
MANAGEMENT OF COLORECTAL CANCER DURING PREGNANCY

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Abstract

Although cancer in pregnancy is uncommon, several types of cancer were encountered. These include malignant melanoma, breast cancer, carcinoma of the cervix, bladder cancer, renal cancer, lymphomas, thyroid cancer, brain tumours, ovarian cancer, gastric and pancreatic cancer and colorectal cancer. Due to the uncommon incidence of the disease and therefore the limited experience coupled with the complexity of the situation which could affect the wellbeing of the foetus and mother, then the management of the pregnant woman with cancer might result in achieving less than the expected optimum. However, from the experience of single case reports and short reviews a reasonable management approach could be reached through multidisciplinary speciality collaboration. The author had encountered two pregnant women with colon cancer, both of them were symptomatic, and one of them had bowel obstruction. Their clinical presentation, diagnosis and management are described followed by a concise review of the literature.

Introduction

Cancer during pregnancy is uncommon. The exact incidence and prevalence are unknown but depending on the type of the cancer it is suggested to be in the range of 1-2 new cases of cancer in every 1000 pregnancies¹. In the USA this disease is estimated to account for about 19% of mortality in women aged between 15 to 34 years old². This coexistence highlight the difficult decisions needed to be taken in managing the mother and tumour with the least harm to the foetus³. Colorectal cancer associated with pregnancy is reported to have an incidence of 1 in 13,000 deliveries⁴. Due to a number of reasons this disease could be a difficult cancer to manage during pregnancy. The similarity of clinical presentation between the cancer symptoms and those attributed to the usual features present during normal pregnancy will often result in delayed diagnosis and therefore an advanced stage. These are coupled with difficulties in proper investigation and satisfactory

cancer staging, taking prompt decisions on the timing of surgical interventions and any need for adjuvant treatment.

Case one

More than 10 years ago, N.H. a 32 years old woman in her 34 weeks of pregnancy presented with increasing abdominal pain and some change in bowel habit, otherwise her current pregnancy seems to be progressing satisfactorily. She gave a previous history of twice ruptured ectopic pregnancy which needed a life-saving operations and therefore unfortunately she lost her two fallopian tubes. Because both she and her husband were desperate to have a baby they decided to undergo an artificial insemination which resulted in the current, successful pregnancy. The patient is generally healthy and fit and denied any family history of bowel problems or cancer.

The patient looked uncomfortable because of the pain and her abdominal examination confirmed the progress of

her normal pregnancy and the possible presence of some fullness in the right upper abdomen. She had an ultrasound scan performed by the author and a mass lesion was seen in the right upper abdomen, most likely related to the region of the hepatic flexure/right upper colon/right side of transverse colon. The liver looked free from obvious lesions. MRI was not available at that time in that hospital. Although colonoscopy, have some risks to the foetus, but because a definitive diagnosis was necessary, I accepted to do it after discussing the situation with the patient and her husband and backed by the support of the obstetrician, and anaesthetist. The procedure had an uneventful event and the presence of what looks to be endoscopically a malignant tumour was confirmed to be present at the hepatic flexure. Again after thorough discussion between all concerned parties the patient underwent an extended right hemicolectomy followed by an uneventful recovery. The operation was performed through a short right subcostal incision, which gave an excellent exposure and allowed complete mobilisation, resection and anastomosis without visualising or interfering of the gravid uterus. The tumour was mobile, and there was no gross evidence of peritoneal, omental or hepatic disease. Enlarged mesenteric lymph nodes were present, which were completely removed. The foetus was monitored immediately after the operation without any harm. Histology confirmed that the tumour was a poorly differentiated adenocarcinoma with lymph nodes metastases. I had a thorough discussion with an experienced medical oncologist and after discussion with an obstetrician, and discussing the several options available with the patient and her husband we agreed to give the patient systemic chemotherapy and allow the pregnancy to continue while the foetus is regularly monitored by the obstetrician for any stress, which could

make a decision of terminating the pregnancy by performing a caesarean section. That line of therapy was mainly taken because the couple were desperate to have a baby and none of us wanted to take any risk from a premature delivery. In addition to that and from the existing information in the literature the data suggest that systemic chemotherapy is well tolerated without obvious deleterious effects to the foetus during that stage of gestation. Fortunately both the patient and foetus tolerated the chemotherapy well, until maturity, which was followed by normal, vaginal delivery without obvious changes or conditions to the baby. The patient had a regular follow up and she was well without a recurrence of the disease for over five years.

