Metastatic unknown primary tumour presenting in pregnancy: a rarity posing an ethical dilemma

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This brief report raises the ethical dilemma encountered by an obstetrician involved in the care of a pregnant woman with life-threatening disease. This is a particularly difficult issue if the maternal well-being is in conflict with the survival of the unborn child.

We report a case of a 40-year-old woman presenting to us in her second pregnancy. Her first pregnancy had ended in a miscarriage and subsequently she underwent prolonged treatment for infertility, including tubal surgery. She was admitted at 22 weeks' gestation with a 3-month history of severe lower back pain radiating down both legs, which was unresponsive to simple analgesia. She had difficulty in swallowing food, and had lost about 6–7 kg in weight. On examination, she was thin and malnourished, with glands palpable in both supraclavicular fossae (Virchow's sign). There were no other palpable lymph glands or any suspicious skin lesions. Examination of breasts, cardiovascular system and respiratory system was unremarkable. Abdominal examination confirmed an enlarged uterus but was otherwise normal. Investigations revealed anaemia (8.5 g/dL), and chest X-ray showed a rounded mass on the hilum of the left lung.

Histological examination of the excised left supraclavicular node showed moderately to poorly differentiated adenocarcinoma of uncertain primary origin. This indicates the presence of cancer of indeterminate origin, which usually carries a poor prognosis. Specialised testing suggested the tumour to be a metastatic adenocarcinoma with a possible primary in breast, salivary gland, oesophagus, stomach or pancreas and less likely to have arisen in kidneys or lung. An ultrasound scan of the abdomen showed normal liver and no evidence of a primary tumour in kidney or pancreas. A CT scan of chest and abdomen revealed numerous hepatic and bony metastases. An endoscopy of the upper gastrointestinal tract and a mammography were normal.

Multidisciplinary management was planned, with input from the medical oncology, radiology, pathology and obstetric departments. Given the extremely poor prognosis of her disease, palliation with appropriate chemotherapy was advised. The patient and her husband were counselled and given the options of therapeutic abortion with immediate chemotherapy, or of continuing the pregnancy and delivering electively at 28 weeks'

gestation. After discussion, the patient was referred to a tertiary fetal medicine centre for consideration of a termination.

An ultrasound scan revealed a healthy, well-grown fetus with growth in the 95th centile. By this stage, the pregnancy had advanced to 24 weeks' gestation and after consultation the mother decided to continue with the pregnancy. It was agreed to delay oncology treatment to allow further maturation of pregnancy. Elective caesarean section was planned at 27+ weeks, with a proviso of performing this earlier if the mother's condition deteriorated.

As it transpired, a caesarean section was carried out at 25+3 weeks because of rapid deterioration in the patient's condition, and a male infant weighing 915 g was delivered. The mother's condition continued to worsen and she died 36 hours after delivery. Placental histology revealed metastasis, confined to the maternal side of the gestational tissues. In view of the widespread metastasis, the coroner did not advise a postmortem examination. The baby progressed well in the neonatal unit and was eventually discharged home.

DISCUSSION

Cancers in pregnancy occur with an average frequency of 1 in 1000 births.¹ There have been only two previous reports of unknown primary tumours presenting during pregnancy.^{2,3} The clinical course is rapidly progressive, with an average survival of 4 months and <25% surviving beyond 1 year. A small group of these patients can now be treated with newer combination chemotherapy, resulting in improved survival.⁴

Diagnosis of cancer is understandably devastating to a mother who is often delighted by the prospect of parenthood, and the management of such cancers poses a great challenge. This was especially true for this case, in which conception had followed a long period of infertility.

The management must be specific for the individual patient, with careful consideration before definitive treatment as to whether termination is necessary or continuing with the pregnancy is possible. The ideal aim is to cure the cancer and deliver a live healthy infant. A multidisciplinary approach should be adopted involving the obstetrician, neonatologist, and surgical and medical oncologists, as for this case. As this case has huge ethical implications, the ideal management, time permitting, should involve a discussion with the local clinical ethics committee, if available.

