

Oropharyngeal carcinoma during pregnancy: clinical and psycho-oncological aspects

Carcinoma dell'orofaringe durante la gravidanza: aspetti clinici e psico-oncologici

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Parole chiave

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Summary

Cancer is uncommon in pregnancy, occurring in approximately one out of 1000 pregnancies, although it has been noted that one out of 118 women diagnosed with cancer is pregnant at the time of diagnosis. In the last 10 years, two oropharyngeal carcinomas, (1 squamous cell carcinoma and 1 adenoid cystic carcinoma) which developed during pregnancy, have been diagnosed and treated in our Department. No cases of oropharyngeal cancer, during pregnancy, have so far been reported in the literature with the exception of one case of oral cancer. This report focuses not only on the clinical history but also the management of oropharyngeal carcinoma during pregnancy, in terms of choice and timing of treatment. A scrupulous psycho-oncological analysis was also carried out in order to throw further light on psychological repercussions of head and neck cancer in the pregnant woman.

Riassunto

L'incidenza di cancro in gravidanza è poco frequente, dal momento che occorre approssimativamente in 1 caso su 1000 gravidanze, sebbene sia stato notato che 1/118 donne con diagnosi di cancro sia gravida al momento della diagnosi.

Negli ultimi 10 anni abbiamo diagnosticato e trattato 2 carcinomi orofaringei (1 squamoso, 1 adenoido-cistico) sviluppati in donne gravide. Al presente non sono stati riportati in letteratura casi di carcinoma orofaringeo in gravidanza ed 1 solo caso di carcinoma orale. In questo lavoro non abbiamo solo cercato di focalizzare la storia clinica delle pazienti ma anche la gestione della suddetta neoplasia in corso di gravidanza, anche in termini di scelta e di timing del trattamento. È stata inoltre condotta un'accurata analisi psico-oncologica che ci permettesse di meglio comprendere le ripercussioni che il cancro del distretto cervico-cefalico determina sulla donna in stato di gravidanza.

Introduction

Whilst cancer is uncommon in pregnancy, occurring in approximately one out of 1000 pregnancies, it has been noted that one out of 118 women diagnosed with cancer is pregnant at the time of diagnosis¹.

The malignant neoplasms complicating pregnancy are those most frequently seen in young women i.e., lymphoma, leukaemia, melanoma, cancer of the breast, cervix, ovary, thyroid and colon².

In a recent review, Ferlito et al. reported that as far as concerns head and neck tumours arising in pregnant women, the 4 most prominent types were, namely, cancer of the larynx, cancer of the thyroid, malignant melanomas and malignant lymphomas of the head and neck³.

In the last 10 years, two oropharyngeal carcinomas (1 squamous cell carcinoma (SCC) and 1 adenoid cystic carcinoma), which developed during pregnancy, have

been diagnosed and treated in our Department.

To date no cases of oropharyngeal cancer during pregnancy have, to our knowledge, been reported in the literature, with the exception of one case of oral cancer.

Oropharyngeal cancer often requires invasive treatment followed by radiotherapy. The side-effects are drastic, considering the aesthetic, functional and psychological aspects, since treatment, in this particular case, is carried out during pregnancy.

Aim of the present report was not only to focus on the clinical histories of these 2 patients but also to describe the management of oropharyngeal carcinoma during pregnancy, in terms of choice and timing of treatment.

A psycho-oncological analysis has also been carried out, in order to better evaluate the psychological repercussions of head and neck cancer in the pregnant woman.

Case reports

Case n. 1. A 32-year-old laboratory technician, in her 23rd week of pregnancy, was admitted to the ENT Department, University of Turin on May 15th, 1992.

Her family history revealed no risk factors: she was neither a smoker nor a drinker; had regular menstruation as far as concerns quantity, periodicity and duration. No exposure to ionizing radiation was reported. The patient had had no previous pregnancies and did not use oral contraception.

The patient had been complaining of a foreign body sensation in her throat and paradox dysphagia since March 1992.

