Abstract. Background: Brain tumors in pregnancy are extremely rare events. A case of a patient with primitive neuroectodermal tumor (PNET) of the brain diagnosed during the second half of pregnancy is reported. Case Report: The first case of PNET of the brain diagnosed in a 26-year-old woman, gravida 1 para 0, in her 20th week of pregnancy is presented. The patient presented with headache, nausea and blurred vision. Magnetic resonance imaging revealed a large ill-defined tumoral mass in the left frontal cortex. Gross subtotal resection was achieved via a left frontal craniotomy. Pathological evaluation revealed histology and immuno-histochemistry consistent with the diagnosis of PNET. Adjuvant radiation therapy to the neurocranium was administered. Additionally, chemotherapy with Temodal 5 mg (Temozolomid) was initiated at 30 weeks of gestation. The patient delivered her baby via Cesarean section at 34 weeks of gestation. After delivery, external beam radiation to the craniospinal axis completed the therapy. The patient is currently being followed-up at the Department of Oncology University of Vienna Medical School, without any evidence of disease, 3 months after diagnosis. Conclusion: This is the first reported description of a PNET in pregnancy. A brief discussion on this disease and its management in pregnancy is presented. The treatment options seem to be reduced in pregnant women and mainly depend on the patient’s condition as well as the gestational age at presentation. In a multidisciplinary approach, an optimal therapy schedule should be assessed depending on these two parameters.

Brain tumors in pregnancy are extremely rare events, with only a few reports existing in the literature (4-6). During pregnancy, symptoms such as headache, mental status changes and seizures are typical manifestations of eclampsia. However, the physician has to bear in mind that such symptoms may also be caused by an intracerebral tumor.

The cornerstone of the treatment consists of gross-total resection of the tumor, adjuvant irradiation therapy to the craniospinal axis plus an increased dose to the tumor site, with or without chemotherapy (7, 8). Treatment options are, however, different in pregnant women.

To the best of our knowledge, this is the first reported description of a PNET in pregnancy. A brief discussion on this disease and its management in the setting of pregnancy is presented.

Case Report

A 26-year-old woman, gravida 1 para 0, in her 20th week of pregnancy presented with headache at the left parieto-temporo side lasting 3 weeks, nausea and defective vision (lasting 1 week). Her past surgical history included only appendectomy and her family history was not significant. Her past obstetrical history was significant for three trials of in vitro fertilization with successful pregnancy after the
third attempt. An ophthalmologic examination was performed and a progressive unilateral papilledema could be detected. The ultrasound examination at this time revealed a normal pregnancy at 20 weeks of gestation.

Due to the above-mentioned symptoms, contrast enhanced magnetic resonance imaging (MRI) was performed immediately and revealed a contrast-enhancing large ill-defined mass in the left frontal cortex which significantly compressed the surrounding tissue with a displacement of the midline. Due to the extent of the tumor, gross subtotal tumor resection was achieved via a left frontal craniotomy. Tissue was prepared by routine histological procedures and the samples were embedded in paraffin and stained with hematoxylin and eosin. Histological analyses of the tissue revealed sheets of hyperchromatic tumor cells with mitotic activity and necrosis, as well as highly malignant anaplastic features. The tumor cells were positive for neuronal markers such as synaptophysin, neuron specific enolase and nestin, thereby confirming the diagnosis of PNET. Immuno-histochemistry was negative for PDGFR-alpha, PDGFR-beta, c-kit, c-abl and arg in the tumor cells. The MIB1 proliferation index was about 80%.

After surgical excision, the patient underwent adjuvant radiation therapy with an increased dose to the tumor site (total dose of 36 Gy with 2 Gy/day applied to the whole neurocranium and a total dose of 56 Gy applied to the residual tumor). Due to the existing pregnancy, external beam radiation therapy to the craniospinal axis could not be performed. The radiation therapy to the tumor site was completed after 2 months at 30 weeks of pregnancy. A follow-up MRI after irradiation revealed residual tumor with no signs of progression compared to the initial MRI. Initially, the time of delivery was planned at 30 weeks of pregnancy. However, as fetal scan examination revealed a small-for-gestational-age baby, the time of delivery was shifted, while adjuvant chemotherapy was started in the meantime. Instead of a first-line chemotherapy regimen (Glivec), Temodal (Temozolomid 5 mg) was used as a second choice. The patient delivered via Cesarean section at 34 weeks of gestation. After delivery, the patient underwent adjuvant whole craniospinal irradiation therapy. The patient is currently being followed-up at the Department of Oncology without any evidence of disease after 3 months.

