Brain Tumor Radiotherapy Role and Variation

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ABSTRACT---
Objectives: We report our experiences of brain tumors management by surgery and radiotherapyWhether It has been used as adjuvant, radical or palliative therapy belonging to benign or malignant tumors over 2 years period at ENT, neurosurgery and radiotherapy departments royal medical services.

Methods: We used a retrospective study design to review all brain tumor patients(benign, malignant or metastatic) operated in neurosurgical department and referred to radiotherapy after discussing each case in multidisciplinary clinic in 2018 and 2019. Patient files, radiological images computed tomography (CT) or magnetic resonance imaging (MRI) scans), histo-pathological reports and radiotherapy management plan were reviewed for patients.

Results: In total, 137 patients with brain tumor managed byradiotherapy 64 patients were metastatic, 37 patients high grad glioma, 12 patients atypical meningioma, 7 patients medulloblastoma, rest of cases discussed in the study

Conclusions: Radiotherapy has been fulfilling crucial part in the treatment of CNS tumors, where it has been implemented as adjuvant therapy or even being the solitary resort where surgery is inapplicable or used as palliative therapy in different regimens according to histopathology, performance status and different sites.

Keywords--- brain tumor, benign, malignant,radiotherapy,adjuvant, palliative

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1. INTRODUCTION

The indications for radiotherapy that is used in brain tumors in general are high grade gliomas (1), post-operative residual disease, and recurrentdisease (2) or in benign tumors and for palliative radiation as whole brain in brain metastasis.

Radiotherapy is used in malignant tumors such as high grade gliomas (GBM,Anaplastic Astrocytoma , Anaplastic Oligodendroglioma), high grade meningioma (3), blastoma (4) , in metastatic brain tumor (5) and CNS lymphoma(6) .

Radiotherapy can be used to treat benign tumors such as low grade meningioma, pituitary tumors, hemangiopericytoma ,hemngioblastoma , chordoma , schwannoma and many others such as craniopharyngeoma ,AVM and glomusjagulare tumors (7,8)

The aim of this study is to demonstrate the role of radiotherapy in the treatment of CNS tumors, particularly in brain tumors. Whether it has been used as adjuvant therapy or palliative therapy belonging to benign or malignant tumors at the Royal Medical Services /Radiation Oncology Center we will also discuss the protocols used in radiotherapy department for different tumors.

We will also put light on our protocol at RMS for radiotherapy management of brain tumors

2. MATERIALS AND METHODS

Patients

All patients diagnosed at King Hussein Medical Centre (KHMC) for brain tumor (benign, malignant or metastatic) operated in neurosurgical department and referred to radiotherapy after discussing each case in multidisciplinary clinic 2018-2019 were included. Ethical approval was granted by the research department ethical committee at the Royal Medical Services.

The methodologies for collecting data were categorizing and sorting incoming referred patients to palliative or adjuvant cases based on radiologic diagnostics or based on pathology. Cases medical reports were reviewed .Radiation therapy at our center was investigated regarding the doses, timing and if given concurrently with chemotherapy.

This study was conducted in our Radiation oncology department 2018-2019 using 2 devices of (3D-CRT) 3 dimensional conformal radiation therapy type, Electa Synergy digital linear accelerators connected to FOCAL stations for contouring and XIO planning system, CT simukator was used in addition to fusion with MRI images when clinically needed.

3. RESULTS

Between2018-2019, 137 patients with brain tumors were referred to our center (table 1).

Table 1: Number of patients in each brain tumor type.

Brain Tumor	Number of patients
Metastatic	**64**
Metastatic Lung	28
Metastatic breast	17
Metastatic colon	5
Metastaticendometrial	4
Metastaticrenal cell carcinoma	3
Metastatic prostate	1
High grad glioma	**37**
GBM	26
Anaplastic astrocytoma	11
Atypical and anaplastic meningioma	**12**
Medulloblastoma	**7**
Pituitary adenoma	**4**
Schwannoma	**3**
Hemangiopericytoma WHO G III	**3**
Oligodendroglioma WHO GII, G III	**3**
CNS Lymphoma	**2**
Anaplastic Ependymoma WHO G III	**1**
Clivaschordoma	**1**

64 patents had received palliative therapy as whole brain radiotherapy WBRT as metastatic brain tumor. Patients' cases were distributed as28 patients with lung cancer origin,17patients withbreast cancerorigin,5 patients with colon cancer origin,4 patients with endometrial cancer origin,3 patients with renal cell carcinoma originand one patient with prostate cancer origin, 6 patients with unknown primary due to no biopsy.

25 patients diagnosed with GBM WHO G IV had received 3D conformal EBRT concurrently with Temozolomide followed by adjuvant Temozolomide.

One patient with multifocal multicentricGBM received WBRT with total dose of (30Gy/10Fx) followed by intrathecal MTX.

Two patients had been re-irradiated at our center successfully, cases were recurrent GBM and inoperable WHO G III glioma.

A 9 patientswhom were diagnosed with Anaplastic Astrocytoma WHO G III had been treated with EBRT with total dose of (59.4Gy/33Fx)over two phases concurrently with Temozolomide followed by adjuvant Temozolomide .Two patients had Anaplastic oligodendroglioma WHO GIII , one of them had received EBRT with total dose of (54Gy/27Fx) followed by PCV ,The second received EBRT with total dose of (60Gy/30Fx) concurrently with Temozolomide followed by adjuvant Temozolomide. One patient had Oligodendroglioma WHO GII was treated with (54Gy/30Fx) followed by chemotherapy.

