Case Report

Targeted Chlorine e6 based Photodynamic Therapy for Nasal Cancer—A single case report

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Summary

Objective: To improve local tumour control by using chlorine e6 based photodynamic therapy (PDT) as part of a multimodal approach in a patient with locally advanced nasal carcinoma.

Case report: In this case study we report the treatment outcome of using photodynamic diagnosis (PDD) and chlorine e6 based PDT as part of adjuvant therapy in a patient with locally advanced nasal carcinoma. The patient had previously refused surgical ablation of the nose for cosmetic and psychological reasons. Chlorin E6 was given IV at a dose of 1 mg/sqm BSA three hours before PDT procedure. PDD was performed with blue light (405 nm) prior to PDT with red light laser (670 nm). PDT effect is based on a defined local photodiagnostic measurements of chlorine E6. The multi-modal approach resulted in local tumor control with an acceptable cosmetic outcome.

Conclusion: The case study illustrates the successful use of adjuvant PDT in combination with electrotherapy in a patient with nasal carcinoma. Exact photodiagnostic measurement is necessary to improve the anti-cancer effect of PDT.

Introduction

Photodynamic therapy (PDT) is a minimally invasive therapeutic procedure that can exert a selective cytotoxic activity toward malignant cells. The procedure is clinically approved and involves administration of a photosensitizing agent followed by irradiation at a wavelength corresponding to an absorbance band of the sensitizer. In the presence of oxygen and with the support of additional oxygen a series of free radicals lead to direct tumor cell death, damage to the microvasculature, and induction of a local inflammatory reaction [1].

Foscan based photodynamic therapy was approved in 2004. It is reserved for patients that failed prior therapies and were unsuitable for radiotherapy, surgery or systemic chemotherapy. Endocavitary and interstitial placement are possible application forms of red laser [2]. PDT seems to have similarities to brachytherapy with regards the ability for interstitial use.

Fotolon® is a purified chlorine e6 formulation that accumulates in tumor cells [3]. There are some reports showing efficacy in head neck cancer patients. It is not used in the primary treatment of ENT cancer until today [4,5].

This case report demonstrates PDT as part of an alternative treatment approach and report about necessary photodynamic diagnostics in order to improve and specify anticancer-effects in the head and neck region.
Case Report

D.S. (male, 49 years) suffered from squamous cell cancer of the nose since 2 years when he was seen by ENT surgeons in March 2016. They recommended a total ablation of the nose and adjunctive radiotherapy because of the findings demonstrated in figure 1a,b. The full case history is summarized in Table 1. In detail we would like to describe the steps of our last intervention. This PDT session was done to treat the last remaining residual tumor figure 2a Fotolon® (Apo Care Pharma, Bielefeld, Germany) was administered intravenously (IV) at a dose of 1 mg/kg body weight three hours before the photodynamic procedure. The following steps were then followed:

- Blue light (405 nm wave length) application for optical control of Fotolon® accumulation of the tumor figure 2b.
- Touching spectrometry by fiber on reference point, and defined and documented points of the tumor figure 2c.
- Red light (670 nm wave length) application at the point of highest Fotolon® accumulation via same interstitial bare fibre.
- 2nd blue light application to get optical control of Fotolon® concentration.

Our observations during the photodynamic diagnostic (PDD) session were as follows:

- Optical dosimetry has shown accumulation of photosensitizing substance in the whole region of septum and the neighbor areas of the nose (skin, ethmoid cells).

Figure 1a: MRI scan showing an infiltrating cancer of nose. Recommended therapy ablatio nasi.

Figure 1b: MRI scan showing an infiltrating cancer of nose. Recommended therapy ablatio nasi.
Table 1: Case report D.S., 49 years, male, nose cancer.