Clinical examination revealed a large fungating lesion at the right base of the tongue, extending from the postsulcal part of the dorsum of the tongue to the right glosso-epiglottic vallecula (Figs. 1, 2).

Staging consisted of no-teratogenic tests (cervical magnetic resonance imaging (MRI), no cervical computed tomography (CT) scan, no chest X-ray).

Biopsy revealed SCC, T₂ N₀ M₀ of the oropharynx.

A multidisciplinary team, including the otorhinolaryngologist, radiotherapist, obstetrician, anaesthesiologist, family physician, oncologist, paediatrician, neonatologist and psycho-oncologist decided to carry out surgical treatment.

On May 28th, the patient underwent resection through a conservative transmandibular approach,



Fig. 1. Cervical MRI: axial image.

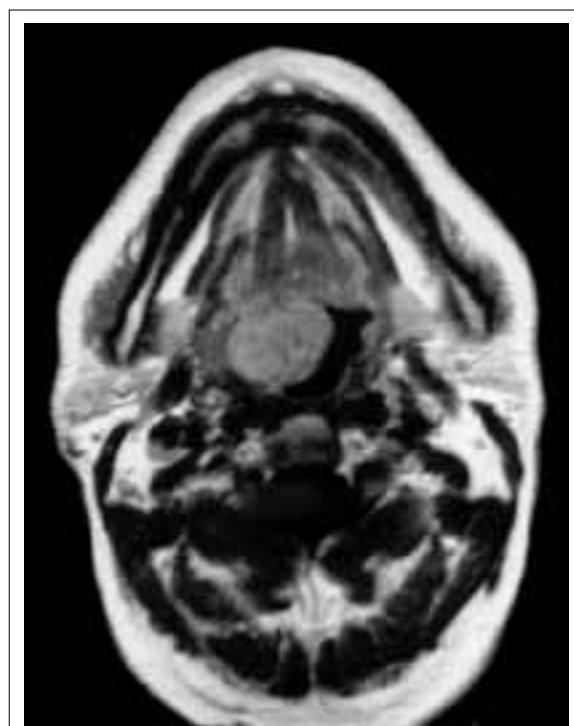


Fig. 2. Cervical MRI: coronal image.

selective neck dissection (levels I to IV) and tracheostomy. Repair of the oropharyngeal defect was carried out by direct suture.

Anaesthesia was induced using thiopental sodium as a short-term hypnotic drug followed by succinylcholine chloride as a muscle relaxing agent. Hypnosis and relaxation were obtained using nitrogen protoxide and pancuronium bromide. Fentanyl citrate associated with haloperidol decantoate for sedation were used as painkillers.

Great care was taken to avoid foetal asphyxia. Intra-operative monitoring of the foetal heart rate was carried out. Operating time was reduced to avoid compression of the aorta and vena cava due to the supine position.

Histological examination of the specimen confirmed a poorly differentiated SCC, with basaloid aspects pT₂ pN₁. No complications were observed during the post-operative period.

The patient began oral intake on the 20th post-operative day and tracheostomy was removed on the 23rd day.

Since post-operative radiotherapy was indicated (poorly differentiated carcinoma, stage III, basaloid aspect), delivery was artificially induced at the 32nd week of pregnancy. The patient gave birth to a healthy and beautiful baby girl weighing 2250 g. The

baby was admitted to the Neonatal Unit. Histology did not reveal any placental metastases. Two weeks after delivery, the patient underwent 50 Gy external beam radiotherapy. The patient is disease free after the 9th year of follow-up and her daughter has completed the second year at primary school.

