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Case Report

Pathology Section

Early Onset Radiation Induced Sarcoma Following Treatment for Glioblastoma: A Case Report and Review of the Literature

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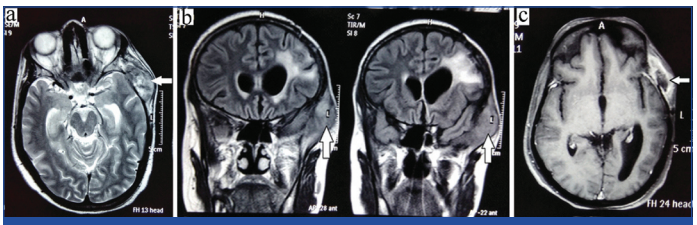
ABSTRACT

Radiation induced sarcoma after irradiation of brain tumour is a rare complication of radiotherapy, with an incidence of 0.03 to 0.3%. It is associated with poor prognosis and frequently occurs five years after completion of treatment. Herein we report a case of a 35-year-old female who had been diagnosed with glioblastoma of the left frontal region. After surgical resection of the tumor, she was treated with external beam radiotherapy. Subsequently she developed a scalp swelling of the left temporal region within two years of completing treatment. Histopathologic examination of the swelling aided by immunohistochemistry in collaboration with the history and the latency period suggested the diagnosis of radiation induced sarcoma. We report this case for its rarity and to highlight the short latency period (within two years) of development of a secondary neoplasm after postoperative radiotherapy.

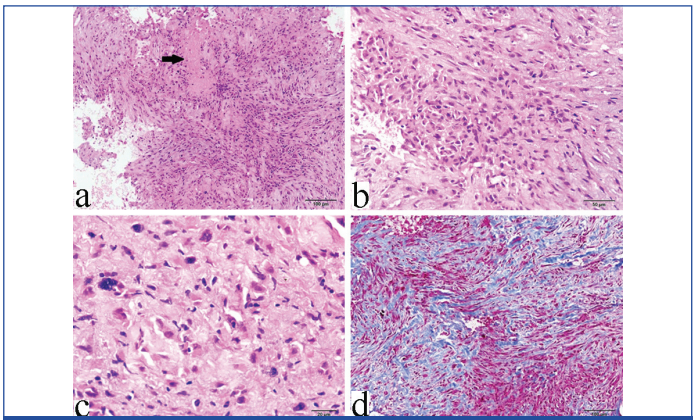
Keywords: Latency period, Radiation therapy, Secondary neoplasm

