

Ethmoid sinus carcinoma during pregnancy

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ABSTRACT

Objectives: The neoplastic pathology in the pregnant woman is highly uncommon, but always raises an important clinical problem. We present the case of a 34-year-old woman diagnosed with ethmoid sinus carcinoma during the 38th week of pregnancy.

Methods: The diagnosis is based on tumour biopsy and CT/MRI evaluation. The therapeutic management, according to the complexity of pathology, requires a multi-specialized team and a multi-modal treatment. The sequence of the therapeutic means was decided by the patient's emergency condition, the location and the histological type of the tumour, as well as the patient's biological status.

Results and Conclusions: The favourable follow-up and tumour regression after the radiation therapy applied post-partum is a topic worth studying and debating for the future.

Key words: ethmoid sinus carcinoma, pregnancy, paranasal cancer, 3D conformal radiation therapy

INTRODUCTION

Diagnosis of cancer during pregnancy is one of the most extreme scenarios in medicine: the creation of a new life might coincide with the mother's death.

On rare occasions cancer coincides with pregnancy (1). As regarding the association with pregnancy, there is a frequency of 0.8% among all cancers (2).

A cancer diagnosis occurs in approximately one of 1,000 pregnant women. It is a relatively

rare combination, but compelling when it occurs. Treatment decision must balance the health of the mother with the health of the foetus, and also the emotional and ethical views of the patient and her family are to be taken into consideration. Every case requires highly individual care (3).

Researchers and clinicians have been painfully aware of the lack of data about the management of cancer in pregnancy. In order to counterbalance this lack of data, Motherisk

established the Consortium of Cancer in Pregnancy Evidencer (CcoPE) with the purpose of developing up-to-date, evidence-based information on the diagnosis and fetal outcome of cancer in pregnancy (4).

Specific cancers in pregnancy are: bone malignancies, brain tumour, breast cancer, cervical cancer, hepatocellular carcinoma, Hodgkin's diseases, leukemia, lung cancer, malignant melanoma, non Hodgkin's lymphoma.

The most encountered tumour types mentioned in the head and neck area of the pregnant woman are: cancer of the larynx, cancer of the thyroid gland, malignant melanomas and malignant lymphomas (4).

Pregnancy itself does not cause cancer, and pregnant women are not more susceptible of cancer than other women. The cancers that tend to occur during pregnancy are those that are more common in younger people, such as cervical cancer, breast cancer, Hodgkin's lymphoma, malignant melanoma and thyroid cancer. Because age is the most significant risk factor for cancer, doctors expect an increase of the cancer rate during pregnancy as more and more women postpone pregnancy for an older age.

As most statistics show, the incidence of the face sinus cancer tends to slightly decrease during the past decades. Its frequency lies at the level of 0.5% in the general oncological pathology and 5.8% in the ear – nose – throat (ENT) cancer (5).

The cancer of the superstructure (superoposterior to Ohngren's line) may occur at the level of the upper wall of the maxillary sinus and develops towards the upper side of the sinus and in the base of the orbit and progressively invades the malar bone and the ethmoido-maxillary cells (6). The clinical signs could be sinus, ocular and neurological, according to the affected region and taking into account the complexity of the anatomical relations with the orbit, epipharynx and the base of the skull.

The complexity of this case consists in the tumour location, as the superstructure cancer is a rare finding, and, moreover, its association with pregnancy. No such type of cancer associated with pregnancy has been found by us in the medical literature. The tumour usually has an aggressive development, and the survival rate at 5 years in young patients is as low as 20% (7). Moreover, the immunological changes related to pregnancy and the general immunotolerance

status, lead to an acceleration of the tumour growth as well as to an increased risk of hemorrhagic complications. □

CASE REPORT

We present the case of a 34-year-old Caucasian woman, R.M, with no particular family or personal oncological history and with a normal course of pregnancy until the 34th week. No toxic substances were documented in the work history. At that moment she addressed herself to an ETN clinic for moderate epistaxis. The conclusion of the clinical examination followed by a biopsy was: undifferentiated squamous cell carcinoma, type III (WHO classification) (8) at the level of the right nasal fossa.