<table>
<thead>
<tr>
<th>Month</th>
<th>Event Description</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>March 2016</td>
<td>Total ablation of the nose was recommended</td>
<td>Suicidal thoughts</td>
</tr>
<tr>
<td>April 2016</td>
<td>2 cycles PDT with Fotolon® (endocavitary)</td>
<td>Ineffective, leaving the therapist</td>
</tr>
<tr>
<td>July 2016</td>
<td>PDT 2 cycles with electrotherapy (interstitial)</td>
<td>Re-opening, residual tumor</td>
</tr>
<tr>
<td>August 2016</td>
<td>Neck Dissection</td>
<td>N1-status, locoregional control</td>
</tr>
<tr>
<td>September 2016</td>
<td>Irradiation, 66 Gy</td>
<td>Local partial remission</td>
</tr>
<tr>
<td>November 2016</td>
<td>PDT 1 cycle (endocavitary)</td>
<td>No change</td>
</tr>
<tr>
<td>January 2017</td>
<td>PDT 1 cycle (interstitial)</td>
<td>No change</td>
</tr>
<tr>
<td>February 2017</td>
<td>PDT 1 cycle (interstitial)</td>
<td>No change</td>
</tr>
<tr>
<td>March 2017</td>
<td>Lateral rhinotomy, 1 PDT cycle (interstitial&amp;endocavitary)</td>
<td>Tumor reduction, fistula</td>
</tr>
<tr>
<td>April 2017</td>
<td>PDT 1 cycle (endocavitary)</td>
<td>No change</td>
</tr>
<tr>
<td>May 2017</td>
<td>PDT 1 cycle (endocavitary)</td>
<td>No change</td>
</tr>
<tr>
<td>June 2017</td>
<td>PDT 1 cycle + electrotherapy (interstitial)</td>
<td>Tumor mass reduction</td>
</tr>
<tr>
<td>June 2017*</td>
<td>PDT 1 cycle (interstitial)</td>
<td>In residual Fotolon® accumulation area only</td>
</tr>
<tr>
<td>July 2017</td>
<td>Device forming</td>
<td>Partial epithesis for closing the fistula</td>
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*see text.

- Touching spectrometry registered normal Fotolon® concentrations in normal skin as reference figure 3a. Surrounding regions have shown minimal levels of accumulation corresponding to bacterial super-infections figure 3b. Fotolon® accumulation was seen in the central point of septum on the border between bone and cartilage figure 3c.

- The postoperative blue light application has shown a reduction of Fotolon® accumulation after red laser application in position III figure 4b.
PDT procedure: According the measurement we have placed the laser fibre into the central position III figure 4a. The red light application (photodynamic therapy - PDT) was given after the patient has received a local anesthesia with Lidocaine 2%. The patient received Cox-2-inhibitors and antibiotics after the procedure. After 5 days we observed a demarked region in the former tumor-involved septal mucosa figure 4c.

Discussion

Rigual and colleagues [6] have studied an intra-operatively PDT-integration concept.
in recurrent diseases in 2013. Adjuvant intraoperative photodynamic treatment was an alternative option to re-irradiation in selected cases. The effect of radiotherapy are often limited in nose cancer cases. In this case report we observed a partial remission after radiotherapy. Initial cycles of PDT were also not able to reduce the tumor size adequately. Our adapted therapy concept with open surgery, photodynamic therapy, and additional electrotherapy has resulted in a favorable local tumour response.

Fotolon® accumulates in tumor tissue only. Optical dosimetry (blue light) has shown more accumulation as punctual measurements could register local substance
concentration. As we know from the dermatological literature [7], any bacterial superinfection will cause this low-level accumulation, which is typical for the mucosal area of the head neck region. False positive measurements have to be avoided. More defined and localized measurements are necessary to focus the work the active tumor tissue. We have shown in this case that touching the mucosal surface with a bare fiber and performing localized measurements offers reproducible results. So, we were able to focus the laser application on the central point of interest. As more specific the placement is as higher energies could be given. Furthermore it is possible to protect normal tissue by the reduction of PDT application volume.

As mentioned, PDT is normally reserved for patients without surgical or radio-oncologic treatment options. We know such integration models in bronchial cancer. Freitag et al. [8], have suggested the early PDT integration in detail. They argued that PDT is only able to work if the tumor volume is not too extensive. Interestingly, they had combined PDT with high dose rate brachytherapy (HDR). In head neck cancer cases it should be combined with other procedures of tumor reduction, for example surgery or electrotherapy. Our patient benefit from surgery plus PDT as well as electrotherapy plus PDT again. The low residual tumor masses were identified and treated by PDT at the end.

ENT surgeons are able to place the PDT fiber anywhere via interstitial application. Large vessels are the only limiting factors. If they are involved by tumor, PDT should not be performed. Former trials have shown carotid artery ruptures as major complications in such situations. Indication and limitation could be transferred from other interstitial treatment approaches like brachytherapy techniques [9].

References