CASE REPORT

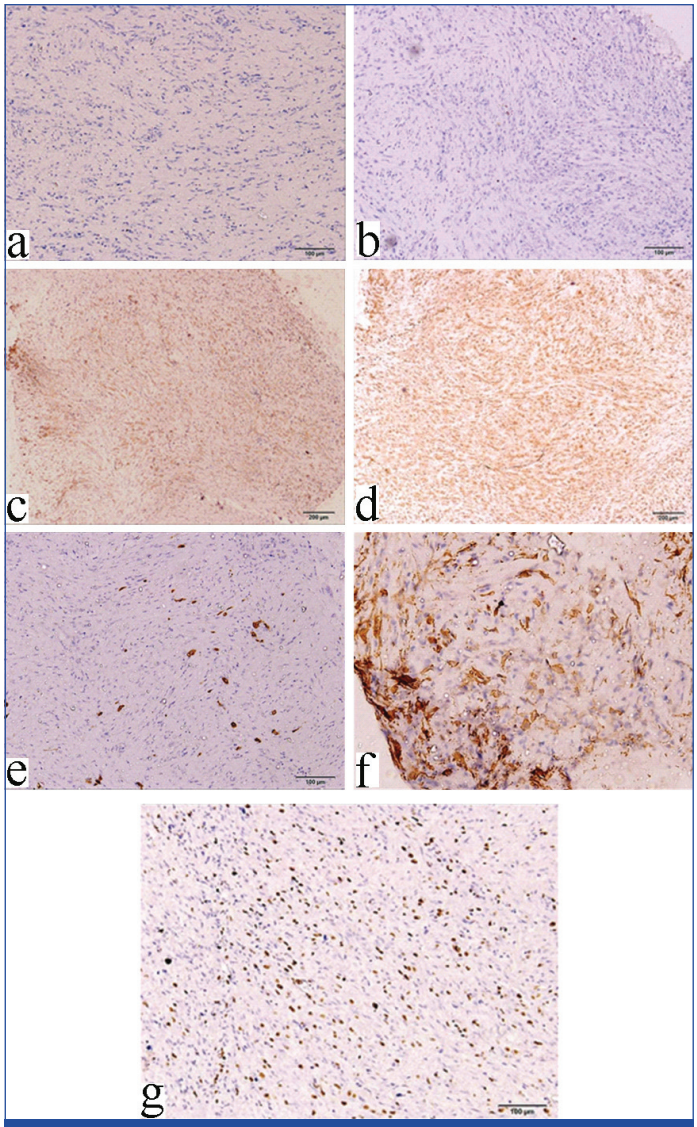
A 35-year-old female presented with a scalp swelling in the left temporal region of three months duration, accompanied by fever since last one month. There was no history of trauma or seizures or vomiting or loss of consciousness. Physical examination findings showed a 4-5 cm tender mass on the scalp of the left temporal region. There were no other significant findings, including absence of any lymph nodes anywhere. She had a past history of left frontal craniotomy for resection of a left fronto-parietal mass two years ago. Magnetic Resonance Imaging (MRI) then had shown a heterogeneously enhancing (5×4.2×3.7 cm) mass in the left fronto-parietal region, suggestive of glioma. Frozen sections were suggestive of high grade glioma. Complete resection of the tumour was performed. Histopathologic Examination (HPE) was consistent with a diagnosis of glioblastoma; Immunohistochemistry (IHC) marker for Glial Fibrillary Acidic Protein (GFAP) had showed strong positivity in the tumour cells. Thereafter, she received adjuvant chemotherapy with temozolamide (100 mg daily throughout radiotherapy) and concurrent external beam radiation therapy with Cobalt-60 machine, full dose regimen (60 Gy/30 fractions). Within two years of completion of treatment, she developed the current scalp swelling. Contrast enhanced MRI this time revealed an ill-defined T2/FLAIR heterointense, T1W1 iso- to hypointense heterogeneously enhancing extra-cranial lesion measuring 5.7×2.9×5 cm in size on the left temporal convexity with infiltration into the dura as well as between the inner and outer tables causing expansion of the temporal bone and also extending into the left temporalis muscle [Table/Fig-1]. The site of the primary tumour (i.e., glioblastoma) did not show any residual lesion. In the operating field, there was no evidence of invasion into the brain parenchyma. The tumour was excised en masse. HPE revealed strips of fibrocollagenous stroma infiltrated by sheets of medium to large sized pleomorphic neoplastic cells having irregular ovoid to plump spindle hyperchromatic to vesicular nuclei, prominent nucleoli and moderate to abundant cytoplasm; no glioblastoformic elements were identified. Necrosis, myxoid change and mitosis were also noted [Table/Fig-2]. Masson trichome and Alcian blue stains exhibited positivity for collagen and myxoid respectively [Table/Fig-2]. A provisional diagnosis of sarcoma was made based on the histomorphology and the special stains. Review of the previous biopsy of the primary brain tumour seconded the diagnosis of glioblastoma. On IHC study, the tumour cells were negative for GFAP and Epithelial Membrane Antigen (EMA) (conclusively ruling out glioblastoma/gliosarcoma whether primary or metastasis), but showed diffuse positivity for Vimentin and CD 34, focal sparse positivity for desmin and Smooth Muscle Actin (SMA). Other markers such as Pan CK, p63, CD 31 and S100 were negative, with Ki-67 index being approximately 35-40% [Table/Fig-3]. Correlating with the history, latency period, morphology and IHC findings, final diagnosis was radiation induced sarcoma with myofibroblastic differentiation. There were no distant metastases to other internal organs or skeletal system as confirmed by abdomino-pelvic Computed tomography scan and whole-body bone scan. The patient was treated with adjuvant palliative chemotherapy, and is on follow-up.



[Table/Fig-1]: Irregular enhancing lesion (arrow) involving bone without intracranial extension on left temporal scalp (a: T2 weighted axial section; b: FLAIR axial section; c: Contrast enhanced axial section).



[Table/Fig-2]: Tumour mass composed of fibrocollagenous stroma infiltrated by sheets of irregular pleomorphic neoplastic cells accompanied by areas of necrosis (arrow) and myxoid change along with presence of bizarre hyperchromatic giant cells; H&E (a) 10X, (b) 20X, (c) 40X. d) Masson trichrome stain exhibited positivity for collagen (10X).



