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Fractionated Stereotactic Radiosurgery for Pituitary Metastasis in a known Case of Cervical Squamous Cell Carcinoma – A Case Report

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Abstract

Background *- Pituitary metastasis of cervical squamous cell carcinoma is an exceedingly rare phenomenon. Management becomes a challenge in such a setting when the patient is either not willing for any surgical intervention or deemed unfit for the same especially in a limited resource peripherally located setup in the country. Fractionated Stereotactic Radiosurgery (FSRT) is a valuable treatment option in such cases as presented below.*

Case Description *- We present a case of a 55-year-old female with cervical squamous cell carcinoma and no comorbidities, diagnosed to be in a metastatic stage owing to her distant metastases. She was diagnosed in the month of December 2018 as per the PET CT and biopsy report. Eventually the patient had undergone palliative Radiation Therapy (RT) to the cervical lesion, in view of local symptoms. Further the patient was treated with palliative chemotherapy using weekly Paclitaxel to a dose of 80 mg/m2 and Carboplatin AUC 2 for 6 cycles and completed the same in March 2019. Follow-up PET CT done in April 2019 was suggestive of Complete Metabolic Response (CMR). After a DFI of around 10 months the patient developed sudden onset diplopia for which she was re-evaluated using PET CT. PET CT in February 2020 showed presence of isolated pituitary metastasis with no uptake anywhere else in the body. The patient was further advised MRI brain which was reported to be suggestive of pituitary metastasis. Visual field examination and hormonal evaluation were further advised for reconfirmation, however, attendants had denied the same in view of financial constraints. So also the patient was not willing for any type of surgical intervention. With lack of surgical intervention the possibility of pituitary adenoma could not be entirely ruled out. Case was therefore, subsequently discussed in the Tumor Board and isolated pituitary metastasis diagnosis was finalised owing to her known metastatic condition and a rapid onset of the symptoms. Accordingly, patient was planned for fractionated SRS (FSRT) to the gross disease, considering it as the only FDG avid lesion, to a dose of 25 Gy in 5 fractions delivered every alternate day. Treatment was uneventful with major clinical benefit in terms of reversal of visual symptoms by the end of 4 weeks. Follow-up scan was planned at 6 weeks, however, unfortunately the patient was lost to myocardial infarction before the same. The objective response could not be documented in our case, nevertheless, we wish to report it, in view of rarity of its occurrence and clinical benefit as mentioned before.*

Conclusion *– Fractionated Stereotactic radiosurgery may be considered as a valuable option while treating rare metastatic spreads to organs like pituitary gland, especially when the patient is deemed unfit or not willing for surgical intervention.*

Introduction

Metastatic lesions to the sella are believed to comprise only 1% of all pituitary lesions, of which the most common sites of primary tumor origin are the breast and lung [1–3]. Compression of parasellar anatomical structures may produce symptoms such as visual feld loss, headache and ophthalmoplegia [4]. Cerebral metastasis of cervical malignancy is uncommon [5]. To our knowledge, only one other case of cervical carcinoma with pituitary metastasis has been reported in a non-autopsy setting [6]. Here, we report a case of sellar metastasis in a patient with cervical squamous cell carcinoma that could not be debulked surgically as patient had denied the same and hence was treated with definitive Fractionated Stereotactic Radiosurgery (FSRT). We wish to highlight the clinical findings and natural history of this rare presentation, and review the literature.

