Case Report: Down-staging locally advanced head and neck cancer in an HIV infected patient in a limited resource setting

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Introduction

Head and neck cancers are a common group of malignancies. They rank sixth among the cancers, and accounting for 6% of all cancer cases globally[1]. In early stages the disease is highly curable with either radiotherapy or surgery, and these modalities offer equivalent survival outcomes. However, most patients up to 60% present with advanced disease which confers a poor prognosis[2]. The role of chemotherapy in head and neck cancers has evolved over time. The first big meta-analysis of chemotherapy in head and neck cancer (MACH-NC) involving over ten thousand patients failed to demonstrate benefit of neo-adjuvant chemotherapy in head and neck cancers, which was only demonstrated in concurrent chemo-radiation. The meta-analysis was largely looking for survival benefit. The Veteran approach of neo-adjuvant chemotherapy for laryngeal preservation was one of the first trials to report a positive role of neo-adjuvant chemotherapy but for laryngeal preservation other than survival benefit.[3] Later, TAX trials demonstrated that induction chemotherapy with Cisplatin, 5- Fluorouracil and Taxotere (TPF) regimen followed by concurrent chemo-radiation for patients with locally advanced head and neck cancer is more effective and tolerable[4]. The neo-adjuvant chemotherapy in this protocol demonstrated survival advantage. This is the recent standard of care for locally advanced head and neck cancers in good performance status patients. Palliative radiotherapy forms the main stay of treatment in locally advanced cases that are not fit for radical treatment. However, the management of HIV infected locally advanced head and neck cancer is not clearly established. HIV infected patients tolerate chemotherapy poorly, are more likely to suffer severe toxicity, with higher possibility of declining CD4 count, rebound in HIV viral load and septic complications[5,6,7]. Further challenges exist in areas where radiotherapy access is a major challenge. We report a case of a locally advanced head and neck cancer of squamous cell histology, HIV infected who was down-staged using non-TPF neo-adjuvant chemotherapy in a setting where there is no radiotherapy and achieved near complete response and enabled a potentially curative resection procedure be performed.

Presentation

A 36 year old female patient HIV reactive on antiretroviral therapy (Triommune: Neverapine, Stavudine and Lamivudine fixed dose combination) for five years. She was referred to our hospital, Queen Elizabeth Hospital (QECH) at the Oncology Unit, with a main complaint of progressive swelling of the right cheek for 4 months. The patient reported having an episode of toothache prior to this, following which she had a tooth extraction. She was prescribed different antibiotics but there was no marked improvement in the swelling.

Clinical examination

Patient weighed 47kgs, height 154.5cm, BMI 19.7kg/m^2. Inspection revealed a left cheek tumour with a surface that was partially ulcerated, with pus discharging sinuses. The tumour was oval in shape, hard measuring 7cm X 6cm. Oral evaluation revealed a mass on the left cheek with ulceration of the mucosal surface and no other findings. (See Figure 1 pre-chemo). There was trismus of about a centimetre, which precluded detailed oral assessment. There was no clinically palpable submandibular, cervical and supraclavicular regional lymphadenopathy. Examination of the rest of the systems were non-remarkable with no obvert stigmata of HIV infection.

Investigations

Incision biopsy was performed and pathological examination of the submitted specimen confirmed ulcerated oral mucosa with an invasive poorly differentiated squamous cell carcinoma extending to the lateral and deep margins of the biopsy. X-rays of the affected region demonstrated destruction of the left aspect of the body of the mandible sparing the angle. The base-line full blood count done demonstrated a leucocytosis with white cell count of 22 and lymphocyte predominance. Haemoglobin revealed mild anaemia and there was mild thrombocytosis as shown in table 1, column of base-line values. Her CD4 count had increased to 560cells/mm^3 from the initial 42 cells/mm^{3}done five years prior. The baseline urea, electrolytes and creatinine were normal, and the rest of the blood test results generated during the patient's different visits to the oncology unit is as shown in Table 1.

