

CASE REPORT

Sino-nasal mucosal malignant melanoma

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SUMMARY

A 49-year-old man with a history of left nasal discharge and nasal cavity blockage for 5 months was diagnosed with sino-nasal mucosal malignant melanoma on nasal biopsy. On CT scan, the tumour involved the nasal cavity, left maxillary sinus, ethmoid sinus and medial left orbit. The tumour was grossly excised and adjuvant radiation therapy was offered. The patient was planned for an Intensity Modulated Radiotherapy technique to keep tolerance doses of organs at risk within normal limits and at same time deliver the intended dose of radiation to the tumour site, using 66 Gy in 33 fractions. Owing to the anatomical complexity of the sino-nasal region, precision radiotherapy (RT) is mandatory to optimally irradiate the tumour area while sparing critical surrounding normal structures from late toxicity of RT. Established dose constraints for at-risk organs can only be accomplished through this novel technique of RT. However, despite advances in techniques, current treatment modalities have not significantly made an impact on survival of these patients.

BACKGROUND

Mucosal malignant melanoma (MM) is a rare malignancy. It comprises about 1% of all melanomas.^{1,2} The sino-nasal region of the head and neck is the most common site for this rare tumour.¹ MM are managed with an aggressive surgical approach with the intention of complete excision of the tumour followed by adjuvant radiotherapy. Prognosis, however, is generally poor even with this aggressive treatment strategy. The literature has reported survival rates of under 5 years after combined modality approach.^{2,3} The sino-nasal region is a difficult site for radical doses of radiation. Intensity modulated radiotherapy (IMRT), a refined form of three-dimensional conformal radiotherapy (3DCRT), is a preferred treatment technique to achieve optimal therapeutic ratio at this site.⁴⁻⁷ We report a case of MM of the sino-nasal tract in a 49-year-old man who had been irradiated up to 66 Gy postsurgery by IMRT technique at our institute. It was possible for us to deliver this dose, while keeping normal tissue constraints, by employing the IMRT technique. To the best of our knowledge, this is the first case report of sino-nasal MM from our region, where IMRT is used to deliver radical doses of adjuvant RT.

CASE PRESENTATION

A 49-year-old healthy married man, with no known comorbidities, a cook by profession, presented with a history of intermittent bleeding from the left nasal cavity with ipsilateral nasal blockage. His symptoms started 5 months earlier when he

reported of continuous nasal discharge that was non-purulent and watery. There were no associated symptoms such as bleeding, pain, swelling and visual disturbance. He consulted many doctors who prescribed various medicines but did not get relief. His symptoms increased progressively to the extent that he started bleeding from the left nasal cavity 2 months prior to presenting. There was no associated pain, visual disturbances or other significant ear or throat problems. The patient finally consulted the ear, nose and throat (ENT) clinic at our institute where, on local examination, a mass was found in the lateral wall of the left nostril, which was black in colour and bled on touch. There was no palpable lymphadenopathy clinically. His systemic examination was unremarkable. His medical history was not significant and he was well before these symptoms started. Considering the presenting symptoms and findings, it was decided to perform a biopsy of the nasal mass and investigate further.

INVESTIGATIONS

The biopsy of the tumour was taken by an ENT surgeon and turned out to be mucosal MM, as the tumour cells showed positivity for HMB-45 and melan-A, while being negative for cytokeratin CAM 5.2 and cytokeratin 5/6 immunohistochemically (figures 1–3).

The patient was investigated with a CT scan of the para nasal sinuses, which revealed a soft tissue density lesion in the left nasal cavity that was extending into the left maxillary and left ethmoid sinuses (figure 4). The mass was also causing dehiscence of the floor of the sphenoid sinus, as well as invading the medial wall of the left orbit through the lamina papyracea. Further staging work up, which included CT scan of the chest and abdomen, was carried out for distant metastasis; it was unremarkable.

