

# Cancer in pregnancy

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## Abstract

Cancer in pregnancy is an uncommon event and the diagnosis may be delayed. Presenting signs and symptoms may be masked by the pregnancy and there may be reluctance to investigate because of fears of harming the pregnancy. Optimal treatments for the malignancy may conflict with the potential wellbeing of the fetus and a truly multidisciplinary approach is needed to create a treatment plan which minimises the risk to mother and baby, in both the short and long term.

**Keywords** cancer; chemotherapy; palliative; pregnancy; radiotherapy; teratogenicity

## Introduction

Although a new presentation of cancer in pregnancy is uncommon, the very significant shift in the age at which women choose to have their children has made it less so and more women than ever are having to face a diagnosis of malignancy before they conceive, or during their pregnancies. Others must consider the possibility of a relapse or recurrence when choosing whether to start or extend their families. Although evidence suggests that, stage for stage, the outlook for most malignancies is unaffected by pregnancy, there is a real risk of a delay in diagnosis occurring because symptoms may be attributed to the pregnant state, signs may be masked and/or appropriate investigations may be deferred because of fears of harming the fetus. Surgical treatments for abdominopelvic malignancies may be limited by the pregnancy, although tailored chemotherapy outside of the first trimester is mostly well tolerated. Radiotherapy is mostly avoided, except for sites very distant from the uterus. A multidisciplinary approach is vitally important in planning and delivering care, and premature delivery of the baby, or even termination of pregnancy, may need to be discussed when considering all options. The treatment plan must be decided in partnership with the woman and her family, and they must be offered specialised support in helping them to come to terms with the diagnosis, and its possible implications. They may face extremely hard choices, and may have to accept compromising

either their own well-being or that of their unborn baby, or both. The choices they make may not always be absolutely in tandem with those of their various care-givers, and truly informed consent and patient autonomy is an important principle which must be strictly adhered to. For the survivors of cancer, careful consideration must be given as to whether to further extend the family, or not. Relapses and recurrences are associated with a poorer long term survival with the risk that a woman may leave her children without their mother.

The following three case studies illustrate these points, focussing on the potential harms of chemotherapy during pregnancy, radiation treatment during pregnancy, and some of the psychosocial aspects of a diagnosis of cancer during pregnancy.

## Case 1

### Anal cancer in pregnancy

A 37 year old primiparous patient presented to primary care with worsening constipation, per rectal mucus and per rectal bleeding. The symptoms were attributed to minor irritations of pregnancy and the patient was placed on several over-the-counter laxatives. Her symptoms did not improve and, at 18 weeks' gestation, she was referred to the general surgeons. In an urgent outpatient clinic they were unable to complete a rigid proctoscopy due to pain. The patient therefore had a sigmoidoscopy under general anaesthesia and a large ulcer was found 8 cm from the anal verge. Histology showed a moderately differentiated anal squamous cell carcinoma.

MRI staging was undertaken which revealed locally invasive T3, N0, M0 disease. Optimum treatment of this stage of anal cancer is chemoradiation (1,2,3) and due to her gestation (then 20 weeks) she was offered a medical termination to allow full external beam pelvic radiotherapy. The patient declined this after full counselling by the oncology team.

At the colorectal oncology multidisciplinary team (MDT) meeting the decision was made to proceed with four cycles of carboplatin and paclitaxel chemotherapy alone. The pregnancy progressed well with normal growth scans. Delivery was timed with combined obstetric and oncology input and an elective caesarean section was performed at 34 weeks (intravenous dexamethasone was administered at the chemotherapy cycles). The caesarean went smoothly and a boy weighing 2.045 kg did well.

Four weeks following the birth external beam pelvic radiotherapy and chemotherapy with Mitomycin C and 5-Fluoro-Uracil was commenced. This was augmented with anal brachytherapy boosting. During neoadjuvant treatment, the patient was counselled about ovarian irradiation and the likelihood of subsequent infertility. She was offered cryopreservation of ovarian tissue but declined, stating her family was complete. Hormone replacement therapy until the age of natural menopause, to minimise osteoporosis and cardiovascular morbidity, was discussed.

Clinically the tumour showed a good regressive response to treatment and the oncologists counselled the patient that the outlook for cure was reasonable. The five year survival rate for this stage of anal cancer is 78%.

## Discussion

Anal cancer in pregnancy is extremely rare and the literature is scanty. With the decision to continue the pregnancy, a risk benefit assessment with respect to commencing chemotherapy was necessary. The decision to withhold radiotherapy with the

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patient still pregnant was based on the inability to shield the developing fetus from the radiation beam field because the malignancy was pelvic. This case serves to illustrate the implications and evidence of harm of radiotherapy in pregnancy and also the evidence for the relative safety of chemotherapeutic agents during pregnancy. Finally, as the diagnosis in this patient was delayed by the assumption that her symptoms were secondary to constipation, a common minor irritation of pregnancy, this case also serves as an example of how the diagnosis of cancer is often delayed in pregnancy.