	BASELINE	Pre 1st Cycle	Pre 2nd cycle	Pre 3rd cycle	Pre 4th cycle
WBC (10^3/µL	22	18.2	11.8	7.1	5.2
HGB	9.8	11	8.7	9.8	9.8
PLT	463	549	684	346	436
MCV	84	80	80	86	95
UREA (mg/dl)	6	9	8		21
POTASSIUM (mmol/L)	3.9	5.9	4	3.7	3.8
SODIUM(mmol/L)	137	188	142	139	147
Chloride(mmol/L)	104	133	107	104	111
CREATININE	0.6	0.72		0.59	0.81

Table 1 showing blood results during different patient's visits

Treatment

The patient received 5 days course of Metronidazole and flucloxacillin to control the infection before commencing her on chemotherapy.

One month after initial presentation the patient was commenced on chemotherapy. Prior to commencing chemotherapy, patient's performance status was ECOG 1, had reasonable haematological counts and a good renal clearance. She was started on Paclitaxel at 135mg/m^2 day 1

and Cisplatin calculated at 70mg/m² day 2given three-weekly for four cycles were administered. Prior to her second cycle of treatment, the haemoglobin decreased to 8.7 and required transfusion of whole blood.

Assessment post-chemotherapy (four cycles) revealed remarkable tumour regression. The patient had near complete response (see figure 1 post-chemo).

The patient was assessed jointly with oncology team and a plastic surgeon and excision was agreed upon. This was discussed with the patient who consented for the procedure.

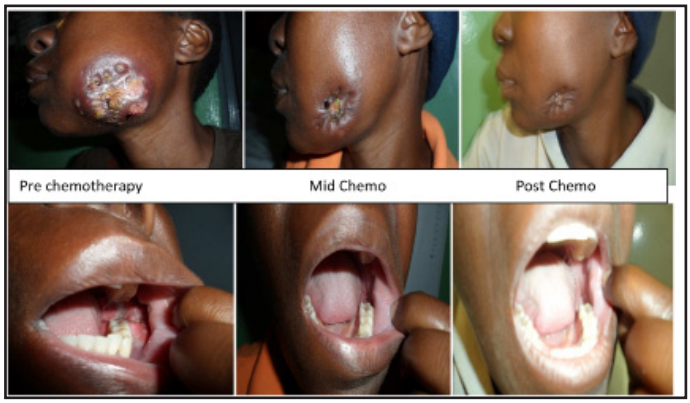

Figure 1 shows pictures taken before and after chemotherapy

The patient underwent radical surgery in order to improve her survival period. Therefore 1 cm margins of normal skin and bone were taken. The resulting through to through defect was reconstructed using a pectoralis major osteomyocutaneous flap containing the fifth rib to fill the bony defect. The rib was plated to the mandible.

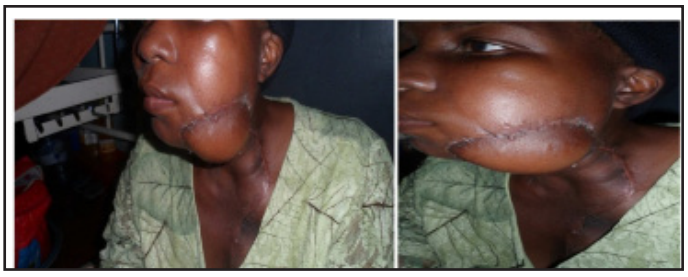

Figure 2 demonstrates post-resection with the osteomyocutaneous flap

The patient had an uneventful postoperative course. The flap took up successfully with no ensuring defect or septic complication (see Figure 2).

Further follow-up

Following successful resection the patient was being planned for external referral to a foreign country for radiotherapy but patient defaulted. The patient had a documented recurrence at 9 months after resection with a lesion on the cheek 3 x 3 cm plus a sternal recurrence on the incision line following a this disease free duration. This time she had a super-imposed infection that was cleared with anti-biotics. She was assessed in a combined surgery-oncology review and decision was to re-challenge her with chemotherapy (Cisplatin-5FU) but patient died only after a single cycle with neutropenic sepsis.