Case n. 2. A 38-year-old patient, 6 weeks pregnant, was admitted to our Department on November 2nd, 1999. The patient was 11 years old at menarche, had regular menstruation as far as concerns quantity, periodicity and duration. She had had a previous successful pregnancy. She had smoked 15 cigarettes a day for 15 years, but had not been smoking for the last 5 years. The patient had been complaining of a swelling at the base of the tongue since October 1999. Clinical examination of the oral cavity revealed an irregular mass immediately behind the lingual V, extending below the base of the tongue. No palpable nodes were found in the neck. Biopsy revealed an oropharyngeal adenoid cystic carcinoma (T₂ N₀ M₀). Cervical MRI and chest X-ray were performed. The decision to proceed with surgical treatment was taken by the same multidisciplinary team, taking care of Case n. 1. On November 19th, 1999 the patient underwent resection through a conservative transmandibular approach, suprahomoyoid neck dissection (level I→III) and tracheostomy. After resection, all margins, in particular distal and proximal nervous stumps, were checked and found to be negative at frozen sections. Although with some difficulty, repair of the oropharyngeal defect was performed by direct closure. General anaesthesia was carried out according to the same pharmacological protocol as that used in Case n. 1. Histological examination of the specimen confirmed an adenoid cystic carcinoma of the oropharynx pT₂ pN₀. Radiotherapy was not indicated. During the post-operative period, recovery of the mandibular osteotomy was delayed, therefore, treatment with interdental fixation plates was necessary. Food intake was started on the 28th post-operative day and the tracheostomy was removed on the 32nd post-operative day. The patient duly delivered a beautiful baby boy weighing 3.7 kg who was regularly breast fed, for 6 months. The pathological examination did not reveal any placental metastases. The patient is now considered disease free after the 24th month of follow-up and the baby is doing very well.

Psycho-oncological assessment

Six months after surgery, psychological assessment of the patients has been carried out by a clinic psychologist psycho-oncologist who evaluated the patients on three different occasions. During the first visit, a semi-structured interview on the following aspects has been performed:

- the relationship between the patients and their parents, especially with the mother,
- the pregnancy period,
- the emotional aspects related to cancer.

The second interview included Rorshach's Test, a projective test used to evaluate the personality structure. During the third interview, the following instruments have been used in the psychological assessment of the patients:

- Beck Depression Inventory (BDI), evaluating the presence of mood disorders ⁴;
- STAY1 and STAY2 Scales, to assess state and trait anxiety ⁵;
- self-administered MINI MAC Scale, to identify the patient's copying style, while facing the disease ⁶.

Results

Rorshach's Test, in both patients, revealed cognitive inhibition due to the peculiar emotional situation, thus on a stable and adaptive personality base. Cancer had weakened the patients' defense mechanisms (from a psychodynamic point of view these are a way to fight against distress), leaving them more vulnerable, especially in situations in which strong emotions of uncertainty and lack of foresight were felt ⁷. The inner worries of these two patients concerning their body affected by a cancer, their own image modified by the operations and the possibility of recurrence, are underlined by the high percentage of anatomic answers given to Rorshach's Test ⁸. Albeit, these answers may be considered normal when testing any person affected by an organic disease. These two patients did not show any significant sign of anxiety or depression in their way of behaving; this aspect is confirmed by the result of the MINI MAC Scale, studying the copying styles. Their style, defined as "fighting spirit", is, in fact, characterised by moderate levels of anxiety and depression and several "active" cognitive and behavioural reactions, when facing a difficult situation in a positive and constructive way. The possible feeling of discomfort, therefore, does not weaken the adaptive behavioural strategies, even if it still represents a risk factor.

From the interview, other common aspects emerged in these two patients: a late pregnancy (36 and 37 years old) and a good, satisfying marriage. Moreover, the role of the husband, at the time of diagnosis and during the course of treatment, was fundamental, as he acted as a strong and emotionally significant support.

It may be assumed that the choice of having a baby, after having discussed this possibility for a long time with one's husband, brought the couples to strongly invest in the pregnancy, constantly aware of the possibility of losing the baby.

Both patients, during the interview, felt confused and lost on account of their lack of knowledge about the risks their babies might run; once reassured by clinicians, the babies themselves became an important stimuli to survive and fight for.