When cancer is diagnosed in pregnancy, the usual advice is to avoid radiotherapy until delivery due to concerns regarding the teratogenic effects of radiotherapy on the fetus. This was certainly the case in this patient and is the case for management of commoner malignancies such as breast cancer in pregnancy. However, robust evidence that radiotherapy harms the fetus is lacking and is generally based on animal data. Radiotherapy has the potential to cause miscarriage, teratogenicity, microcephaly, fetal growth restriction, learning difficulties, induction of childhood malignancies and haematological disorders. Factors influencing outcome for the pregnancy include the level of radiation dosage, the gestational age and the location and extension of the radiation field.

An increased risk of fetal malformation and learning difficulties occurs with radiation dosages greater than 100–200 mGy, however, radiation dosages this high are generally not reached even with curative radiotherapy during pregnancy. The gestational ages which seem to be at greatest risk from harm are between 8 and 15 weeks and exposure before this gestation appears to have an ‘all or nothing’ effect, i.e. miscarriage.

With regards to the radiation field, if tumours are located sufficiently far from the uterus and there is adequate shielding to protect the fetus against leakage radiation and scatter, the risks of radiation-induced childhood malignancies and learning difficulties can be reduced. Clearly this was never achievable in this patient’s case due to the nature and site of her malignancy. Furthermore, even lower dosages might be causal in the development of childhood cancer, sterility or learning difficulties, based on cohort studies of children exposed in utero to ionising radiation from the 1945 atomic bombs in Nagasaki and Hiroshima. In summary, it is understandable from a clinician’s view and also the patient’s view that, if possible, radiotherapy, especially abdominal and pelvic radiation, should be avoided but a carefully considered alternative management plan involving oncologist, obstetrician and patient is paramount.

One must also consider that radiotherapy can be acutely life-saving in various malignancies and treatment, especially when clinically urgent, should not be precluded by pregnancy. There have been several case reports of successful administration of ‘rescue’ fractions of radiotherapy in glioblastomas in pregnancy to reduce raised intracranial pressure and keep the mother alive until a reasonable gestation to deliver the pregnancy with a good fetal outcome. The same is true for metastatic brain tumours, for example melanoma, breast or lung metastases presenting in pregnancy. The RCOG states in its ‘Pregnancy and Breast Cancer’ guideline that radiotherapy can also have a role in mobility preservation in the case of spinal cord compression from a metastasis or a primary spinal tumour. Radiotherapy in these cases of tumours *remote from the uterus* can be administered and

exposure to the fetus minimised by using precise radiation field techniques and appropriate shielding of the abdomen as outlined above.

All cancers in pregnancy are rare, occurring in approximately 0.02% of all gestations but early diagnosis is crucial in optimising maternal morbidity and mortality rates. Furthermore, as mean maternal age rises, the incidence of cancer colliding with child bearing is likely to increase. Sadly, symptoms of pregnancy themselves can often confuse the clinical picture or even mask diagnosis; Headache and backache in pregnancy are common, glioblastoma multiforme or spinal metastases are not.

Gynaecological malignancies such as cervical cancer are generally diagnosed in a reasonably timely fashion, perhaps as patients place greater importance on vaginal bleeding during pregnancy. There is however, ongoing reticence to refer women to colposcopy and, once there, to perform biopsies on the pregnant cervix. This can delay diagnosis and subsequently worsen prognosis. Similarly, breast cancer can be a challenge to diagnose in the pregnant or lactating patient and there is often a delay. This is because breast lumps, skin changes and nipple changes are all common both in pregnancy and certainly postnatally. Urgent referral to a ‘one stop’ breast clinic with access to imaging and biopsy techniques such as a fine needle aspiration or Tru-Cut biopsy should always be made when there is a clinical suspicion.

Pregnancy is a time of physiological anaemia, often resulting in tiredness. However, lymphadenopathy should never be dismissed in a pregnant patient and indeed leukaemia and non-Hodgkin’s lymphoma are some of the commoner malignancies diagnosed in pregnancy. Furthermore while shortness of breath can occur in response to anaemia, or be physiological during pregnancy, symptoms such as intractable cough or haemoptysis warrant urgent investigation to exclude a lung malignancy.

While constipation is common in pregnancy, rectal bleeding should always alert the clinician to sinister pathology, with swift expedition of a flexible sigmoidoscopy. Similarly, intractable haematuria should be investigated with a flexible cystoscopy. This is especially prudent in women from Africa or the Middle East where schistosomiasis is common and can lead to rarer squamous cell carcinomas of the bladder.

## Case 2

### Ovarian cancer in pregnancy

A 25 year old woman with a previous normal birth was seen at booking with a dating scan demonstrating an intrauterine pregnancy with a crown rump length (CRL) of 10 mm (7 weeks and 1 day gestation). Also noted was a right sided thin walled pelvic cyst measuring 26.5 × 25.7 × 4.8 cm, extending above the fundus of the uterus. The right ovary was not seen separately. The woman was asymptomatic and there was no family history of cancer. It was thought to be ovarian in origin and a Ca-125 value was 45. Seven litres of fluid was aspirated from the cyst under ultrasound and cytology showed mild atypia of uncertain significance, and no overt features of malignancy. She was reviewed in antenatal clinic at 20 weeks where she reported right sided abdominal pain and a repeat ultrasound scan showed re-accumulation of the cyst. A decision was made for laparotomy at which was found an intact large right-sided ovarian cyst extending above the umbilicus. The left fallopian tube and ovary,

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