Neoadjuvant chemotherapy in Albinos with locally advanced skin cancer at a Blantyre Hospital: - Case Series

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Abstract

Albinism in Africa remains a public health concern with increasing numbers of advanced skin cancer in this population at presentation. There are challenges with availability of Radiotherapy (RT) units in Africa which is an important modality for controlling loco-regional disease alone or in combination with surgery. Proposed chemotherapy regimens have not been well validated through Randomized Controlled Trials thus posing difficulties for standard of care for units that do not have access to functional RT facilities. Malawi is one such country without radiotherapy.

Case summary

Seven patients with locally advanced skin cancer were seen in the adult oncology unit at Queen Elizabeth Central Hospital in Blantyre (QECH), Malawi between 2010 and 2013. QECH is one of the teaching hospitals in the country. All were subjected to neo-adjuvant chemotherapy. The primary treatment aim was cyto-reduction followed by surgery whilst the secondary outcome was general symptom control. Three patients achieved complete responses of which two underwent resection and a pectoralis major myocutaneous flap. One had a near complete response and three showed partial responses.

Conclusion

Neo-adjuvant chemotherapy may be a possible.

Introduction

Albinism is an inherited disorder characterised by a reduced or lack of melanin; a photo protective chemical responsible for pigmentation in the body. Two major forms are described; Oculocutaneous (OCA) and Ocular albinism[1]. This makes albinos prone to the effects of ultraviolet radiation[2,3] such as skin cancer of which squamous cell carcinoma (SCC) is the commonest histology[4,5,6].

There is lack of data on the standard management of advanced skin cancer cases in albinos especially in limited resource settings. There are challenges with limited Radiotherapy (RT) units in developing regions like Africa generally, a modality which has been shown to be important for controlling loco-regional disease[7]. Whereas the European standard for radiotherapy services is 250 000 people per machine, the International Atomic Energy Association (IAEA) through its programme of action for cancer therapy (PACT) reports that the majority of sub-Saharan African countries range from no machines to very few that serve approximately 10 million people per machine[8].

Malawi is one such country with no functional radiotherapy facility hence chemotherapy forms the mainstay of treatment in advanced non-resectable skin cancers in albinos. The waiting time for a government funded external radiotherapy referral is a minimum of six months. Considering this and advanced disease at presentation, chemotherapy in these cases was administered to down-stage the disease for resection or symptom control as surgery upfront was not possible. However, the proposed chemotherapy regimens have not been well validated through Randomized Controlled Trials (RCTs).

It is with this background that we present a case series to report feasibility of using chemotherapy in albinos and demonstrating their responses to neo-adjuvant chemotherapy.

Patient Summaries*

1: A 23 year old female had wide local excision and left superficial parotidectomy done for SCC lesions on her forehead and left cheek respectively. 3 months later she presented with a recurrence on the left cheek. She was started on Cisplatin and 5-Fluorouracil (PF) to which there was complete clinical response. Following this; she refused further surgery and presented 7 months later with another recurrence (6 × 6.5 cm) at the same site. She was then rechallenged with Adriamycin and Cisplatin (AP) with complete tumour regression. A total of 4 cycles were administered but she never returned for further treatment or follow up.

2: A 35 year old male presented with a left pre-auricular 4 × 5 cm ulcer. He was started on PF. There was complete clinical response to 3 cycles of chemotherapy which was followed by Pinnectomy and a Pectoralis major myocutaneous flap. Further pathological analysis of the surgical specimen was reported as a Basal Cell Carcinoma with squamous differentiation. He was recommended for radiotherapy but never received. However, he has remained disease free for over 12 months.

3: A 19 year old boy presented with a 5 year history of a left parietal ulcer. An excision biopsy was reported as invasive SCC. He was started on AP. There was a near complete response following 4 cycles. Subsequently there has been poor treatment compliance and multiple treatment interruptions which resulted in progressive disease.

4: A 50 year old man presented with a left preauricular mass for 7 months that was associated with pain and hearing difficulties ipsilaterally. The lesion was 10 × 8 cm and a tru-cut biopsy confirmed an invasive poorly differentiated SCC. He was started on AP. Partial response was noted after 6 cycles.

5: A 34 year old man presented with a 3 months history of recurrent left cheek swelling. He had initially undergone 2 wide local excisions at the same site and histology confirmed an invasive SCC. The tumour was 10 × 9 cm and he received 3 cycles of AP. Partial response was noted. He presented with progressive disease due to poor treatment compliance. AF was given as re-challenge but was also not completed.

6: A 38 year old man presented with locally advanced SCC infiltrating into the maxillary antrum and buccal mucosal. There was partial response to 5 cycles of PF but did not turn-up for further treatment. He presented with progressive disease almost a year later.

7: A 30 year old female with advanced SCC of the right cheek;

she was started on Carboplatin and Adriamycin. There was complete response after 6 cycles followed by resection and a myocutaneous flap. 9 months later there was a recurrence on a different site (right shoulder area). She was rechallenged with PF but did not return to complete her treatment. This case was reported prior by Mapurisa and Masamba (2011) [9] and formed the basis for this series.

*Summary of patient details in Table 1.

Treatment Details and Outcomes

Study population

Seven cases are here reported, two females and 5 males. The median age was 32 years (range 19 to 50 years) and all the lesions were in the head and neck region; specifically the cheek. The average symptom duration was 20 months. Two patients presented with recurrent disease within 6 months following prior surgical excision (case 2.1 and 2.5). All were chemotherapy-naive at presentation.