Case Presentation

55-year-old female with moderately differentiated squamous cell carcinoma of cervix and no comorbidities, was diagnosed to have upfront metastatic disease, owing to distant metastasis to lungs, retroperitoneal lymph-nodes and right pubic bone. She was diagnosed in the month of December 2018 as per the PET CT report dated 03.12.2018 and biopsy report dated 01.12.2018. eventually undergoing palliative Radiation Therapy (RT) to primary cervical lesion in view of local symptoms, to a dose of 30 Gy/10 fractions over 2 weeks using 15 MV photons and 3DCRT technique. Further the patient was treated with palliative chemotherapy using weekly Paclitaxel to a dose of 80 mg/m2 and Carboplatin AUC 2 for 6 cycles and completed the same on 27th March 2019. Follow-up PET CT dated 05.04.2019 was suggestive of Complete Metabolic Response (CMR). After a Disease Free Interval (DFI) of around 10 months the patient developed sudden onset diplopia for which she was re-evaluated using PET CT. PET CT dated 07.02.2020 [Figure 1,2] showed presence of isolated pituitary metastasis with no uptake elsewhere in the body. There was focally increased uptake seen in a well-defined enhancing nodular lesion in the sellar region measuring 12 x 11 mm, SUV max 10.3 which increased to 11.9 in the delayed images. The lesion also had eroded the posterior wall of sella turcica. The patient was further advised MRI brain plain plus contrast which was reported as on 18.02.2020 [Figure 3 – a,b,c] to be suggestive of pituitary metastasis. Visual field examination and hormonal evaluation were further advised for reconfirmation; however, attendants had denied the same in view of financial constraints. So also, the patient was not willing for any type of surgical intervention. With lack of surgical intervention, the possibility of pituitary adenoma could not be entirely ruled out.

Case was therefore subsequently discussed in the Tumor Board and a diagnosis of isolated pituitary metastasis was established based on panel consensus, owing to her known metastatic condition and rapid onset of the symptoms. Accordingly, patient was planned for fractionated SRS to the gross disease, considering it as the only lesion, to a dose of 25 Gy in 5 fractions alternate day [Figure 4,5]. The Target

Volume (TV) was 19.74 cc while the marginal dose i.e the minimum dose received by 100 percent of Target Volume, achieved was 21.92 Gy [Figure 6]. Treatment was uneventful with major subjective clinical benefit in terms of reversal of visual symptoms by the end of 4 weeks. Follow-up scan was planned at 6 weeks, however, unfortunately the patient was lost owing to myocardial infarction before the same.

Discussion

Cervical carcinoma typically disseminates locally via the lymphatics to the retroperitoneal lymph nodes; distant hematogenous metastasis most commonly occurs to the liver, lung and bone [11]. Brain metastasis is rare with an estimated prevalence of 0.5-1.0% and portends a particularly poor prognosis [5]. Metastases to the sellar region have been hypothesized to occur either hematogenously, such as from the pituitary stalk or cavernous sinus, or via leptomeningeal spread [7]. Pituitary metastasis typically occurs late in disease course, carrying a poor prognosis [8]. FDG-PET provides information that is not obtainable with other imaging modalities like MRI, and is very effective in the diagnosis and management of patients with various types of cancer. [9] Nevertheless, on MRI, contrast enhancement has been reported to be a prominent feature more commonly observed in metastatic lesions [10]. In this case, MRI done was strongly suggestive of a metastatic lesion and hence a firm derivative could be made. So also, SUV max and the CT component of PET-CT being suggestive of significant erosive component directed us more towards a metastatic lesion than pituitary macroadenoma in this known case of metastatic carcinoma cervix. Pituitary metastases are symptomatic in only 7 % of the cases [12,13], with predominance of Diabetes insipidus (DI) [14-16]. This is an important characteristic in the differential diagnosis of invasive sellar lesions, as DI occurs in less than 1% of non-functioning pituitary adenomas in the first manifestation [16]. However, the patient in question did not present any clinical and laboratorial evidence of DI. To our knowledge, only one other case of cervical carcinoma metastasis has been reported till date. In a 2000 study, Salpietro and colleagues described a sellar/suprasellar metastasis of an epidermoid cervical carcinoma in a 44-year-old female who presented with diabetes insipidus and diplopia. For brain metastasis from cervical cancer, combination therapy of either chemotherapy or stereotactic radiosurgery followed by whole-brain irradiation has been shown to extend median survival to up to 4.6 months [17, 18]. The majority of these studied cases have been squamous cell carcinomas with an intra-parenchymal location. Additionally, the majority of these lesions have been histologically poorly differentiated with high tumor grade [19]. Multimodality therapies are generally recommended with adjuvant chemoradiation therapy following maximal safe surgical resection. However, in resource limited settings where finances still play a major role in the treatment management, and so also in settings where the patients deny or are unfit for surgery, FSRT may be considered based on clinical discretion and panel consensus. This case highlights the importance of

initiating FSRT therapy expeditiously under such circumstances though the objective benefit could not be documented.