In fact, in every pregnant woman affected by cancer, we observe two contrasting emotions: the cancer associating her with death and a new life growing inside her⁹.

For our patients, the fact that they realized that their body was not only ill and damaged, reinforced their self-confidence and stimulated them to fight.

Discussion

Cancer and pregnancy cause many opposite reactions and feelings.

When a pregnant woman is diagnosed with cancer, her first reaction is a mixture of denial and loss and these same feelings are common to the husband, the family and the doctor in charge of the case.

When an oropharyngeal carcinoma is diagnosed, great care must be taken in adopting the correct therapeutic protocol.

A review of the literature showed that head and neck cancer and pregnancy can be managed together with a good outcome for the baby and without making the mother's prognosis worse.

The doctors, patient and family must be aware of all the diagnostic, moral, ethical and religious problems related to this condition.

From our personal experience and from the few papers available in the literature, there is no evidence that these tumours are more aggressive, apart from the early appearance. Furthermore, there is no evidence of an increased incidence of malignant neoplasms in pregnant women. In the past, pregnancy was thought to have a deleterious effect on some cancers, but, except for the case in which diagnosis is delayed, no convincing data exist that pregnancy *per se* adversely influences the prognosis or biology of the maternal tumour.

Immunological derangement during pregnancy results in a decrease in killer cells, reduced helper T-cell pop-

ulations, development of serologic blocking factors, immunosuppressive effect of hormones (such as oestrogen, progesterone and chorionic gonadotropin), presence of suppressor T-cells, presence of leucocyte migration enhancement factor in amniotic fluid, and alteration of surface antigenicity¹⁰.

While smoking and heavy alcohol intake are the most significant aetiological agents, for oropharyngeal SCC, other genetic and/or chemical factors etc. may also be involved¹¹.

Surgery is indicated as primary treatment of oropharyngeal cancer during pregnancy, just like all other head and neck cancers. Surgical treatment can be satisfactorily carried out, without modifying the extent of the resection.

In the two cases described, resection was performed via a conservative transmandibular approach with selective neck dissection, as would have been carried out on a non-pregnant patient.

Pedicle or free flaps were not considered as reconstructive options. Only in the second case were the aesthetic and functional results considered unsatisfactory. At present, at the patient's request, we are focusing on a secondary reconstructive option, in order to reduce impairment of lingual movements.

In those cases in which direct suture of the pharyngeal defect is impossible, reconstructive surgery may lead to severe technical and ethical problems.

Reconstruction using the pectoralis major, either myocutaneous or only myofascial, should be avoided since it interferes with the anatomy and physiology of the breast, which during pregnancy results in an unpredictable change. The patient, in this case, would be exposed to further complications.

Reconstruction through the forearm free flap can be taken into consideration, flap harvesting being performed together with the demolitive operation, thus reducing the total operation time.

In that case, there might be a slight percentage of risk related to loss of the flap (5%), which would require further surgery to repair the defect.

Trapezium and platysma flaps should, in our opinion, be avoided due to the high percentage of unsuccessful outcomes. Our choice of reconstruction, if necessary, is the forearm free flap.

Specific precautions must be taken regarding general anaesthesia: it is important to take into account maternal apnoea periods and the mother's haemodynamic parameters, avoiding inhalation of stomach contents and monitoring foetal heart rate after the 16th week of gestation. Non teratogenic drugs are mandatory, especially if administered in the first trimester.

During the first trimester of pregnancy, hypotension and foetal hypoxia may occur on account of compression of the aorta and vena cava due to the supine position.

Knowledge of the various alterations, associated with pregnancy, is also mandatory for optimal management of these patients. The managing physician requires a thorough knowledge of the physiologic maternal adaptations to pregnancy to minimize maternal iatrogenic risks. The potential effects of the planned procedure, diagnostic tests, therapeutic drugs and anaesthesia must be considered preoperatively. Any potential risks to the foetus must be discussed with the patient.