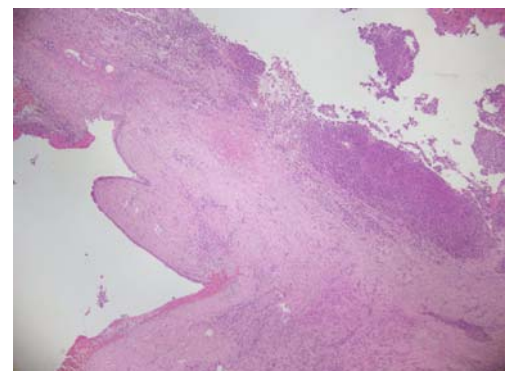


Figure 1 Mucosal melanoma—H&E stain slide with magnification $\times 40$.



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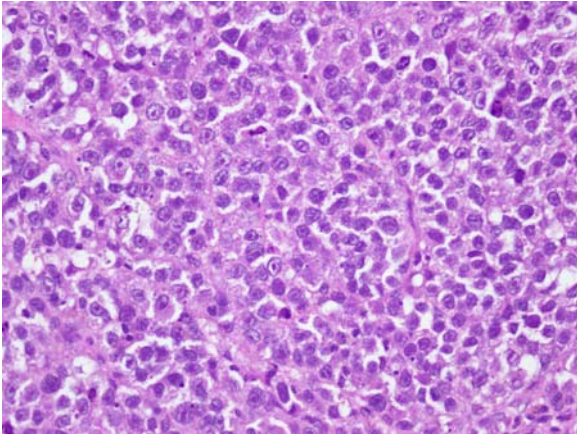


Figure 2 Mucosal melanoma—H&E stain slide with magnification $\times 400$.

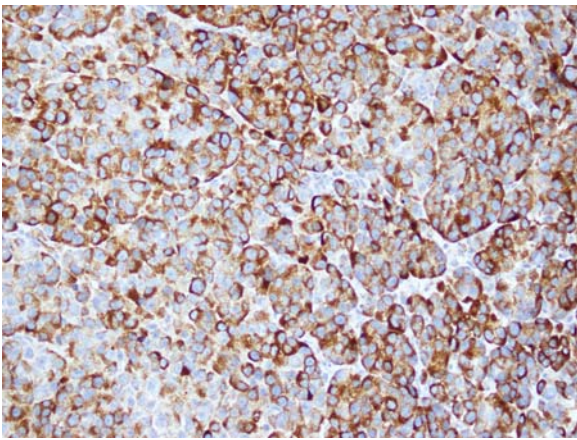


Figure 3 Histopathology slide—tumour cells showing positivity for HMB-45 immunostain.

TREATMENT

After all work up was complete, the patient underwent a left medial maxillectomy and left lateral rhinotomy with the intention to remove the tumour completely. The ENT surgical team removed the maximum tumour bulk in piecemeal from all the involved sites of the sino-nasal region. The histopathology of the surgical specimen was consistent with malignant melanoma.

This case was then discussed in a head and neck multidisciplinary tumour board meeting for further management strategy. Considering the extent of the tumour, it was staged as

T4aN0M0 as per the 2013 AJCC Staging System for Mucosal Melanomas of the Head and Neck. It was decided that adjuvant radiotherapy would be beneficial for this patient.

He was planned for a total dose of 66 Gy of RT in 33 fractions, at a daily dose fraction of 2 Gy over 6.5 weeks using the IMRT technique. With the help of inverse planning of the IMRT technique, we were able to keep the tolerance doses of organs at risk such as the optic chiasm, optic nerves, retina, pituitary and parotids within normal limits and at the same time deliver the intended dose of radiation to the tumour site (figures 5–9). The patient received treatment according to plan and tolerated it well. He was reviewed weekly during the treatment by our team. There were no significant side effects observed except moderate skin reactions on the irradiated skin and occasional left nasal blockage at the end of treatment. He was advised to follow-up after 4 weeks.