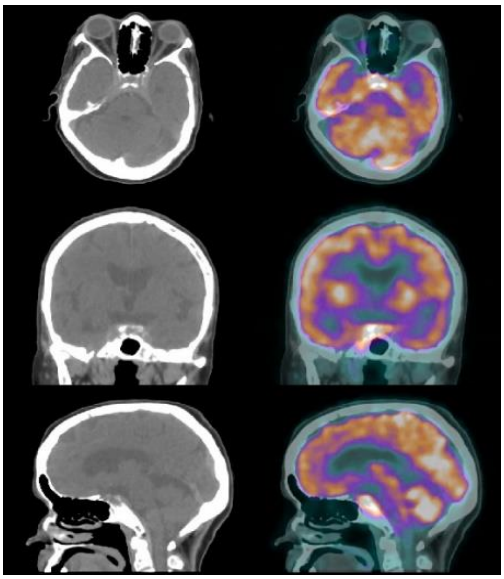
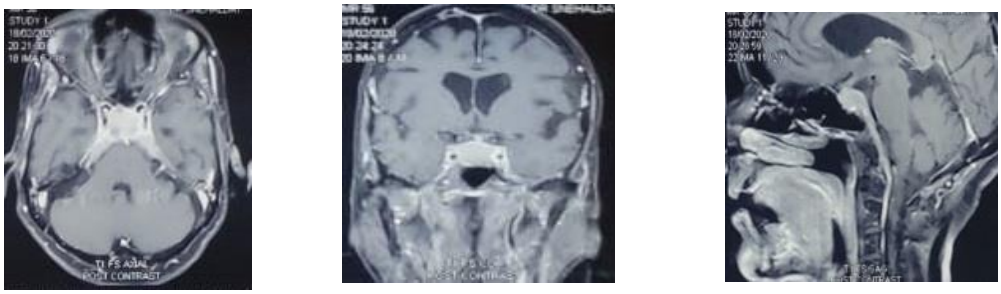


Figure 1 – PET CT (Feb 2020) s/o isolated pituitary metastatic lesion

Figure 2 – MIP of PET CT (Feb 2020) with no lesion elsewhere in the body.



(a) (b) (c)

Figure 3 – Axial (a), coronal (b), and sagittal (c) views of T1 contrast MRI Brain (Feb 2020)

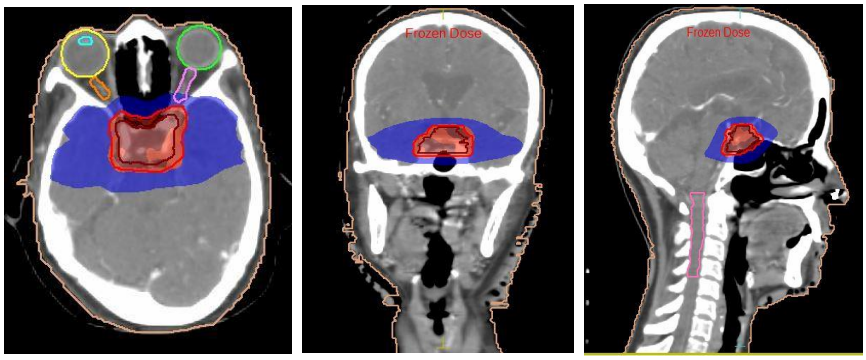


Figure 4 – Axial, coronal and sagittal views of Treatment Planning CT Scan with iso-dose (ID) distribution (Blue – 50 % ID, Red – 100 % ID and Brown - > 100 % ID)

