Case Report

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Nasopharyngeal Carcinoma in Pregnancy: Management Approach Case Report at Moi Teaching and Referral Hospital, Eldoret-Kenya

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Abstract

Nasopharyngeal carcinoma is an uncommon tumour, which raises management dilemma in pregnant women. The condition has a considerable effect on the pregnancy outcome, considering the risk of preterm delivery. This paper reports a case of 26 years old Gravida 7 Para 6 admitted at 28 weeks of gestation with epistaxis, hematemesis and a neck mass. The head CT scan showed a right paranasal space soft tissue mass with bony destruction and bilateral cervical adenopathy, consistent with neoplastic carcinoma. Histopathological examination confirmed the diagnosis of nasopharyngeal carcinoma. Deterioration of the patient's condition, necessitated emergency caesarean delivery at 32 weeks to accommodate further management.

Keywords: Nasopharyngeal carcinoma; Pregnancy; Chemo-radiation

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Introduction

Nasopharyngeal carcinoma (NPC) is a rare tumour with challenging antepartum management in resource-limited settings. Because of its rarity in most countries (<1 per 100,000 per year), most of obstetricians in developing countries are unfamiliar with NPC, its clinical presentation, and its management during pregnancy. In addition, the diagnosis of cancer in general and particularly NPC in sub-Saharan Africa is challenging due to several factors such as, scarce of facilities providing diagnosis and treatment of cancers [1] lack of public awareness of the disease and poor health literacy, socio-cultural disadvantage, and predominantly low socio-economic status of most people translates to poverty reducing access to health care. To date, a number of researches have shown that malignant tumours can be managed successfully during pregnancy with use of a multidisciplinary approach to maximize the maternal and perinatal outcomes [2]. This case study emphasises the multi-disciplinary management approach of nasopharyngeal carcinoma in pregnancy, as well as challenges related to its diagnosis in resource-limited settings.

Case Report

A 26-year-old Gravida 7 Para 6 was admitted at 28 weeks gestation by ultrasound as a referral from a remote peripheral facility for further management of right lateral neck mass, persistent headache, epistaxis, nasal obstruction and hematemesis complicated with severe anaemia. She developed these symptoms 3 months prior to first contact with a primary clinician. Her previous medical history was unremarkable. She had 6 successful homebirths. This was her first admission. Her father was undergoing treatment for advanced stage NPC. Her psychosocial history was significant by poor quality of family and social support correlated with her low education level. However, her past psychiatric history and mental status was unremarkable.

Episodes of epistaxis and pain were frequently managed with Tranexamic acid, Tramadol and sometimes with antibiotics at a remote peripheral health facility with improvement of symptoms. On physical examination, she was sick looking and afebrile, blood pressure (BP) 110/66 mmHg. There were bilateral neck masses, the right measured 6 × 4 cm and the left 3 × 3 cm. Macroscopically, these represented a posterior nasopharynx mass covered by the soft palate, bleeding in response to touch. The gravid abdomen's fundal height measured 26 cm. She was pale without jaundice. There were no palpable contraction, vaginal bleeding or discharge, and the cervix appeared closed on pelvic examination.

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She was anaemic, with a Red blood cell count of 1.49 × 10^6, haemoglobin 4.6 g/dl, haematocrit 13.4%, MCV 89.9 µm³, platelet 266 × 10^3. Patient's blood group O rhesus positive. Urea electrolytes and creatinine as well as liver function tests were normal. Coagulation profile was unremarkable. Obstetric ultrasound showed a viable single intrauterine foetus at 28 weeks and 2 days gestational age in cephalic presentation with an estimated foetal weight of 1196 grams, umbilical artery study with resistive index of 0.635, and an amniotic fluid index of 13.2 cm the foetus was grossly normal.

Locally, magnetic resonance imaging (MRI) was expensive and unavailable. A multidisciplinary team of obstetricians, oncologists, ENT (Ear, Nose and Throat) specialists and haematologists and radiologist consultants recommended computed tomography scan (CT scan) of the head, neck and chest. For the head and neck there was a right paranasal space soft tissue mass with bony destruction and bilateral cervical adenopathy, consistent of neoplastic carcinoma. Nasal endoscope-guided core needle biopsy (CNB) was recommended. Chest CT scan was normal. Biopsies performed under anaesthesia (EUA) revealed a tumour composed of syncytial clusters of pleomorphic epithelial cells with irregular vesicular nuclei and prominent nucleoli. Dense lymphoplasmacytic response was seen. The diagnosis of nasopharyngeal carcinoma was made, and patient was classified as T3N2M0. For management plan, the patient had to stay in the hospital until delivery and was frequently given intravenous Tranexamic acid 1 gram 3 times daily to stop bleeding, blood transfusions to correct severe anaemia (total of 16 units in 4 weeks as she had several episodes of bleeding during hospitalization), intramuscular dexamethasone 6 mg (6 hourly for 24 hours) for foetal lung maturity. Postpartum chemo-radiation after delivery at 34th week of gestation to allow foetal lung maturity) was made in collaboration with a hospital which is the only centre in Western Kenya which offers radiation. At 32 weeks of gestation, the patient's condition deteriorated with uncontrollable profuse bleeding. An emergency caesarean delivery with patient requested bilateral tubal ligation was performed under spinal anaesthesia. The outcome was alive male infant with Apgar score of 9 at the first and fifth minutes and a birth weight of 1,700 grams. The new-born was admitted to the new-born unit for prematurity. After delivery, the patient's condition markedly improved.