OUTCOME AND FOLLOW-UP

The patient was reviewed after 4 weeks. Skin reactions almost resolved, only mild erythema of irradiated skin was seen. The patient was doing well. He was advised to have a CT scan performed after 4 weeks to check on the treatment response.

DISCUSSION

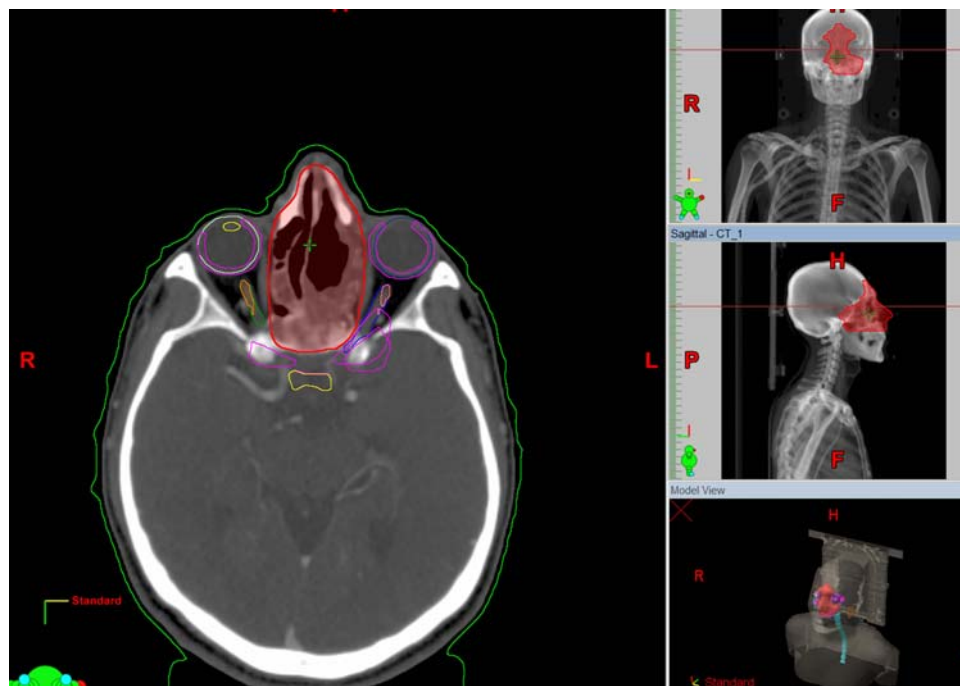
MM of the head and neck remains a rare disease entity with an aggressive natural history and poor long-term prognosis.^{1 2} It is more common in the older age group and the primary tumour arises mostly from the nasal cavity or paranasal sinuses. It usually presents as a localised disease at the time of diagnosis. This disease has a propensity to recur locally and to develop distant metastases. The prognosis is generally poor but comparatively better in the younger age group. Most patients with head and neck MMs will not be expected to survive beyond 5 years.⁸ Local recurrences have been reported to occur commonly in most series, ranging from 40% to 79.4%. Distant metastases are also common, with reports ranging from 19.2% to 64.3%. Manolidis *et al*⁹ noted a 51.5% rate of distant failure in a pooled analysis from 332 patients.

It is also evident that the current treatment modalities have not significantly made an impact on the survival of these patients. However, the goal of treatment should attempt to cure with a treatment modality that preserves a reasonably good quality of life. The established therapeutic approach is attempt at complete removal of the tumour with clear margins of resection followed by adjuvant radiotherapy. Despite advances in surgical techniques and methods of adjuvant therapy, the 5-year survival rate of patients with nasal melanoma is very low.

Figure 4 Presurgery CT scan showing tumour extent in axial and coronal views. The tumour is involving the nasal cavity, right maxillary sinus, ethmoid sinus, medial wall of left orbit and frontal sinus.



Figure 5 Contouring of planning target volume (PTV), optic chiasm, optic nerves, retina and lenses on planning CT scan. Complexity of PTV evident in the planning system in three-dimensional images.



