>
<tr>
<td>&lt;8</td>
<td>8-12</td>
<td>&gt;12</td>
<td>&lt;8</td>
</tr>
<tr>
<td>Hydatidiform mole</td>
<td>2</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>Invasive mole</td>
<td>-</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Choriocarcinoma</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>2</td>
<td>9</td>
<td>10</td>
</tr>
</tbody>
</table>
Discussion

Out of 99 cases of the GTN managed in 10 years there were 88.88% cases of hydatidiform mole, 8.08% of invasive mole and 3.03% of choriocarcinoma. Overall incidence of GTN was 0.29 % of all births. Most women were very young (20-25 years) and no one was more than 35 years old. Maternal age has consistently been identified as an important risk factor and extremes of age are known risk factors but most of our patients were young. Age specific incidence reports usually reveal a J curve; teenagers and women over 40 years old have higher rates. Thirty (30.30%) women had previous abortions, a figure statistically significantly higher than overall 10 -12 % abortion rate (P < 0.01). In a Italian study, an elevated risk of hydatidiform mole in nulliparous women with a history of miscarriage has been reported. Data concerning the effect of gravidity independent of age are inadequate and no firm conclusions can be drawn. It is believed that poor obstetric histories associated with increased fetal wastage may increase the risk of GTN.

One woman with invasive mole died within hours after evacuation and was found to have metastatic deposits in the lungs. One case of choriocarcinoma on chemotherapy had to undergo abdominal hysterectomy because of hemorrhage and sepsis but hysterectomy does not protect against distant metastasis. So chemotherapy is still needed.

Methotrexate has been found to achieve complete remission in most nonmetastatic and low risk GTN. Etoposide and actinomycin have been found successful as second line of treatment with 97% response in low risk disease. In the present study these drugs were used in two cases of persistent disease. Almost 90% of the invasive mole patients who were given methotrexate responded well. Others also report that low risk metastatic GTN has a 100% chance to respond to single agent chemotherapy and those with high risk disease have great chance to respond to multiagent chemotherapy such as etoposide, methotrexate, actinomycin, and cisplastin. GTN is considered the most curable gynecologic malignancy. In the present analysis, one death occurred in a case which was thought to be hydatidiform mole with severe anemia, but turned out to be a case of metastatic invasive mole. Another death was a case of choriocarcinoma who died within hours of hospitalization due to a severe bout of hemoptysis.

Conclusion

The disease spectrum in GTN varies from benign to malignant. While it can almost always be treated successfully even hydatidiform mole can be fatal if
unattended. It is important that the condition be diagnosed early for intervention and chemotherapy, which is curative in almost all cases, can be started. Single drug therapy is often sufficient.  

References  