Case two

Recently, V.K. a 33 years old pregnant woman in her 31 weeks second pregnancy presented with increasing abdominal pain, change in bowel habit and anaemia over the previous month. She had a normal previous vaginal delivery of her first child two years previously and she usually enjoys good health. The patient had a far relative who was found to have colon polyps but there is no family history of bowel cancer. The patient was admitted as an emergency under the care of the obstetrician because of her uncontrolled abdominal pain. The patient was in pain, looks pale and probably lost some weight. Her abdominal examination was limited by the gravid uterus, but there was no obvious significant abnormality. A single plain abdominal film was taken and showed a significantly distended caecum and right colon. An abdominal MRI showed the presence of a tumour mass with very narrow lumen in the hepatic flexure region. The differential diagnosis was thought of either a neoplastic or inflammatory mass. Due to the significant dilatation of the proximal right colon, I decided to perform an emergency

laparotomy. Preoperatively the condition was thoroughly discussed with the patient in the presence of her husband and mother. They accepted the surgery and therefore I thoroughly discussed the condition with the obstetrician, and anaesthetist who were very supportive. During the operation, the patient was tilted slightly to the left side to avoid a possible pressure of the gravid uterus on the inferior vena cava. Similar to the first case and because of the identical site of the tumour, the abdomen was explored through a short right subcostal incision, which gave an excellent exposure. The significantly distended proximal right colon was delivered to the wound level without extending the incision. There was a very tight, white-looking tumour involving the proximal part of the right colon/hepatic flexure for about 10.0cm, with obvious involvement of the serosa. There was complete obstruction of the remaining part of right colon including the caecum, which showed evidence of several gangrenous spots and breaches in the serosa without perforation. The team was upset to find widespread peritoneal and omental disease in addition to enlarged mesenteric lymph nodes. Resection and immediate anastomosis was achieved followed by uneventful recovery without any obvious harm to the foetus. The tumour was poorly differentiated adenocarcinoma involving the whole bowel wall up to the serosa with multiple lymph nodes metastases. Detailed discussion was subsequently carried out between me, two medical oncologists and the obstetrician. We decided to terminate the pregnancy by caesarean section (CS) after 32 weeks of pregnancy when the foetus is expected to have reached an acceptable maturity to achieve survival and to insert at the same time a portacath to be used later on for systemic chemotherapy. Provided the patient will recover well then the CS will subsequently be followed on the next day of surgery by a staging CT scan to the

chest, abdomen and pelvis so and to start systemic chemotherapy as early as possible after satisfactory recovery. The patient and her family accepted the plan. The patient recovered well from the SC but unfortunately the CT scan showed multiple liver metastases involving both lobes with no obvious pulmonary metastases. The patient is going to start systemic chemotherapy soon and the future plan is to try to treat her disease aggressively by all available means depending on her follow up and response. This might include laparotomy and cytoreductive surgery and local ablative therapy to the hepatic lesions.

Discussion

Although the most common cancers in pregnancy are cervical, mammary, ovarian, malignant melanoma, lymphoma and leukaemia, there are small series or case reports of colorectal, renal, thyroid and almost all other known cancers^{5,6}. Hypothetically it was thought that pregnancy might affect the biological behaviour of tumours in particularly through the effect of high concentrations of oestrogen and progesterone hormones secreted during pregnancy but there is no definitive acceptance to this theory^{5,6}. Transplacental cancer spread to the foetus is rare and therefore should not be considered as an indication to terminate the pregnancy⁷. On the other hand, treatment of cancer might have an adverse outcome to pregnancy; however, most of these are speculative as pregnant women are specifically excluded from almost all cancer trials and nearly all drug trials.

