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Difficulties with diagnosis of malignancies in pregnancy

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Diagnosis and staging of cancer during pregnancy may be difficult due to overlap in physical signs, uncertainties on safety and accuracy of diagnostic tests and histopathology in pregnant women. Tumour markers should be used with caution due to pregnancy-induced elevation. Ionizing imaging and staging techniques such as computed tomography (CT) or positron emission tomography (PET) scans and sentinel node procedures are safe during pregnancy when fetal radiation threshold of 100 mGy is maintained. Ionizing imaging techniques can increasingly be avoided with the technical devolvement of non-ionizing techniques such as magnetic resonance imaging (MRI), including whole body MRI and diffusion-weighted imaging, which hold potentially great opportunities for the diagnostic management of pregnant cancer patients. Pathological evaluation and establishing a diagnosis of malignancy can be difficult in pregnant women, and a note to the pathologist of the pregnant status is essential for accurate diagnosis. This chapter will give an overview of possibilities and difficulties in diagnosing pregnant women with cancer.

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Introduction

For patients with symptoms that might be caused by a malignancy, quick and proper diagnosis is of utmost importance. Some tumours, especially in the case of a visible or palpable mass, are more easy to detect when compared to more internally localized cancers. The physiologic gestational changes may contribute to this masking of cancer symptoms. As cancer during pregnancy is relatively rare with an estimated incidence of one in 1000 pregnancies, it might not be high on the list of different potential diagnoses [1]. It has been reported that due to pregnancy, delay in diagnosis occurs, leading to a higher stage of disease at diagnosis [1]. Pregnant women with cancer enface an even more complex problem as standard interventions in diagnosing, staging and treatment of cancer may be harmful for the unborn child. However, as these interventions are standard patient management, alternatives should be applied with caution in order to accurately assess the maternal condition [1]. In this review, we focus on the difficulties of diagnosing and staging pregnant women with cancer.

Clinical presentation

Symptoms of normal pregnancy can be vague and diverse, and most of these complaints are self-limiting. Primary caretakers who are confronted with pregnant women easily consider these complaints as pregnancy-related. A malignancy may not be the most obvious cause, but it has the greatest impact on the mother and the unborn child. Table 1 shows the most common overlapping symptoms. This large overlap makes it more understandable that both patient's delay and doctor's delay may occur [2–4]. Andersson et al. [5] found fewer new cancer diagnoses during pregnancy than expected based on population-based numbers with a ratio of 0.46 (95% confidence interval (CI): 0.43–0.49). A subsequent rebound effect postpartum for melanoma, nervous system malignancies, breast cancer and thyroid cancer was also observed, which might be caused by the delay in diagnosis or by altered tumour biology during pregnancy and lactation [5].

Laboratory testing

Specific tumour markers can be measured at diagnosis, treatment evaluation or in the detection of recurrence during follow-up. These markers are produced not only by tumour cells but also as a response to (para)neoplastic conditions (e.g. inflammation). Sensitivity and specificity are therefore low, and increased levels of tumour markers are also associated with other benign situations such as pregnancy [6]. In pregnancies complicated by obstetrical problems, the variation of these markers is even greater [7]. The use of tumour markers during pregnancy or in pregnancy following a previous cancer is therefore limited. Carbohydrate antigen 15-3 (CA 15-3) is used in breast cancer patients, and it is significantly increased during pregnancy, especially in the third trimester, with 3.3–20.0% above cut-off levels [6]. Squamous cell carcinoma antigen (SCC) is used in the management of squamous cell carcinomas (e.g., cervix, head and neck, oesophagus and lung). While mean concentrations stayed below cut-off value 3.1–10.5% raised above this value, especially in the third trimester [6,8]. Cancer antigen 125 (CA 125) is used in monitoring non-mucinous epithelial ovarian cancer, and it is also

Table 1
Overview of common overlapping symptoms of pregnancy and malignant disease [2–4].

Symptoms
Nausea and vomiting
Appetite changes
Constipation/haemorrhoids
Abdominal discomfort/pain
Anaemia
Increased volume and consistency of breast tissue/palpable mass in the breast
Hyperpigmentation/changed nevi
Fatigue