Details of the surveillance and treatment plan arranged with free maternity care between the family and tertiary hospital were completed. Her adherence to this treatment plan was difficult due to the distance from her residence to hospital and unaffordable transport costs to the tertiary hospital despite 100% waiver of direct healthcare fees. She received one of 7 planned chemo-radiation cycles. She died 7 months postpartum.

Discussion

Nasopharyngeal carcinoma is a rare tumour, accounting for 2% of all head and neck squamous cell carcinomas. It is of particular interest because of the interaction of complex genetics, environmental, viral and dietary factors resulting in a remarkable geographic distribution in the world [3]. Historically, the first case of NPC was reported in 1901 and its clinical characteristics were described in 1922 [4]. In their study, Mu-Sheng Zeng et al. reported that the incidence of NPC is higher in endemic regions of Epstein-Barr virus (EBV), particularly in Southern China, Southeast Asia, Japan and Middle East/North Africa with an incidence of up to 50 cases per 100,000; whereas in western countries, the incidence is 1/100,000. It is the third most common malignancy among men than women [5]. However, in sub-Saharan Africa, there is paucity of data regarding NPC despite high exposure of the population to risk factors which include Epstein-Barr virus and consumption of salted fish. Furthermore, studies have shown that the NPC affects all age groups, however it is highly frequent among people aged 50-60, and less frequent in late childhood. In addition, it is widely acknowledged that EBV infection is not sufficient to induce cancer and that other cofactors such as genetic factors play an important role in NPC pathogenesis [6]. In this case, the patient was 26 years, with a positive first-degree relative history of NPC, supporting the hypothesis of genetic factors.

With regards to the diagnosis, NPC is difficult to diagnose at early stage due to a paucity of symptoms and signs. The symptoms and signs include nasal bleeding, nasal obstruction and discharge in 78% of cases; hearing impairment, ear infection and tinnitus in 73% of cases; headache (61%); and lump or neck mass in 63% of cases [7]. This lump or neck mass is described as painless and it is caused by the cancer spreading to lymph nodes in the neck, making them larger than normal [8]. From the same source, ear infections are common in children. However, in the presence of ear infections without upper respiratory infection in adults NPC is a more likely diagnosis. Similarly, the case report presented with the described nasal symptoms, headache and bilateral neck swelling without ear symptoms and signs. In some studies, it has been argued that hearing impairment may be either due to the tumour itself, treatment (radiotherapy dose and adjuvant chemotherapy), irritation, or injuries of sensory nerves respectively [8]. According to the same authors, hearing loss may be of sensorineural, conductive, or mixed type, which can be diagnosed through tone audiogram and impedance audiometry [8]. The literature supports that the auditory system is affected because NPC is often located in the fossa of Rosenmuller near the opening of the Eustachian tube into the nasopharynx [9]. Consistent with this, radiation technique and middle ear effusion can to lead to hearing loss [10].

Further, investigation related to its diagnosis is challenging during pregnancy because local physical examination is done under anaesthesia which may be associated with risks to the foetus. Biopsy, an important diagnosis procedure, may be associated with catastrophic bleeding. CT-scan exposes the foetus to radiation. Similarly, Sukhminder [11] found that anaesthesia for non-obstetric surgery during pregnancy is challenging. In total, 1-2% of all pregnant women present for emergency non-obstetric surgery at least once in their lifetime [12]. In reality, studies have shown that anaesthesia in second trimester is safe and the risks of spontaneous abortion and preterm delivery associated with anaesthesia, respectively in the first and third trimester are reduced. Thus, the biopsy was performed under anaesthesia at

the end of the second trimester to minimize any foetal event. In addition, complications related to biopsy, especially bleeding seem to increase with increased gestational age. For example, progesterone, a gestational hormone is a known vasoactive hormone, inhibiting agonist-induced vasoconstriction [13]. Consequently, during biopsy, this may contribute to uncontrolled bleeding or thromboembolic events. The current case report had continuous bleeding from the tumour related to any stimulation, initially controlled by drugs. This was mistaken for hematemesis because any contact of tumour with the patient's tongue trigged profuse bleeding, inhaled by the patient. Biopsy is most accurate to establish the diagnosis of any malignant process. The risks and benefits of the procedure should always be weighted in pregnant woman and under some circumstances, we agree that pregnancy status should not delay the procedure because the result is essential for initiating treatment. Regarding imaging investigation, both CT- scan and MRI can provide sufficient information about the nature of the tumour and its extension to other organs. Recently, the America Society of Clinical Oncology (2017) reported that CT- scan of the head and chest is safe during pregnancy because it does not directly expose the foetus to radiation. The case report benefited from imaging and pathology, described as a high-quality diagnostic procedure. Other laboratory studies including complete blood count, renal and liver function tests, uric acid and coagulation profile are important. Liver function test results may be abnormal and suggestive of hepatic metastasis; Uric acid levels may be elevated in patients with rapidly growing nasopharyngeal carcinoma NPC [8]. In this case, baseline blood work results were normal. Epstein barr virus (EBV) titres that include immunoglobulin A (IgA) and G (IgG) antibodies to the viral capsid antigen are thought to be useful as well as serum EBV-DNA level (marker) for pre-treatment risk categorization, initial treatment response, and at the end of treatment [8]. Epstein barr virus titres were not done in this case because the patient could not afford the cost of laboratory tests only available in a private laboratory.