Pre-Chemotherapy Work-up

Pre-chemotherapy assessment involved history taking, clinical examination and blood tests which included a full blood count, liver and renal function tests. A baseline chest radiograph and Liver ultrasound scan were done to rule out distant metastases. The desirable parameters for chemotherapy were a performance status as per the Eastern Cooperative Oncology Group (ECOG) of ≤ 2, a haemoglobin count of ≥ 8 g/dl with an absolute white cell count of ≥ 2000/mm3 on full blood count, and a glomerular filtration rate (GFR) of ≥ 60 ml/min based on the Cockroft-Gault formula.

3.3: Chemotherapy Regimen and Administration

The chemotherapy regimen included a platinum; either Cisplatin given at 60-70 mg/m2 on D1 if GFR was $\geq$ 60ml/min, or Carboplatin. The Carboplatin was calculated using Calvert's formula at area under the time-concentration curve 6 (AUC 6). The platinum was given with either 5-Fluorouracil (5FU) at 750-1000 mg/m2 D1to D4 or Adriamycin at 60 mg/m2 D1 only cycled at 21 days. Only 1 patient received Adriamycin with 5FU (case 2.5). The average cycles given were 6.4.

Treatment Goals and Outcome

The primary treatment aim was cyto-reduction followed by surgery whilst the secondary outcome was general symptom control. Tumour response was evaluated using the RECIST criteria (Appendix 2). [10] Of the three patients who showed complete tumour response; two underwent surgical excision, Pinnectomy and a Pectoralis major myocutaneous flap but one refused surgery. One patient showed a near complete response. Of the three patients who showed partial responses two of them did not complete their treatment and were lost to follow up.

Discussion

As already demonstrated from several studies, squamous cell carcinoma (SCC) is the commonest histology noted in the African albino. Management of skin cancers in this population has been compounded by several factors especially within Africa. For example, in this series the time to presentation ranged from 3 to 60 months, emphasizing extreme delay in presentations. As much as this was mainly due to patient related factors, failure of the health system to pick up early stages of the disease and delays in the referral system may also have contributed. This has also been reported and was thought to be due to poor disease understanding (mainly by the patients) and financial constraints[2,11]. As a result many patients initially present with advanced disease.

The common site for the lesions as also previously observed was the head and neck region. This is thought to be due to increased sun exposure in this area relative to other sites. Malawi experiences a tropical climate with more than 75% of the population based in the rural area where they rely on subsistence farming. This means two-thirds of the day is spent outdoors with increasing sun exposure. It is noteworthy that there were more males than females which may reflect gender roles especially in the rural setting and may explain in part the finding above.

As part of preventive and supportive care of persons living with albinism, there is an albino clinic at our hospital that works together with the Albino society to manage different skin related conditions in this population. In addition, they conduct awareness campaigns annually on behavioural change and photo-protective measures where they distribute such items as sunscreen and hats. The hope therefore is that as these programs are sustained and built further, the incidence of skin malignancies in this population should decrease in the near future; an approach which may also prove beneficial for various cancers and other non-communicable diseases.

Of note is that for a long time, the treatment modalities commonly employed for either radical or palliative intents in such patients have been surgery and or radiotherapy with variable responses[4,7,11]. However, there has been no concrete evidence shown for the role of chemotherapy especially for settings without functional RT facilities. Even though the small total number of patients offers some limitation in our series, the down-staging that occurred with neoadjuvant chemotherapy suggests there could be benefit in this line of treatment.

Although in many of the cases there was poor compliance to either treatment, follow up or both; there is evidence that chemotherapy seems to have been delivered safely in all the cases with no significant toxicities recorded. We believe this may partly be attributed to the symptomatic relief achieved once chemotherapy is initiated such that there is complacency in seeking further treatment evidenced by four patients who subsequently presented with either recurrence or progressive disease (case 1, 3, 5 and 6). However, other reasons may be financial constraints and lack of strong social support. This reflects the need to extensively counsel our patient population on disease understanding and treatment implications regardless of response to treatment such as regression of lesions. In addition, it underscores the importance of engaging the civil society to contribute towards social support for patients undergoing treatment with the intent of minimizing treatment disruptions due to financial constraints.

Conclusion

This series is hypothesis generating. Neo-adjuvant chemotherapy seems to be a safe option in locally advanced skin cancer in albinos. However, to determine a true measure of effect of this approach it requires validation in a larger trial setting. This work also highlights the pressing requirement for radiotherapy and all areas relevant to cancer care for optimal management of this group of patients in the developing countries.

6. Recommendation

We recommend multi-centre trials to validate the role of neo-adjuvant chemotherapy in albinos presenting with advanced skin cancer in low in-come regions like sub-Saharan Africa with limited access to radiotherapy services.

7. Acknowledgement

To the entire oncology nursing team, data clerks and clinicians at our hospital who labour tirelessly to ensure optimal delivery of care to all our patients and the development of cancer services in the country.

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Table 1: Patient summaries, treatment and response

Case No.	Age in yrs/ Sex	Site	Duration of Symptoms (Months)	Size in cm	Chemo-Regimen	Number Of Cycles	Response*
1	23/ F	L Cheek (Recurrent)	7	6 x 6.5	PF AP	6 4	Complete
2	35/ M	L Ear	24	4 x 5	PF	3	Complete
3	19/ M	L Ear	60	8 x 10	A P	5 3	Complete
4	50/ M	L Cheek	7	10 x 8	AP	4	Partial
5	34/ M	L Cheek (Recurrent)	3	10 x 9	AP AF	3 3	Partial
6	38/ M	R Cheek		4 x 3	PF	5	Partial
7	30/F	R Cheek		-	AP PF	6 3	Complete

*KEY: *RECIST criteria, P: Cisplatin or Carboplatin, F: 5-Fluorouracil, A: Adriamycin*