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Evaluation of Multımodality Imagıng For Management of Recurrent Intracranial Nongermınomatous Germ Cell Tumors (NGGCT) With Precise Radıatıon Therapy (Rt): An Origınal Article

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Abstract

Objective: Nongerminomatous germ cell tumor (NGGCT) may be considered as a distinct entity partly due to differential response to treatment especially in the central nervous system (CNS) and other extragonadal localizations. Initial diagnosis for NGGCT is at younger ages compared to germinoma, and overall survival rates for NGGCT is typically poorer given the resistance to administered therapies. Management of NGGCT warrants multidisciplinary input from medical oncology, surgery, and radiation oncology departments. Localized field radiotherapy, whole ventricle radiotherapy, whole brain irradiation, and craniospinal radiotherapy with local boost may be utilized alone or in combination with respect to patient, disease, and tumor characteristics. Despite aggressive management, intracranial recurrences may occur. In this original research article, we assess multimodality imaging for management of recurrent intracranial NGGCT with precise radiotherapy.

Materials and Methods: Patients referred to Department of Radiation Oncology, Gulhane Medical Faculty, University of Health Sciences for radiotherapeutic management of recurrent intracranial NGGCT were assessed to investigate whether multimodality imaging contributes to target and treatment volume definition, interobserver and intraobserver variations. A comparative evaluation and analysis was performed for radiaotherapy target definitions based on computed tomography (CT) simulation images only or by integration of Magnetic Resonance Imaging (MRI) in the radiation treatment planning procedure.

Results: As a result of this study, we have found that ground truth target volume was identical with CT-MR registration based imaging for radiotherapeutic management of patients with recurrent intracranial NGGCT.

Conclusion: This study supports the utilization of multimodality imaging for improved target definition for recurrent intracranial NGGCT. Clearly, there may be the requirement for additional supporting data from future studies.

Keywords: Recurrent intracranial NGGCT; Radiotherapy; Magnetic resonance imaging (MRI); Target definition; Multimodality imaging

Introduction

Primary intracranial germ cell tumors are relatively infrequent tumors accounting for a small proportion of central nervous system (CNS) malignancies [1-3]. However, the frequency may be higher in children and adolescents, and incidence may vary among different geopraphical locations throughout the world. These tumors are mostly located in midline CNS localizations including the pineal and suprasellar regions. Germ cell tumors may be histologically categorized into two distinct groups including the undifferentiated germ cell tumors or germinoma (referred to as seminoma and dysgerminoma in the testis and ovary, respectively) and differentiated or nongerminomatous germ cell tumors (NGGCT) which include teratoma (mature and immature), teratoma with malignant degeneration, embryonal carcinoma, choriocarcinoma, endodermal sinus (yolk sac) tumor, and mixed germ cell tumor. Teratomas consist of a mixture of tissues derived from germ cell layers with varying levels of differentiation (immature, mature, or mature with malignant degeneration). Mature teratomas include fully differentiated ectodermal, mesodermal and endodermal elements. Nevertheless, immature teratomas possess embryonal or fetal primitive elements with malignant potential. Pure mature

teratomas have benign behaviour and may be cured by surgery. However, teratomas may commonly possess a mixture of mature and immature elements which render their behavior quite challenging to predict.

NGGCT is considered as a distinct entity partly due to differential response to treatment especially in the CNS and other extragonadal localizations. Initial diagnosis for NGGCT is at younger ages compared to germinoma, and overall survival rates for NGGCT is typically poorer given the resistance to administered therapies [4-6].

Serum and/or cerebrospinal fluid tumor markers such as alpha-fetoprotein and human chorionic gonadotropin may assist in diagnosis of yolk sac tumors and choriocarcinoma. Management of NGGCT warrants multidisciplinary input from medical oncology, surgery, and radiation oncology departments. In terms of radiotherapeutic management, response-adapted field designing and different dose regimens have been addressed [3,7-9]. Localized field radiotherapy, whole ventricle radiotherapy, whole brain irradiation, and craniospinal radiotherapy with local boost may be utilized alone or in combination with respect to patient, disease, and tumor characteristics. Despite aggressive management, intracranial recurrences may occur. In this original research article, we assess multimodality imaging for management of recurrent intracranial NGGCT with precise radiotherapy.

Materials and Methods

Patients referred to Department of Radiation Oncology, Gulhane Medical Faculty, University of Health Sciences for radiotherapeutic management of recurrent intracranial NGGCT were assessed to investigate whether multimodality imaging contributes to target and treatment volume definition, interobserver and intraobserver variations. A comparative evaluation and analysis was performed for radiaotherapy target definitions based on computed tomography (CT) simulation images only or by integration of Magnetic Resonance Imaging (MRI) in the radiation treatment planning procedure. A ground truth target volume was defined individually by board certified radiation oncologists following thorough assessment, colleague peer review, and consensus to be utilized in actual treatment and comparison purposes. Decision making process for radiotherapeutic management of patients has included thorough multidisciplinary assessment individually. Treatment protocols and strategies have been considered on an individual basis by taking into account patient, disease, and treatment characteristics. Lesion size, location and association with normal tissues, expected results of suggested therapies, patient symptomatology and preferences along with logistical issues were taken into account for achieving optimal treatment outcomes.

Synergy (Elekta, UK) linear accelerator (LINAC) has been used to deliver precise radiotherapy at our tertiary cancer center. Included patients underwent CT simulation at the CT simulator (GE Lightspeed RT, GE Healthcare, Chalfont St. Giles, UK) for acquisition of high quality radiation treatment planning images. After the CT simulation process, acquired treatment planning images have been transferrred to the contouring workstation (SimMD, GE, UK) by use of the network. Structure sets including target volumes and normal tissues were determined. Target volume definition has been performed by either the CT simulation images only or by registered CT and MR images. We have performed a comparative analysis for evaluation of target definition by CT only and with incorporation of CT-MR registration based imaging to explore the impact of multimodality imaging.