Radical surgical resection of sino-nasal MMs, however, is limited by anatomic and functional considerations. Adjuvant RT has to be delivered with modern radiation techniques such as IMRT for precision, conformity and sparing of normal organs surrounding this complex site.

Memorial Sloan-Kettering Cancer Centre reported their case series of 27 patients of head and neck mucosal melanomas treated with adjuvant RT. The sino-nasal region comprised of 85% of their cases. The majority of the patients were irradiated using the IMRT technique. Their 3-year and 5-year estimates of local progression-free survival, and overall survival were 47% and 35%; and 40% and 33%, respectively. There were no late complications seen related to the optic structures.¹⁰

Combs *et al*¹¹ reported that IMRT showed good results with respect to local control as well as survival, while treatment-related toxicities were minimised. After IMRT, local progression-free survival was 71.4% at 1 year and 75% at 3 years.

Gilligan *et al* reported, in a retrospective survey, 28 cases of malignant MM of the nasal cavity and para nasal sinuses that were treated by definitive radiotherapy. Initial complete regression was observed in 22 out of 28 cases (79%). In their study, absolute local control by radiotherapy alone was achieved in 17 out of 28 cases (61%) but follow-up was limited in many cases by early death due to metastatic disease; actuarial local disease-free survival was 49% at 3 years. The approach of radical radiotherapy for melanoma of this site could be justified on the basis of the local control achieved, low treatment morbidity in patients who are typically elderly and the propensity to disseminate disease. Doses of radiotherapy required to achieve local control need to be radical.¹²

Wide surgical resection has become the mainstay of initial therapy when feasible. Owing to the location and extent of these tumours in the head and neck region, a wide surgical resection is sometimes not possible. For these reasons, RT has

Figure 6 Dose wrapping with intensity modulated radiotherapy (IMRT), conforming tightly to the planning target volume (PTV), while sparing the retina.

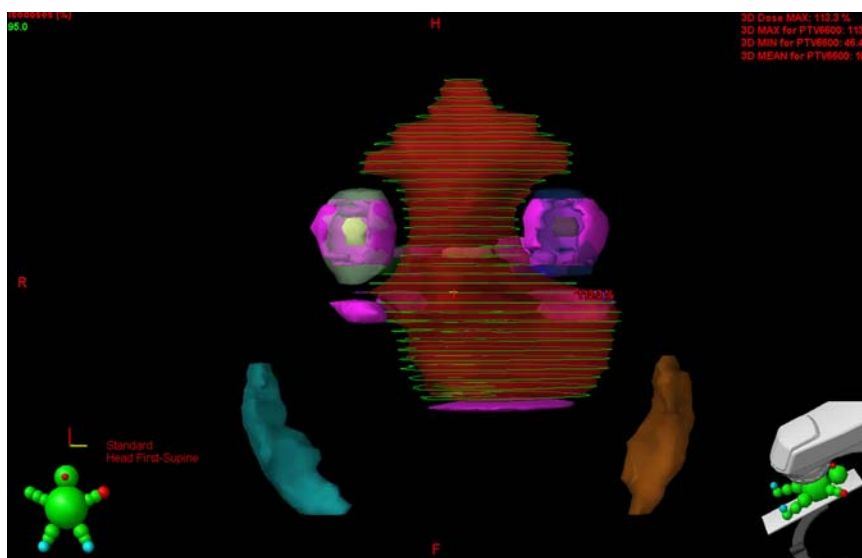


Figure 7 Multiple non-coplanar intensity modulated radiotherapy (IMRT) beams showing entry and exit routes. Sparing of surrounding organs was made possible through this setup.