Despite this situation and medical advice the patient did not accept any treatment at that moment and in the 38th week of pregnancy the epistaxis recurred and, this time, it was associated with painful rhythmic uterine contractions.

The head and neck and neurological examinations showed:

- a) moderate bilateral and antero-posterior epistaxis, nasal bilateral obstruction, as well as a spreading and advancing tumour growth in the right nasal fossa with involvement of the left one
- b) Exophthalmia (clinical remark) at the right eye and diplopia at the lateral left sight.
- c) Periorbital paraestheses and frontal migraine.
- d) The ear symptomatology – defective hearing.

In this situation we performed an anterior right nasal packing with one anatomical non-adhesive pack of 4 cm and in the left side with two packs of 11 cm. The epistaxis ceased.

The obstetrical examination showed an increased uterine tonus and alterations of the fetal cardiac rhythm, with prolonged decelerations, as low as 60 bpm. Additionally, a moderate vaginal blood loss was observed. The ultrasound scan confirms the clinical suspicion of *abruptio placentae*, as a moderate retro-placental haematoma was observed.

The decision was immediate delivery by cesarean section. The patient delivered a healthy 3100 grams little girl and the immediate post-surgical follow-up was marked initially by moderate bleeding through the packs and, finally, a massive bleeding occurred from behind the nasal fossae after 12 hours. This required a

new nasal packing, namely an anterior/posterior classical packing and a bilateral one, respectively.

After delivery we reconsidered this case including complementary examinations required for the complete tumour evaluation and staging.

A. Loco-regional tumoral extension was identified by a fibroscopic naso-pharyngo-laryngeal examination and a cranio-cervical Magnetic Resonance Imaging (MRI):

1. The fibroscopic naso-pharyngo-laryngeal examination pointed out the presence of a spreading and advancing tumour growth characterised by recent bleeding and associated over-infection. The tumour occupies completely the right nasal fossa, partially the left one, the upper anterior wall of the rhino-pharynx and both the terminal orifices of the Eustachian tube.
2. MRI examination of the face sinuses showed a 35/25/40 mm central tumour, with further extent from the posterior half of both nasal fossae, partially to the right maxillary sinus, the sphenoid sinus, the right anterior ethmoidal cells and to the bilateral posterior ethmoidal cells, respectively. It invades the right orbit and pushes laterally the right inner muscle; it penetrates the cribriform plate of the ethmoid bone and enters the anterior level of the base of the cranium but it does not reach the inside of the skull. (Figure 1).



FIGURE 1. The ethmoid and sphenoid sinus are occupied by the tumour invading the right orbit

B. The complications of cancer extension were identified by neurological and audiometry record.

1. The neurological examination finds a conscious and cooperant patient who presents low hearing, closed rhinophonia, but no motion deficiencies, nor disfunctionality in coordinating the movements. Also, the following symptoms are observed: anxiety, transient diplopy when directed towards the left side.
2. Acoustic immittance measurements and audiometry: bilateral conductive medium hearing loss, type B tympanogram with reduced compliance and absence of the bilateral acoustic reflex.

Finally, the tumour was staged as T4aN0M0 in accordance with the American Joint Committee on Cancer classification (9). The tumour presented with large extension involving anterior orbital contents, minimal extension to the anterior cranial fossa and without lymph nodes or visceral metastasis. □

PATHOLOGICAL REPORT

Undifferentiated carcinoma is a poorly differentiated malignancy that arises from Schneiderian mucosa. These fast-growing tumours are made of sheets, nests or trabeculi of cells with pleomorphic nuclei, variably prominent nucleoli and moderate eosinophilic cytoplasm. Abundant mitotic activity and areas of necrosis are often seen (10) (Figure 2).