Results

In this original research article, we have assessed patients who have been referred for radiotherapeutic management of intracranial recurrent NGGCT at our tertiary referral institution. Target definition by either CT-only imaging or by CT-MR registration based imaging was comparatively evaluated. Assessed tumor-related parameters included the lesion size, localization and association with normal tissues. Also, patient age, symptomatology, performance status, logistical issues, lesion location and association with other critical structures were considered. We additionally took into account the reports by American Association of Physicists in Medicine (AAPM) and International Commission on Radiation Units and Measurements (ICRU) in precise radiation treatment planning. Through meticulous consideration of contemporary guidelines and clinical experience, radiation physicists generated radiation treatment plans by taking into account the relevant normal tissue dose limitations. Tissue heterogeneity, electron density, CT number and HU values in CT images were also considered by radiation physicists for radiation treatment planning. Most critical endpoint of radiation treatment planning was achieving optimal target coverage without violation of normal tissue dose limitations. Definition of ground truth target volume was performed by the board certified radiation oncologists following detailed assessment, colleague peer review, and consensus. Ground truth target volume was used for actual treatment and for comparison purposes also. Image Guided Radiotherapy (IGRT) techniques such as kilovoltage cone beam CT and electronic digital portal imaging were utilized, and radiation treatment was administered using Synergy (Elekta, UK) LINAC. As a result of this study, we have found that ground truth target volume was identical with CT-MR registration based imaging for radiotherapeutic management of patients with recurrent intracranial NGGCT.

Discussion

Although primary intracranial germ cell tumors comprise a small proportion CNS malignancies, their incidence may be higher in children and adolescents, and incidence may vary among different geopraphical locations throughout the world [1-3]. These tumors are usually localized in midline CNS locations

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such as pineal and suprasellar regions. Germ cell tumors may be broadly categorized into two different groups including the undifferentiated germ cell tumors or germinoma (referred to as seminoma and dysgerminoma in the testis and ovary, respectively) and differentiated or NGGCT including teratoma (mature and immature), teratoma with malignant degeneration, embryonal carcinoma, choriocarcinoma, endodermal sinus (yolk sac) tumor, and mixed germ cell tumor.

NGGCT may be considered as a distinct entity partly due to differential response to treatment especially in the CNS and other extragonadal localizations. NGGCT is typically diagnosed at younger ages compared with germinoma, and overall survival rates for NGGCT may be poorerdue to the resistance to delivered treatments [4-6].

Yolk sac tumor and choriocarcinoma diagnosis may be assisted by use of serum and/or cerebrospinal fluid tumor markers including alpha-fetoprotein and human chorionic gonadotropin. As a rule of thumb, management of NGGCT requires multidisciplinary involvement of related disciplines including medical oncology, surgery, and radiation oncology. As part of radiotherapeutic management, response-adapted field designing and different dose regimens have been utilized [3,7-9]. Localized field radiotherapy, whole ventricle radiotherapy, whole brain irradiation, and craniospinal radiotherapy with local boost may be utilized alone or in combination with respect to patient, disease, and tumor characteristics. Despite aggressive management, intracranial recurrences may occur.

Younger patients still in the process of growing may be more prone to adverse effects of radiotherapy. Nevertheless, radiotherapy may be considered as a viable therapeutic modality as part of multidisciplinary recurrent intracranial NGGCT management. Clearly, radiation induced toxicity should be vigilantly considered to avoid unwanted consequences. Utilization of IGRT techniques, response adapted radiotherapy, adaptive radiotherapy (ART), optimal field designation, and improved target definition may be considered among the several aspects of contemporary radiotherapy strategies to achieve an improved toxicity profile. Target definition is a very critical procedure, and the contribution of multimodality imaging techniques and image fusion methods for improved target definition has been addressed for many tumors, and there is now accumulating evidence in support of multimodality imaging for target definition [10-45].

Multidisciplinary management may be considered for achieving an improved therapeutic ratio for NGGCT. However, it is pertinent to consider that children and adolescents are more commonly diagnosed with NGGCT. Radiotherapy may play an integral role as part of multidisciplinary management of intracranial NGGCT. Nevertheless, while radiotherapy may serve as a viable treatment option for a plethora of malignancies, pediatric patients at younger ages should be more vigilantly considered for irradiation with regard to the adverse irradiation effects and consequences with the potential to deteriorate quality of life. Readily, vast majority of cancer centers use CT simulation for radiation treatment planning for intracranial NGGCT. CT may be considered as a viable imaging modality, however, incorporation of other imaging modalities such as MRI may contribute to improved target definition. In our study, we evaluated radiotherapy target definition for recurrent intracranial NGGCT by use of multimodality imaging and found that target definition could be improved through the utilization of multimodality imaging. From this perspective, our study may add to growing body of evidence in support of improved target definition by multimodality imaging.

In the millennium era, many improvements have taken place in the field of radiation oncology by introduction of automatic segmentation techniques, stereotactic radiotherapy, molecular imaging methods, intensity modulated radiotherapy (IMRT), IGRT, and ART [46-85]. With these state of the art technologies and innovatory improvements, accuracy and precision in target definition has become an indispensable component of sophisticated radiotherapy strategies. Within this context, we cordially believe that our study may have relevant clinical implications for routine adoption of multimodality imaging for target definition of recurrent intracranial NGGCT.

Conclusion

In conclusion, our study supports the utilization of multimodality imaging for improved target definition for recurrent intracranial NGGCT. Clearly, there may be the requirement for additional supporting data from future studies.

Conflict of Interest

There are no conflicts of interest and no acknowledgements.

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