Generally, the first trimester is the most crucial time to the wellbeing of the foetus. Maternal exposure to diagnostic or therapeutic radiation can have teratogenic, developmental and carcinogenic effects⁶. Although it is estimated that foetal exposure up to 0.1-0.2 Gy are unlikely to cause a substantial foetal anomalies⁸, a 0.1 Gy dose can

result in some reduction of intelligence because the developing brain is especially vulnerable to radiation. However, this radiation dose is not reached by 20 conventional diagnostic radiographic procedures or three pelvic CT scans⁸. Radioisotopes scans can also endanger the foetus. Radiotherapy is contraindicated for abdominal and pelvic cancers in pregnancy but the uterus could be screened (shield) from dangerous exposure if radiotherapy is given to control cancer at distant sites away from the pelvis⁹.

Radiology exposure in pregnancy for the purposes of diagnosis and staging of the disease should be limited to essential investigations to limit the exposure dose. Ultrasound scans and MRI are increasingly used however there is some concern about the safety of both enhanced and non-enhanced MRI during the first trimester¹⁰.

Surgery during pregnancy will have few implications to the foetus from transplacental effects of the anaesthetic agents¹¹, some intraoperative complications like hypoxia, decreased placental perfusion secondary to the mother position during surgery in particularly in late pregnancy¹², and possible postoperative problems & complications¹³ which could have serious adverse outcomes to the wellbeing of the foetus. However, there should be a clear distinction between intra-abdominal and extra-abdominal surgery in regards to these implications. For the surgeon the access to intra-abdominal surgery is impaired in particularly if the surgery includes pelvic dissection especially in the advanced stages of the pregnancy which could make an optimum oncological dissection and resection more demanding.

The usage of chemotherapy agents in particularly during the first trimester has deleterious effects because these drugs predominantly affect the rapidly dividing cells¹⁴. These effects are immediate or

late. The immediate effects include spontaneous abortion, teratogenesis, organ toxicity, premature birth, and low birth weight¹⁵. Late effects include carcinogenesis, sterility, slow physical or mental growth & development and teratogenic effects in the offspring¹⁵. However, chemotherapeutic agents are currently increasingly used in late second trimester and early third trimester with what seems to be small risks².

The goals of cancer therapy in pregnancy are to start treatment for the mother as early as possible and to deliver the baby as early as possible. Lungs maturity is the main limiting factor in delivering the baby. However, this should be safely reached at 32 weeks of gestation.

Colorectal cancer during pregnancy is rare with an incidence of 1 in 13,000 pregnancies^{4,16}. In a review by Bernstein and colleagues, 4 of 205 colorectal cancers in pregnancy and adding to the series the experience in their own cases reported that the disease is predominantly detected in its advanced stages presumably due to late diagnosis and a tendency to higher incidence of rectal cancer. The latter had a better prognosis when compared to the experience with colon cancers⁴, but five-year survival is the same for pregnant women when compared with the general population with the same stage of the disease^{4,5}. It was thought that because colorectal cancer is generally rarely develops in the young female population, then their occurrence during pregnancy might have predisposing genetic or other factors. However, these increased risk groups represent only a small portion of the cases diagnosed in pregnancy¹⁷. The hormonal stimulation hypothesis, which involves oestrogen and progesterone receptors in colorectal cancer has been studied but the data to support the role of these receptors in the pathogenesis of colorectal cancer are not convincing^{18,19}.

Depending on the stage of gestation, the tumour status and whether the colorectal

cancer is complicated or not, then bowel resection might be performed at the same time of caesarean section. However, if the cancer is not complicated, then waiting for few weeks is beneficial to allow for the involution of the uterus and reduction of the vascular engorgement of pregnancy²⁰. Subsequent adjuvant therapy will be completed or started after delivery.

The incidence of ovarian metastases from colorectal cancer is higher in pregnant women (25%) when compared to the non-pregnant patients (3% to 8%)²¹.

Prophylactic bilateral salpingo-oophorectomy was suggested by some reporters²²; however the desire of the

patient for future pregnancies should be taken in consideration.

Conclusion

Colorectal cancer in pregnancy is rare. Due to the complexity of the disease which involves the stage of gestation, the need for essential investigation & tumour staging, tumour status, and the presence or absence of complications, then multidisciplinary team approach involving, among others, surgeons, anaesthetists, obstetricians, neonatologists, and medical and radiation oncologists is mandatory in order to minimise any major conflict between maternal and foetal wellbeing.

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