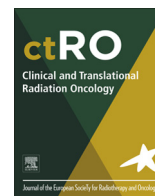




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Case Report

Simultaneous integrated prophylactic cranial irradiation in sino-nasal cancer

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ABSTRACT

Therapy for small cell cancer and high grade neuroendocrine tumours of the paranasal sinuses is extrapolated from the treatment of small cell lung cancer and paranasal cancer of different histologies. Prophylactic cranial irradiation has proven survival benefit in small cell lung cancer.

Two patients with aggressive cancer of the paranasal sinuses received radiotherapy with simultaneous integrated prophylactic brain irradiation, using two sequential plans. Chemotherapy was given before, during and after radiotherapy.

None of the patients had intracranial recurrence. One patient experienced severe, but transient encephalitis-like symptoms that could only be attributed to radiotherapy. No long term side effects in the CNS were observed.

The treatment was feasible, but with possible severe, but transient side effects. It should be considered in cases with head and neck cancer, with a high risk of intracerebral metastasis, as well as a significant overlap between the primary irradiated volume and the brain.

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Introduction

Sinonasal cancers are infrequent cancers with a grave prognosis. The cancers pose great challenges for both the surgical and radio-therapeutic management, due to the abundance of adjacent organs at risk. Small cell and high grade neuroendocrine cancer of the sinonasal area are rare entities [1] with an even poorer prognosis [2], including a high risk of intracranial expansion as well as haematogenous metastases to the brain. For small cell lung cancer (SCLC) the addition of prophylactic cranial irradiation (PCI) to the treatment leads to both a significant risk reduction of brain metastases and prolonged survival [3]. The risk of haematogenous metastases from small cell head and neck cancer is lower than that of SCLC, yet still significant, and PCI has been recommended for selected cases of small cell head and neck cancer [2,4–7]. Adding PCI after radiotherapy for sinonasal cancer is sub-optimal from a dosimetric point of view, as some areas of the brain already received a radiation dose from the primary tumour irradiation, that

may cause late side effects, and probably has a low effect on tumour cells, as the dose per fraction is very low. Furthermore, studies on SCLC indicates, that PCI given during chemotherapy, has superior effect compared to delayed PCI [8]. In two cases we chose to use an integrated PCI during primary radiotherapy to the tumour areas. A description of the cases is given below with emphasis on the technique and results of the PCI.

Case 1

Male, 56 years, no significant comorbidity, but well controlled type II diabetes and hypertension. Two months prior to diagnosis he noticed a slight facial pain and nasal discharge.

MRI and FDG-PET-CT showed a primary tumour of the left maxillary sinus with extension to anterior and posterior wall, gingiva and to the ipsilateral nasal cavity, ethmoid sinuses, orbital content and retromaxillary space. There were regional metastases to parapharyngeal-, retrostyloid- as well as level 1B and 2 lymph nodes. No distant metastasis, ie. T4aN2cM0

Pathology: The tumour was composed of irregular sheets of relatively small, rounded cells with prominent, hyperchromatic nuclei. Immunohistochemical analysis for CD45, S-100 and desmin

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were negative. Positive reactions were seen for cytokeratin (AE1/AE3 and KL-1), p16, CD56, and the neuroendocrine markers chromogranin A and synaptophysin. The tumour was negative for CK5/6 and p63. Proliferation index using Ki-67, was high (70%). The tumour was diagnosed as a small cell neuroendocrine carcinoma.

Due to the advanced stage of the tumour nodes the patient was inoperable. Treatment with curative intent was initiated with chemotherapy: cisplatin 75 mg/m² i.v. day one and etoposide 120 mg/m² i.v. day one to three every three weeks for a total of four series. Three weeks after initiation, he had grade 3 neutropenia (CTCAE 4.0) and the treatment was postponed one week. He subsequently received prophylactic G-CSF and received the remaining chemotherapy as planned without neutropenia. Ten days after initiation of chemotherapy he began radiotherapy.

The target was defined as gross tumour with a 5 mm margin for high dose clinical target given 66 Gy in 33 fractions. A further margin of 5 mm plus the remaining entire involved sinuses, was added for a high risk volume, treated with 60 Gy. No further elective volumes were included (Fig. 1). In addition, the entire brain was treated to 25.2 Gy for the last 14 fractions, as it was estimated, that at least 1.8 Gy per fraction was required to achieve a biological effect. No correction was made for fraction size to reach the biologic effect of 25 Gy in 10 fractions, which is standard at our institution for PCI with SCLC.