In an attempt to define the foetal risk associated with anaesthesia and surgery during pregnancy, Duncan et al.¹² performed a study using health insurance data from the province of Manitoba (1971 to 1978). They analysed data from a group of 2565 women undergoing incidental surgery during pregnancy and paired with a pregnant female population not undergoing surgery. Both groups were linked to a separately maintained provincial congenital-anomalies registry to ascertain the frequency of anomalies. No significant difference was observed in the rate of congenital anomalies between the two groups, implying no strong teratogenic effect. They observed only an increased risk of spontaneous abortion in those undergoing surgery with general anaesthesia in the first or second trimester, most of which after gynaecologic procedures (estimated risk ratio = 2.00). They concluded that surgery with general anaesthesia is associated with a higher incidence of abortion, but it is conjectural, at present, which factors account for the increase observed in foetal risk.

The psycho-oncological analysis revealed that our 2 patients developed adaptive "coping" strategies, that allowed early re-elaboration of the disease and a proper re-orientation of emotional resources. This could be because pregnancy, first seen as the cause of the disease, then becomes the motivation to recovery, strengthening the mother's instinctive survival reaction: this has a positive effect both on pregnancy and the post-operative period.

This strongly discourages voluntary interruption of pregnancy before oncologic treatment is commenced since this would create a complex negative feed-back mechanism.

Timing of treatment is obviously different as far as concerns differentiated thyroid carcinoma, whereas treatment of an oropharyngeal carcinoma cannot be postponed until after delivery.

It should also be taken into account that at least 50% of the patients presenting oropharyngeal carcinoma will undergo post-operative radiotherapy after definition of the histological findings and tumour extent. The 2 patients described in the present report underwent surgery at the end of the 2nd and 1st trimester of pregnancy, respectively.

Post-operative radiotherapy was indicated only in Case n. 1.

Considering that the risk of premature birth rapidly decreases after the 28th week and that, in neonatal units, the risk of death for infants after 32 weeks does not exceed that of those born at term, delivery was artificially induced at the 32nd week, in our patient, in order to enable her to undergo radiotherapy, as soon as possible. This could be a good compromise in order to avoid radiation of the foetus as well as the need to comply with a correct therapeutic protocol for the mother.

The situation is completely different in a mother in the 1st or 2nd trimester of pregnancy when radiotherapy is necessary after surgery.

In this case, before proceeding with radiotherapy, the following points must be taken into consideration: dose rate, field size, radiation energy and gestational age.

Radiotherapy must be initiated after the 8th week of pregnancy in order to reduce foetal malformation. Substantial scatter to the foetus may occur with supradiaphragmatic radiation. Much of the scatter is internal but abdominal shielding can reduce the foetal dose significantly and it may be safe to administer localized radiation to the head and neck areas.

Sharma et al. and Podgorsak, irradiating a phantom, measured the foetal dose, with and without a shield designed to be placed over the patients' abdominal and pelvic regions.

With use of the shield, the inner dose was 3.3 cGy at the cervix to 8.6 cGy at the fundus.

While several studies have demonstrated no increase in abortion, growth retardation or congenital malformation following diagnostic exposures below 0.05 Gy delivered at any time during gestation.

Conclusions

Treatment of cancer occurring during pregnancy is complicated and therapeutic decisions must be tailored to the individual case. These decisions might be facilitated by a multidisciplinary team, including the otorhinolaryngologist, radiotherapist, obstetrician, anaesthesiologist, family physician, oncologist, paediatrician, neonatologist and psycho-oncologist.

This interaction should begin immediately once the patient is diagnosed with cancer.

Considerations must be made for the immediate health of the mother and foetus and the long-term health of infants exposed to potentially teratogenic and carcinogenic drugs and radiation.

The unusual occurrence and insidious onset of these tumours may often delay diagnosis.

Surgical treatment may be based on specific rules, but each case must be considered on its own and the potential benefits of immediate treatment should be assessed against possible risks to which the foetus might be exposed.

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