Discussion

Majority of the patients, close to 60% with head and neck cancer present with locally advanced disease which confers poor prognosis despite disease being highly curable in its early stages. This case represents one of such cases where the tumour was staged as T4 due to bone involvement. The history of an oral tumour being mistaken and treated as toothache is a commonly encountered experience in the developing world. This is likely to explain advanced stage diagnoses in some of the cases and in our patient in particular.

To improve outcomes of the disease, chemotherapy has been incorporated into a combined modality approach involving surgery or radiation. Induction chemotherapy with Cisplatin, 5- Fluorouracil and Taxotere (TPF) has become the standard regimen for patients with locally advanced head and neck cancer instead of Cisplatin and 5-Fluorouracil (PF) induction. The TAX randomised trials demonstrated significant 2 year patients' survival and better loco regional control of disease in the group that received TPF compared to the group that received PF8. However, our patient was treated with Paclitaxel and Cisplatin but managed to achieve near complete response as shown in Fig 1. Paclitaxel has shown marked activity in head and neck cancer with a single agent response of about 40%[9]. Concurrent induction chemotherapy with Paclitaxel and Cisplatin has been shown to achieve greater response in other series. In one prospective study looking at induction chemotherapy with Paclitaxel and Cisplatin to concurrent radiotherapy and weekly Paclitaxel in the treatment of loco-regionally advanced, stage IV (M0), head and neck squamous cell carcinoma demonstrated (n=43) 32 overall tumour responses, 74.4% (23 partial and 9 complete) after three cycles of induction chemotherapy[11]. Assessment of our patient after the four cycles revealed marked tumour regression making it operable in an initially inoperable tumour, suggesting that this approach may be investigated or employed for down-staging advanced tumours before surgery. This may be considered in desperate situations where radiotherapy is not possible, like in our setting to allow surgery in properly selected patients. This regimen however has significant toxicity hematological and non-hematological. Our patient had anaemia prior to her second cycle requiring transfusion of one unit of packed red cells but did not develop any alopecia, mucosal, neurological, nephrotoxic, or neutropenic complications. Our patient tolerated this protocol reasonably well.

Management of HIV infected patients with locally advanced head and neck cancers pose a challenge due to lack of evidence on how such patients ought to be treated. AIDS related immunodeficiency is well established risk factor for development of cancer and also present a unique challenge in patient's ability to tolerate cancer therapy.[2,5,12] The introduction of highly active antiretroviral therapy (HAART), allows most patients live with either mild or moderate degrees of immunodeficiency. In our case, the patient had been on HAART for five years and had a very good immunologic response with CD count of 560 cells/mm³ at the time of chemotherapy commencement. On completion of the four cycles of chemotherapy, the patient achieved significant tumour reduction to near complete response as seen on post-chemotherapy in figure 1 post-chemotherapy pictures. The patient still remained immuno-competent and fit to under-go surgery.

This case suggests that it is possible to down stage a locally advanced head and neck cancer using Paclitaxel-Cisplatin regimen in an HIV positive patient and convert such a stage to a resectable state. Though a combination of HIV infection and locally advanced cancer posed a big challenge in our case due to an irresistible tumour and lack of radiotherapy,

chemotherapy offered an opportunity to shrink the tumour mass remarkably hence offering this patient a possibility of a potentially curative surgical resection. In situations where the patient may not be operated, this may still offer excellent palliation by elimination of mass effect, pain, discharging sinuses and bleeding. This will at the same time improve quality of life.

The therapy offered though did not eventually cure this patient, it still offered a good quality of life for a year. The proposed post-operative radiotherapy in this patient could have prevented the recurrence and prolonged the survival period.

This case suggests benefit of neoadjuvant chemotherapy in head and neck cancer in HIV infected individuals.

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