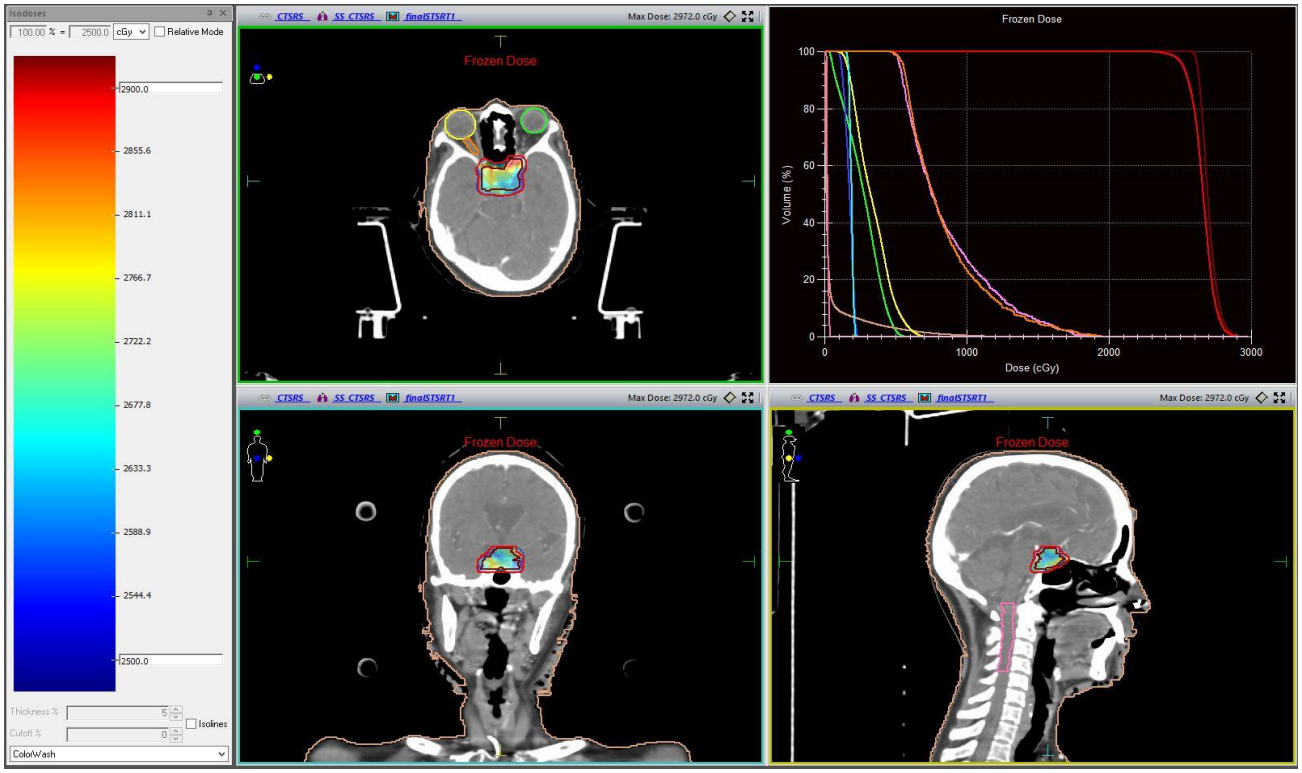
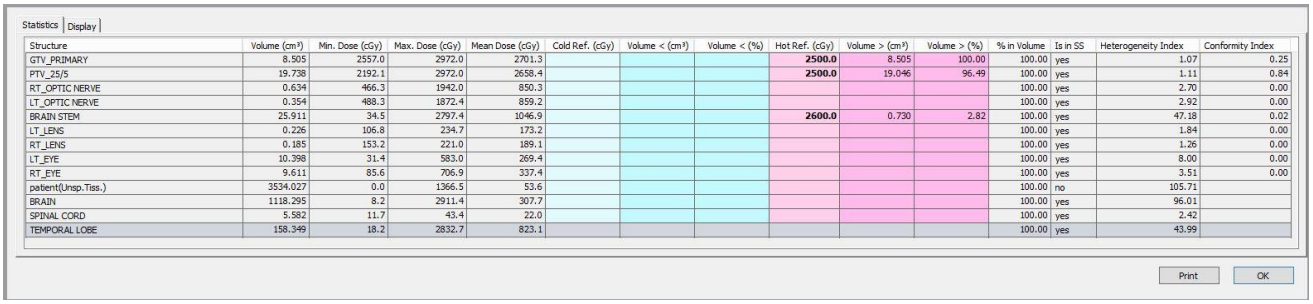