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It has been estimated that 10–20% of fetuses will develop anatomical malformation after exposure to chemotherapeutic agents.⁵ Long-term outcomes of children exposed to chemotherapeutic agents in utero are not well defined. We know that it is safe to give some drugs during the third trimester without causing long-term damage to the baby, for example for Hodgkin's disease or breast cancer. However, the drugs that are used to treat cancers of unknown primary origin have either not been used during pregnancy or have been shown to cause damage. Similarly, exposure to therapeutic and adjunctive doses of radiation can cause harm to the fetus. The effect of radiation on the fetus is dependent on the exposure dose and on the gestational age of the fetus. Radiotherapy should not be used unless a decision has been made to terminate the pregnancy.⁶

Normally if cancer is diagnosed in the second trimester, clinical judgment determines whether the pregnancy can be continued to viability or whether immediate intervention is indicated.

One way of analysing this case from an ethical perspective is to make use of Beauchamp and Childress's "four principles" approach to medical ethics.⁷ This involves consideration of moral problems in medicine through a framework of four moral principles: respect for autonomy, beneficence, nonmaleficence and justice.

Consider first, then, obligations to respect the autonomy of the mother. In this case, the mother was capable of making a competent decision, based upon proper understanding of the situation. Respect for her autonomy entailed respecting her wishes about how to proceed. Obviously, there is no question of respecting the autonomy of the fetus at this stage.

With regard to obligations of beneficence, these concern the promotion of well-being. In the present case, given the advanced nature of her disease, consideration relating to the mother's well-being had to focus on the shorter rather than longer term. It is reasonable to suppose that her well-being would be promoted by giving birth to a healthy child. This suggests that interventions aimed at prolonging her life but which jeopardised the health of the fetus should not have been undertaken. Alternatively, if it is thought that prolonging a mother's life at the cost of the health of the fetus best promotes her well-being, then the obligations generated by this principle should recommend that course of action. However, owing to the significant element of subjectivity in judgements about well-being, the ability of the patient to state which course of action they would take to best promote their well-being presents a good reason for adopting that chosen course of action.

What about the well-being of the fetus? We know that the fetus's well-being is best preserved by postponing medical interventions that will harm it, and we know that the well-being of the fetus is also promoted by developing in the uterus as long as this remains a healthy location.

The issue becomes more complex as we approach the application of the principle of non-maleficence, which concerns obligations to avoid harming patients. A degree of harm to the mother because of the side effects of the treatment is unavoidable, but more importantly, delaying cancer treatment to allow the fetus a fair chance of survival may also be harmful. It is difficult to decide which is least harmful to the mother: a delay in cancer treatment that helps in preserving fetal life or immediate treatment that might have dire consequences for the fetus, but very little real benefit for the mother. The decision regarding this is perhaps best left to the mother, as in our case. From the point of view of the fetus, the least harm was in

continuing the pregnancy and delaying anticancer treatment. This was the course of action chosen by the mother. The principle of nonmaleficence was thus upheld for both the mother and the fetus.

As discussed by Finnerty *et al* in describing a very similar scenario,⁸ justice is fulfilled when society ensures that a person receives what they deserve of society's benefits and that they share in the burdens in an equal fashion. The mother has a justice-based right to the provision of high-quality care. At the same time, the fetus has a justice-based right to the benefit of life. The management in this case thus upheld the principles of justice.

The importance of this case lies not only in the rarity of encountering an unknown primary tumour in pregnancy but also in the management dilemmas at such borderline gestations. Our case provided us with a management challenge. This was not because of the clinical problem, which was relatively straightforward, but because of the complex ethical issues entwined with it. There is a paucity of clear guidance on dealing with such issues. Currently the advice from the Royal College of Obstetricians and Gynaecologists in law and ethics in relation to late termination of pregnancy lists some of the options available, but falls short of providing clear guidance on dealing with the fetus and pregnancy in situations of life-threatening maternal disease.⁹ We suggest that the development of further ethically sound guidance in this difficult area is urgently needed. This should be based on the four basic ethical principles. There is little doubt that currently at least in the UK the wishes of the mother outweigh the right to life of the fetus, even if the fetus is viable. This again needs to be incorporated in such guidelines. An excellent ethical framework of dealing with such a scenario has been provided by Chevernak and McCullough *et al*.¹⁰ This perhaps can be used as a building block for developing much-needed clinical guidelines.

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