[Table/Fig-3]: IHC showing the tumour cells negative for GFAP (a) and EMA (b), positive for Vimentin (c), CD 34 (d), focal positive for Desmin (e) and SMA (f). Ki67 index (g) was approximately 35-40 %; IHC, 10X (a,b,e,g), 4X (c,d), 20X (f).

DISCUSSION

Radiation therapy has an undeniably significant role in postoperative treatment of central nervous system neoplasms. A well-established long-term complication of cranial radiation is the development of secondary tumours, the risk of which has intensified as the survival of patients with brain tumours has increased with the advances in radiotherapy or intensive chemotherapy. The most common tumours noted to have developed following cranial radiation are meningiomas, followed by gliomas, ependymomas, medulloblastomas, sarcomas, schwannomas, and primitive neuroectodermal tumours [1-3]. Development of sarcoma after irradiation of brain tumours is a rare complication of radiotherapy, with an incidence of 0.03 to 0.3% [4]. The latency period, i.e., the time interval between the completion of treatment of the primary neoplasm and appearance of the secondary tumour is substantial, usually more than five years.

Radiation induced tumours were originally explained by Cahan et al., in 1948. Modified by Arlen et al., in 1971, the four characteristics described for a tumour to be classified as such, included: 1) History of radiation therapy; (2) Development of neoplasm within the field of radiation beams; (3) Time relapse between radiation and tumour development; and (4) No other predisposing condition to tumour development [5]. Our patient fulfills all of the criteria for establishment of radiation induced sarcoma.

In a study by Brady SG et al., on 160 patients with radiation-associated sarcomas, breast cancer (26%) was the most common diagnosis which received radiation therapy, followed by lymphoma (25%) and carcinoma of the cervix (14%). Among the radiation-associated sarcomas the most common histologic types were osteogenic sarcoma followed by malignant fibrous histiocytoma and angiosarcoma. High grade tumours (87%) comprised the majority [6]. Although a very rare complication of radiotherapy for brain tumours, radiation induced sarcomas of this part often demonstrate rapid and aggressive growth similar to other location. Risk factors for developing radiation-induced sarcomas are young age at onset of radiation treatment and treatment-related factors, including high radiation dose and simultaneous chemotherapy with alkylating agents [7]. Radiation-induced tumours and also the type of these secondary tumours are related to cumulative dose of radiation exposure. For example, benign tumours, such as meningiomas, tend to occur after lower-dose irradiation (less than 15 Gy), and malignant tumours, such as gliomas or sarcomas, tend to occur after higher-dose radiotherapy (15–60 Gy) [8]. The mean latency of common radiotherapy induced tumours such as meningiomas with high-dose radiation is 18.4 years, compared with 36.8 years for low doses [9]. Thus, latency from radiation to time of diagnosis is mostly more than 5 years. Very few reported cases of radiation induced sarcomas with 1 to 2 years latent period can be found in literature.

The median survival of glioblastoma is approximately 15-18 months after diagnosis [10]. Our case is one of the rare controlled glioblastoma cases with more than 24 months progression free survival, which became complicated with another radiation induced sarcoma instead of recurrence of the primary glioblastoma. The second neoplasm was not a recurrence/relapse of the primary malignancy was conclusively ruled out based on histomorphology and IHC study. Negativity of the tumour cells both for GFAP and EMA excluded the diagnosis of glioblastoma and/or gliosarcoma [10]. Positivity of the neoplastic cells for CD 34, desmin and SMA underlined the myofibroblastic nature of the tumour [11,12]. Prognosis of radiation-induced sarcoma is worse than that of primary sarcoma because of its aggressive clinical behaviour and intractability to treatment strategies [7,13]. As had been done in our case, re-examination of the primary biopsy is absolutely essential to rule out any discrepancy. Development of this second neoplasm occurred within an unusually short span (two years) of completion of therapy of the primary tumour, i.e., latency period <2 years. This shorter latency before the development of post-irradiative brain tumours may be ascribed to larger radiation dosages and higher degrees of malignancy [8,13,14].

CONCLUSION

Radiotherapy is an essential treatment option after surgical resection of neoplasms arising from the central nervous system, but it has its own undesirable effects. Possibility of a radiation induced sarcoma should be kept in mind when a new suspicious lesion is encountered in a previously irradiated field, even if the time interval between radiotherapy and the new lesion is quite short. This fact is borne out by the brief latency period (within two years) in our case. IHC can be of immense help in arriving at the correct precise diagnosis in such tricky cases.

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