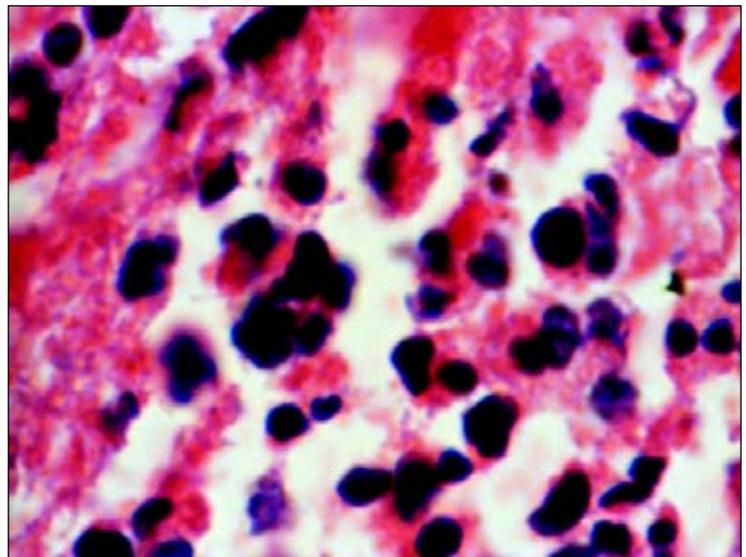


FIGURE 2. Undifferentiated squamous cell carcinoma – histopathological examination

The immunohistochemistry demonstrates a neuroendocrine differentiation, and may point out epithelial markers (e.g. epithelial membrane antigen – EMA, cytokeratin) (11). □

DISCUSSIONS

Theoretically speaking the best choice treatment for the ethmoidal cancer remains surgery (complete tumour excision) followed by local radiotherapy to sterilise the microscopic neoplastic residual foci (12).

As the tumour was considered inoperable, we decided to initiate an immediate post-partum radiotherapy.

A 3-field isocentric technique (anterior and two laterals) was implemented to treat a target volume that includes the ethmoidal sinus, frontal and maxillary sinuses. The orbit and *turcic sellae* were excluded to minimise the side effects of irradiation. The treatment was realised with high energy photon – Cobalt unit.

Because of very rapid growth in the last month of the pregnancy we considered that this tumour has a T_2 (potential doubling time) under 7 days and for this reason we chose a hyper fractionated and accelerated regime hoping to compensate this rapid tumour proliferation. Two fractions are applied daily, with an interruption of a 6-hour interval for a total dose of 60Gy.

The tumour reaction to the radiotherapy (6 months after delivery) can be analysed from the following perspectives: clinically, radiologically, biochemically and histo-pathologically, i.e.

- clinically, the patient does not suffer neither from diplopy, nor from eye protuberance and the ocular paresthesias disappeared.
- the naso-pharyngo-laryngeal fibroscopic examination does not identify any tumour formation at the nasal fossae, but the ostia of the Eustachian tuba presents local fibrosis.
- on MRI, the previously described rhinosinusal tumour shows at present a considerably diminished size, though it maintains the invasive attitude at the level of the right orbit (where it slightly pushes the inner right muscle). A minor invasion towards the anterior side of the cranium base is also to be noted, without presenting tumour growth inside the cranial area. (Figure 3, 4)
- the confirmation biopsy carried out by endoscopic surgery under general anaes-

thesia from the ethmoid and maxillary sinus and nasal fossae points out the existence of stromal edema and inflammatory chronic tissue.

- the immunohistochemistry shows the presence of neuroendocrine cellular markers, interpreted in an inflammatory reparatory context.