Figure 5 – Axial, coronal and sagittal views of Treatment Planning CT Scan with iso-dose (ID) distribution (Blue – 50 % ID, Orange – 100 % ID and Brown - > 100 % ID) and Cumulative Dose Volume Distribution Graph.



Statistics | Display

Structure	Volume (cm³)	Min. Dose (cGy)	Max. Dose (cGy)	Mean Dose (cGy)	Cold Ref. (cGy)	Volume < (cm³)	Volume < (%)	Hot Ref. (cGy)	Volume > (cm³)	Volume > (%)	% in Volume	Is in SS	Heterogeneity Index	Conformity Index
GTV_PRIMARY	8.505	2557.0	2972.0	2701.3				**2500.0**	8.505	100.00	100.00	yes	1.07	0.25
PTV_25/5	19.738	2192.1	2972.0	2658.4				**2500.0**	19.046	96.49	100.00	yes	1.11	0.84
RT_OPTIC NERVE	0.634	466.3	1942.0	850.3							100.00	yes	2.70	0.00
LT_OPTIC NERVE	0.354	488.3	1872.4	859.2							100.00	yes	2.92	0.00
BRAIN STEM	25.911	34.5	2797.4	1046.9				**2600.0**	0.730	2.82	100.00	yes	47.18	0.02
LT_LENS	0.226	106.8	234.7	173.2							100.00	yes	1.84	0.00
RT_LENS	0.185	153.2	221.0	189.1							100.00	yes	1.26	0.00
LT_EYE	10.398	31.4	583.0	269.4							100.00	yes	8.00	0.00
RT_EYE	9.611	85.6	706.9	337.4							100.00	yes	3.51	0.00
patient(Unsp.Tiss.)	3534.027	0.0	1366.5	53.6							100.00	no	105.71	
BRAIN	1118.295	8.2	2911.4	307.7							100.00	yes	96.01	
SPINAL CORD	5.582	11.7	43.4	22.0							100.00	yes	2.42	
TEMPORAL LOBE	158.349	18.2	2832.7	823.1							100.00	yes	43.99	

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Figure 6 – Dose Volume Statistics for various Target Volumes (TV) and Organs at Risk (OARs)

Conclusion

While cerebral metastases of cervical malignancies have been described, metastasis of well-differentiated cervical malignancy to the pituitary region is rare. However, this should be considered in the differential diagnosis of patients with this history and based on the clinical presentation. The development of rapid endocrinopathies, oculomotor dysfunction, and quick radiographic progression suggest a more aggressive neoplasm. Though ideally maximal safe resection should be performed, in our case, due to patient's own denial to surgery we had treated our patient with FSRT achieving a good subjective clinical benefit and may suggest to use it expeditiously as a valuable option under such circumstances.

Abbreviations

FSRT - Fractionated Stereotactic Radiosurgery

PET CT – Positron Emission Tomography – Computed Tomography

RT - Radiation Therapy

Gy – Gray

MV – Megavolt

3DCRT – 3D Conformal Radiotherapy

AUC – Area Under Curve

CMR - Complete Metabolic Response

DFI – Disease Free Interval

MRI – Magnetic Resonance Imaging

MI – Myocardial Infarction

TV – Target Volume

FDG – Fluorodeoxyglucose

SUV – Standardised Uptake Value

DI – Diabetes Insipidus

ID – Iso-dose

MIP - Maximum intensity projection

OARs – Organs at Risk

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