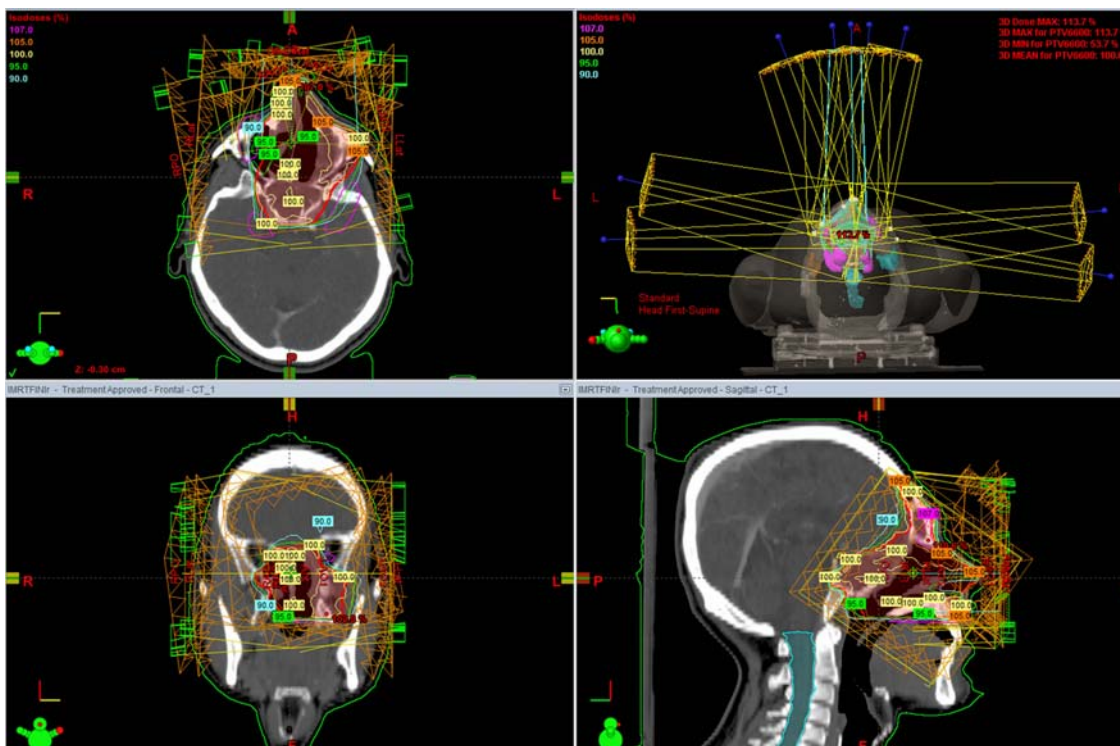
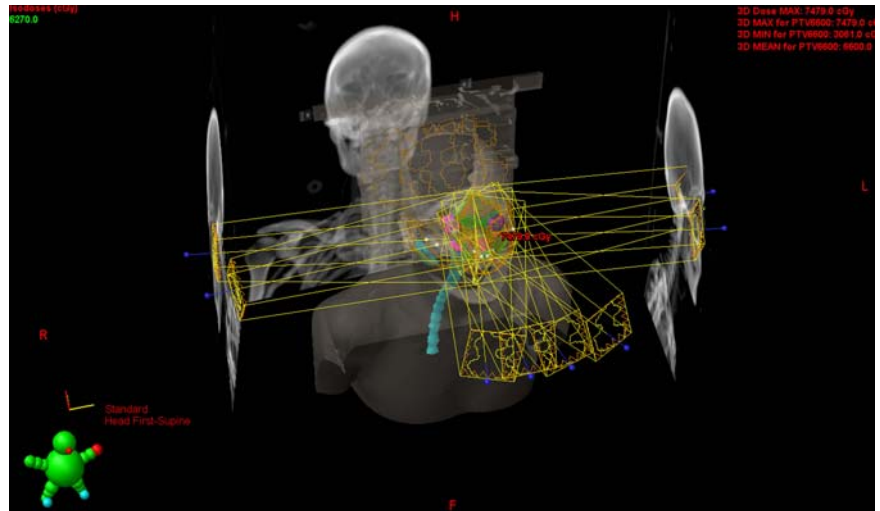
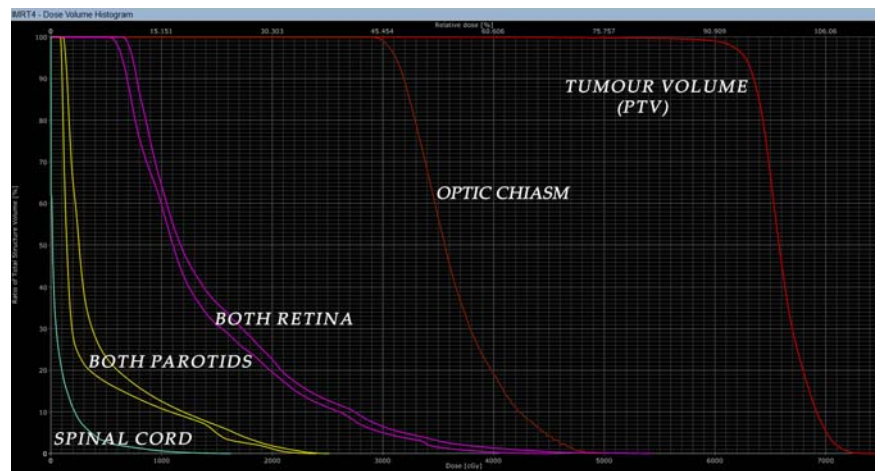