Macroscopically, NPC varies from smooth mucosal bulge, raised nodule with or without surface ulceration, and infiltrative mass lesions [14]. Histologically, according to World Health Organization cited by MU-Sheng Zeng and associates, the NPC is classified in three types based on the degree of differentiation. Type 1 is squamous cell carcinoma (SCC) that mostly arises from the ostium of the Eustachian tube in the lateral wall of the nasopharynx Umar and associates found that the SCC represents 5-10% of total cases of NPC and it is characterized by well-differentiated keratin producing cells, seen by the presence of intracellular bridges in electron microscope. According to Mu-Sheng Zeng and co-workers, type 2 NPC is a non- keratinizing squamous carcinoma that varies in cell differentiation from mature to anaplastic cells. Types 2 and 3 NPC are non-keratin producing. Type 3 NPC has undifferentiated, highly variable cell types (clear cell, spindle cell, anaplastic). cells characterized by a bulk tumour as seen in patients with nasopharyngeal carcinoma. Moreover, in their study, Mu- Sheng Zeng and co-workers reported type 3 NPC that is the most common NPC in endemic regions as it correlates with environmental factors and EBV acting on genetically susceptible individuals. In this case report, histologically, the tumour consisted of syncytial clusters of pleomorphic epithelial cells with irregular vesicular nuclei and prominent nucleoli with dense lymphoplasmacytic response, corresponding to the WHO type 3 NPC classification.

Regarding management of NPC in pregnancy, it is known to be complex, considering the full range of an experienced multidisciplinary team which is not available in resource-limited settings. Additionally, treatment of NPC can affect pregnancy outcome. The American Society of Clinical Oncology recommends treatment options that do not affect pregnancy. Generally, factors that should be considered before initiation of treatment of any cancers during pregnancy include the gestational age; type, location, size and the stage of the tumour; and the wishes of pregnant woman or family members. The primary risk associated with the disease during pregnancy is preterm delivery. Horgan et al. established the relationship between preterm delivery and initiation of chemo-radiation in women with malignant tumours, nasopharyngeal carcinoma included. According to guidelines currently available, NPC can be treated with chemotherapy, radiotherapy or by a combination of these, depending on the stage of the tumour. However, several studies have reported that concurrent chemo-radiotherapy is superior to radiotherapy alone for low-risk patients. Thus, adding neoadjuvant and/or adjuvant chemotherapy is a reasonable approach for high-risk patients. In pregnant woman, chemotherapy or radiation is still a challenge. Some studies have shown that chemotherapy in second and third trimester is associated with intrauterine growth restriction and preterm delivery, and cardiotoxic effects on both the mother and foetus have been reported. For this case, the patients did not receive chemotherapy because of its side effects. However, preterm delivery at 32 weeks was unavoidable due to the patient's poor physical status. Furthermore, delivery was also an option to stabilize the patient and allow further management. To date, there are few studies investigating increased complications of NPC with increased gestational age. In this study, the patient's condition deteriorated during pregnancy, but markedly improved after delivery without chemotherapy or radiation. Further studies will be needed to interrogate this finding. In addition, protocols recommend that stage I and II disease should be treated with radiotherapy alone because the prognosis generally is good. However, stage III and IV disease have poor prognosis and should be managed with combination chemo-radiation. In this case, the patient was stage III (T3N2M0) and could not afford the cost of chemo-radiation. Despite free maternity care and some oncology cost waivers, low psychosocial and economic status affected her treatment adherence. She died, orphaning 7 children after one cycle of chemo-radiation. This is previously undescribed situation in the literature is seen in sub-Saharan Africa where diagnosis and cancer treatment centres are out of reach of most of women.

Conclusion

In conclusion, NPC in pregnancy is uncommon. The management of NPC in pregnancy is a dilemma for clinicians. If the patient's performance status is deteriorating, preterm delivery is an option regardless of gestational age, to broaden management

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options. In resource-limited areas, patients with cancer are out of reach of cancer treatment centres, finally seeking treatment when the tumour is in an advanced stage. Nonetheless, clinicians should be aware about the existence of NPC and must be able to refer the patient for early diagnosis and prompt management at tertiary hospitals. It is possible that increased gestational age can aggravate the symptoms of nasopharyngeal carcinoma. However, further studies are needed to interrogate this finding.

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