According to the criteria established by Miller and tolerated by WHO in evaluating the reaction to the therapy there is a partial reaction (PR),



FIGURE 3. Absent tumour growth at the level of the nasal fossae and right maxillary sinus

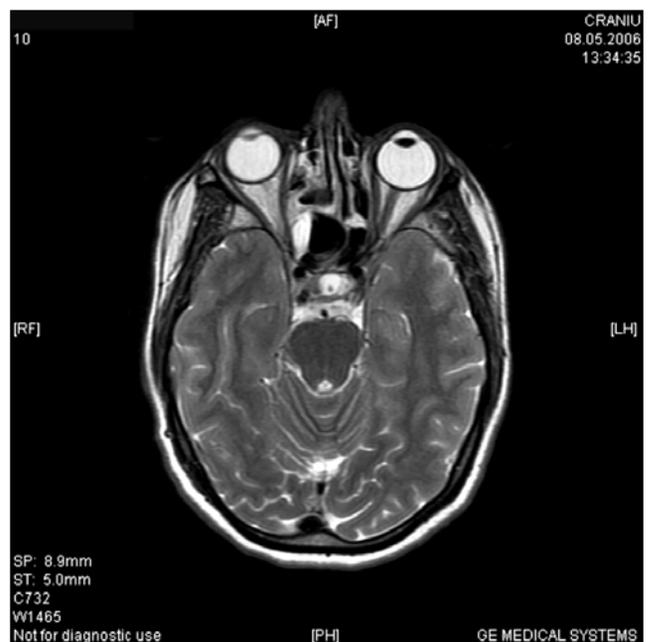


FIGURE 4. Highly regressed tumour which slightly pushes the right inner muscle of the right orbit

the tumour remission exceeding by 50% the initial stage.

Possible serious complications after the radiation therapy include serous otitis media, meningitis, unilateral or bilateral blindness, optic neuritis, cataracts, and central nervous system damage (13). The immediate complication appeared after the radiation therapy is in our case the acute skin toxicity grade II (bright erythema with moderate oedema), according to Radiation Therapy Oncology Group classification.

The oncological commission decided that this case does not require chemotherapy. The radiotherapy can be considered the only viable treatment in case of PR.

The specialised literature does not mention similar cases, therefore we cannot predict a long-term life expectancy. The association of other cancer types (malign melanoma for example) with pregnancy diminishes by half the life expectancy, as opposed to the absence of such an association (2).

The case monitoring is carried out by clinical and naso-pharyngo-laryngeal examinations once in two months and MRI survey once a year, respectively.

Additionally, we would like to mention that the infant presented piloric stenosis surgically solved during the first days following the delivery and no tumour metastases are detected.

In theory, the hormonal, metabolic, haemodynamic, and immunologic changes that occur during pregnancy impose many possible adverse effects in the women. These theoretical concerns are greatest for tumours arising in tissues

and organs that are under hormonal control or that respond to hormonal stimulation. Increased vascular bed, enhanced lymphatic drainage of many organs, and the state of immunologic tolerance that characterises pregnancy may contribute to early dissemination, accelerated growth and aggressive evolution of the malignant process (14,15). A favourable evolution of the patient's condition is possible during the postpartum period. This would be due to the disappearance of the above-mentioned changes during pregnancy under radiotherapy, as it was this case. Evaluation every 6 months post radiotherapy is mandatory, for early relapse detection. □

CONCLUSION

- a) This case is a medical peculiarity through the simultaneous association of pregnancy with the cancer of the paranasal sinuses. It is, as we know, the first case of this type reported in Romania.
- b) In our case, the treatment, as well as the sequence of therapeutical means, was decided by the location, the local extent and the histopathological type of the tumour, by the woman's age and biological condition, but also by the accurate TNM classification. The associated pregnancy limited the therapeutic options at the moment of diagnosis and was responsible for the rapid tumour development and hemorrhagic complications.
- c) Compared with similar cases outside the pregnancy, we found an extremely favourable evolution after radiotherapy only. The dramatic change in the tumour development after delivery and very good response to radiotherapy, are to be considered in such association. □

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