Figure 8 Intensity modulated radiotherapy (IMRT) dosimetry in axial, coronal and sagittal planes.

Figure 9 Dose volume histogram (DVH) of IMRT representing percentage of volumes of critical normal structures receiving specified RT doses.



been considered for MMs of the head and neck in adjuvant settings.

In the past, RT doses in the head and neck, especially for carcinomas of the para nasal sinuses, were limited by the dose tolerance of organs at risk (OAR) in close proximity. Therefore, RT doses applied were insufficient to achieve local tumour control, or, in cases where high RT doses were prescribed, the rate of severe radiation-induced side effects was high. Modern radio therapeutic techniques such as IMRT enable the application of high local doses to complex-shaped target volumes, while sensitive OAR such as the optic chiasm, optic nerves, retina, pituitary, parotids, temporal lobes and auditory structures (including the cochlea and optic structures) can be spared^{4–7} (figures 5–9). Therefore, IMRT is a useful tool to apply the required high RT doses for treatment of MM of nasal cavity and para nasal sinuses. Implementation of high precision RT techniques offers the unique benefit of improved tumour control through the application of high doses, while toxicities are kept very low.

The standard of care for MMs of the head and neck is not well defined owing to the rarity of occurrence. Various groups and institutes have documented small case series and retrospective reviews mainly suggesting multimodality treatment strategies. Currently, one must rely on either single centre or multicentre case series until multi-institutional prospective studies are conducted, the feasibility of which are yet to be determined. Current treatment modalities have not significantly made an impact on the survival of these patients, only a few large case series addressed this disease. Patel *et al*¹³ reported a series of 59 patients with MMs of the head and neck. However, the largest report to date is a multicentre study summarising 74 patients over a 30-year period.¹⁴ These figures express rarity of the disease and the need for multicentre collaboration that will establish clinical guidelines.

Learning points

- ▶ Mucosal malignant melanomas of the head and neck are a rare disease entity with an aggressive natural history and poor long-term prognosis.
- ▶ The established therapeutic approach is complete surgical removal of the tumour followed by radiotherapy.
- ▶ Owing to the anatomical complexity of the sino-nasal region, precision RT is mandatory to optimally irradiate the tumour area sparing the critical surrounding normal structures from late toxicity of RT.
- ▶ Despite advances in surgical techniques and methods of adjuvant therapy, the 5-year survival rate of patients with mucosal melanoma is very low.

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Contributors KK is radiation oncologist of this patient. MI was the ENT surgeon who operated on this patient. NA assisted in major planning of radiotherapy. MUK had the idea to report this case. KK and MUK have played a major role in writing this case report. All the authors made a significant contribution to this study.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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