Progress of pregnancy and neonatal outcome. The first visit to the Department of Gynecology and Obstetrics revealed a normal pregnancy at 20 weeks of gestation with normal fetal development. A single umbilical artery (SUA) was detected, but the patient refused a chromosomal examination via amniocentesis. At 28 weeks of pregnancy, the beginning intrauterine growth restriction was detected and the amount of amniotic fluid was diminished. The umbilical artery Doppler impedance, however, was still in the normal range. Due to the start of intruterine growth restriction with an estimated fetal weight <1000 g (EFW of 893 g at 30 weeks of gestation) a conservative waiting management was chosen instead of delivery. At 34 weeks of gestation, the patient was administered 2x12 mg dexamethasone to achieve fetal lung maturation and a Cesarean section was performed at 34 weeks of completed pregnancy. The Cesarean section was done under general anesthesia and tracheal intubation.

A female baby was delivered with a birth weight of 1372 g. The APGAR score was 7/8/9 and the arterial cord pH was 7.28. The follow-up of the newborn revealed a healthy infant.

Discussion

Medulloblastomas are the most common malignant brain tumors of childhood, their pathogenesis being unknown and their relationship to other embryonal CNS tumors questionable. Patient response to therapy is difficult to predict (3) and the therapeutic treatment options are reduced in pregnant women.

Brain tumors in pregnancy are extremely rare events, with only a few reports existing in the literature (4-6). Isla and colleagues reported seven cases of pregnant women who presented with neurological symptoms during their pregnancy and subsequent diagnosis included two meningeomas, two ependymomas and two gliomas (4). In 1938, Cushing and Eisenhardt were the first to describe the relationship between pregnancy and the rapid increase of neurological symptoms in women with meningeomas (5). However, it is unquestionable that a hormonal relationship in the appearance of some tumors, particularly meningomas, may play a role (9). A case-control study in Iowa, U.S.A., examined the effect of parity and age at first birth on the risk of various carcinomas (10). The authors reported that the risk of brain cancer was slightly higher in women over 25 years. Compared to women younger than 20, the odds ratios for brain cancer were 1.3 (20-24 years), 1.9 (25-29 years) and 1.3 (>30 years), respectively. This is in line with our observation, as our patient was 26 years old when the PNET was diagnosed.

Treatment generally consists of surgical resection, radiation therapy to the tumor site and the craniospinal axis, with or without chemotherapy. Although the data are primarily derived from studies in children, a similar approach applies to adults (8, 9). Recommended radiation dosages are 50 to 55 Gy to the tumor site and 30-36 Gy to the entire craniospinal axis (neuraxis). Several randomized studies have evaluated the contribution of adjuvant chemotherapy, most often CCNU (lomustine),
vincristine and cisplatin, following surgical resection (11). However, the optimal treatment schedule and duration for combined postoperative chemotherapy and radiation is not entirely clear.

Treatment options during pregnancy are reduced as radiotherapy during pregnancy might cause harm to the developing fetus. Generally, pregnant women with malignant diseases are advised to postpone radiotherapy, if possible, until after delivery. In general, the expected radiation effects, such as mental retardation and organ malformations, seem to arise only above a threshold dose of 0.1-0.2 Gy (12). This threshold dose is generally not reached with curative radiotherapy during pregnancy, provided that tumors are located sufficiently far from the fetus and that precautions have been taken to protect the unborn child against leakage radiation and collimator scatter of the teletherapy machine. Such precautions also reduce the risk of radiation-induced childhood cancer and leukemia in the unborn child (12). Furthermore, Isla et al. observed that the risk to the fetus was minimal when pregnant patients with brain tumors were treated with cobalt 60 after 26 weeks of gestation (4). Our patient underwent adjuvant radiation therapy with an increased dose to the tumor site during the 20th and 30th weeks of gestation. At the end of the radiation therapy, intrauterine growth restriction was observed. The patient underwent external beam radiation therapy to the craniospinal axis not during pregnancy, but after delivery. However, it is unclear whether the intrauterine growth restriction was caused by the radiation and chemotherapy applied during the second half of pregnancy.

In conclusion, symptoms such headache, mental status changes and seizures are common manifestations of eclampsia, but the awareness of intracerebral tumors during pregnancy as a differential diagnosis is also important. Treatment options seem to be reduced in pregnant women and mainly depend on the patient’s condition as well as on the gestational age at presentation. In a multidisciplinary approach, an optimal therapy schedule should be assessed depending on these two parameters.

References


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