For the first part of the treatment, 5 planar and 5 non-coplanar fields were used in order to minimize the dose to the brain. For the last part, 6 coplanar and 2 non-coplanar fields were chosen (Fig. 2A and B). As the left part of the visual pathways was partly included in the target volumes, constraints for the organs at risk could not be met. Because of the non-coplanar fields the bilateral parotid glands received a higher dose than typically allowed. Fixed beam angles were chosen over arcs, due to their superior dose distribution in the low dose volume, ie. the majority of the brain volume.

The PCI was planned for the last fractions in order to estimate side effects and response for the first part of radiotherapy and chemotherapy.

One month after initiation of radiotherapy, the patient was admitted 4 days due to dehydration, weight loss, pneumonia, oral candidiasis, mucositis and pain. He was treated with i.v. antibiotic, i.v. fluid and a nasogastric tube.

At the fourth series of chemotherapy, 14 days after cessation of radiotherapy, he had severe fatigue, but no neurological symptoms, still dependent on the nasogastric tube for sufficient nutrition, but the mucositis were healing as expected.

Three weeks later he was admitted to a local hospital with fever and increasing fatigue. No neurological symptoms, no neutropenia, low c-reactive protein. He was treated with oral antibiotics and discharged the same day. At home he experienced continuous fever with temperatures reaching to 39 °C.

Eleven days later he returned to the department of oncology for an acute evaluation due to intermittent fever 38–39 °C, insomnia, intense dreams, headache and neck pain. Objectively his general condition had deteriorated and he was confused and dehydrated. He had no focal neurological symptoms objective abnormalities. MRI of the head and neck and CT of the thorax and abdomen showed regression of the tumour, with no new tumour manifestations. C-reactive protein was continuously low. Cerebrospinal fluid contained increased mononuclear cells, elevated protein and normal level of glucose. The patient was rehydrated and received antibacterial and antiviral treatment as well as high dose steroids on the suspicion of meningitis. No positive microbiology or serology were present. ECG showed unspecific signs of encephalopathy but not consistent with herpetic encephalitis, and CSF-autoimmune encephalitis antibodies were all negative. The patient was discharged after 5 days and continued high dose steroids. The neurological symptoms slowly regressed over months, with no lasting deficits.

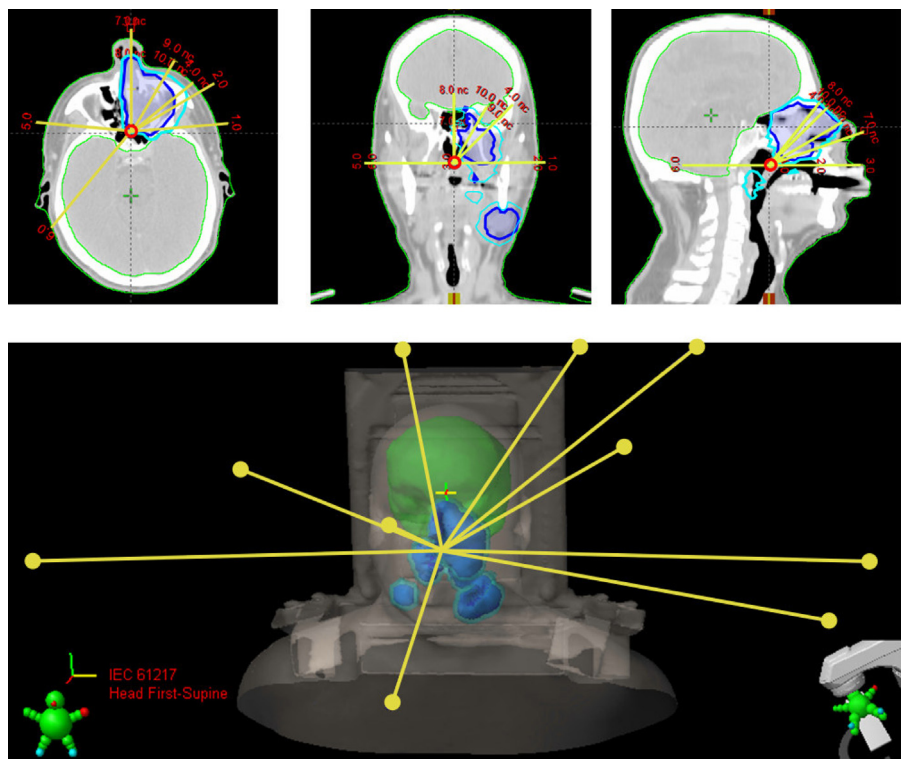


Fig. 1. Target and beam angle selection for part 1 of radiotherapy. Case 1. CTV1 (66 Gy): dark blue and CTV2 (60 Gy): light blue. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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