7 patients were referred to our center for CSI (craniospinal irradiation) .two patients who had Medulloblastoma had received CSI with total dose of (23.4Gy/13Fx) followed by posterior fossa boost with total dose of (30.6Gy/17Fx) both phases concurrently with weekly Vincristine followed by PCV.Another patient with Medulloblastoma had received CSI with total dose of (36Gy/20Fx) followed by posterior fossa boost with total dose of (18Gy/10Fx) both phases concurrently with weekly Vincristine followed by PCV. One patient with Medulloblastoma did not receive CSI due to unsuccessful verification attempts in coordination with the Anesthesia team.

A pediatric patient was diagnosed with Anaplastic Ependymoma WHO G III, had received two cycles of CTX post biopsy, after that received EBRT with total dose of (50.4Gy/28Fx).

12 patients diagnosed with atypical and anaplastic meningioma WHO G II and G III had received EBRT with total dose of (54Gy/30Fx).

Twocases of inoperable pituitary adenoma were treated with EBRT with total dose of (54Gy/30Fx). Another two cases of atypical pituitary macro adenoma were treated with EBRT with total dose of (52Gy/26Fx).A case of clivusChordoma was treated with EBRT with total dose (54Gy/27Fx). Three patients were diagnosed with Hemangiopericytoma WHO G III were referred to our center and were treated with EBRT with doses of (54Gy/30Fx) and (60Gy/30Fx).Three patients were referred having schwannoma and they were treated with EBRT with total doses of (50.4Gy/28Fx) and (52Gy/26Fx).

A case of recurrent hemangiopericytoma WHO GII was referred to our center for re-irradiation who had second surgery (GTR) in 2019 and was not given radiotherapy due to high risk of toxicity .One of the patients who had been referred had been provided with thebest supportive care only.

4. DISCUSSION

External beam radiotherapy (EBRT) is directed to treat brain tumors in the following ways : 3D- CRT 3 dimensional conformal radiation therapy using images from MRI or CT to form 3D model for the tumor in order to spare normal surrounding tissues ,IMRT intensity modulated radiation therapy; a type of 3D -CRT but giving higher doses to the tumor with higher level of sparing the normal tissues ,Proton therapy , SRS stereotactic radiosurgery; where it uses a single high dose directed to the tumor under certain conditions for radical or metastatic cases with different types such as Gamma knife and cyber knife, FSRT fractionated stereotactic radiation therapy ; where it uses multiple fractions to deliver radiotherapy in stereotactic precision close to sensitive structures. (9) (10)

It is remarked that brain metastasis is the most common intracranial tumor as it is evident in our data. (11)

As it is clear, the most common primary site for brain metastases is lung followed by breast origin and this result conforms what is evident in brain metastases. (12) 6 patient from those who had brain mets were treated without histopathology confirmation as 4 of them had the clinical picture of wide spread bone and lung metastasis while 2 of them were not fit for any surgical intervention with KPS less than 40% .

It is observed that glioblastoma multiform GBM is the most common primary malignant CNS tumor,Malignantgliomas make up 35-45% of primary brain tumors. Nearly 85% of these are glioblastomamultiforme(13) .In randomized controlled trials of post-operative radiotherapy versus no radiotherapy, median survival is approximately doubled from 14-23 weeks to 23-47 weeks with the addition of radiotherapy.(14)

The general treatment paradigm for GBM is surgery followed by radiotherapy to 60Gy concurrently with Temozolomide (75mg/m2) followed by 6 cycles of adjuvant Temozolomide (150-200mg/m2) every 28 days for 5 days after a break of one month post radiotherapy.(14) The general guidelines for radiotherapy target volume delineation in GBM according to RTOG are delineating the initial volume based on T1 enhancement ,T2 ,FLAIR up to 46Gy with 2 cm margins to obtain the clinical target volume and boost to T1 enhancement only to 14 Gy with 2 cm margins or based on USCF guidelines including the gross tumor volume based on T1 enhancement and mass like FLAIR up to 60Gy with (1.5-2)cm margins to

get the clinical target volume (15) Then adding (0.3-0.5)cm compensating for internal margin and setup uncertainty to get the planning target volume.

Radiotherapy has been utilized in Meningioma after surgery if the patient had subtotal resection or anaplastic histology or if there is a brain invasion or recurrent disease .Observation should be considered with incidental asymptomatic stable lesions. (16) Radiotherapy doses employed for benign meningioma are 45Gy-54Gy , for atypical type (54Gy-60Gy) and for malignant tumors 60Gy.(17)

Craniospinal irradiation (CSI) is indicated for medulloblastoma and some rarer tumors with signs of leptomeningeal spread, particularly germ-cell tumors, atypical teratoidrhabdoid tumors and others. (14)

Regarding Medulloblastoma tumors where cases are classified to standard risk or high risk (18), the patients are treated with CSI with total dose of 23.4Gy in standard risk or (36-39)Gy in high risk with boost to posterior fossa reaching up to 54Gy concurrently with Vincristine followed by PCV chemotherapy. (19)(20).

5. CONCLUSIONS

Radiotherapy has been fulfilling crucial part in the treatment of CNS tumors, where it has been implemented as adjuvant therapy or even being the solitary resort where surgery is inapplicable or used as palliative therapy in different regimens according to histopathology, performance status and different sites.

More efforts should be done to imply new techniques which will be hopefully seen at our department when new machines are installed.

Further follow up to patients in future will provide information about acute or late toxicities.

This study can be used as a cornerstone to develop clinical practice guidelines for CNS tumors at RMS.

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