ISSN 1220-8841 (Print)
ISSN 2344-4959 (Online)

ROMANIAN
NEUROSURGERY

Vol. XXXVII | No. 3 September 2023

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DOI: 10.33962/roneuro-2023-062

Romanian Neurosurgery (2023) XXXVII (3): pp. 349-353
DOI: 10.33962/roneuro-2023-062
www.journals.lapub.co.uk/index.php/roneurosurgery

Post-irradiation bilateral basal ganglia calcification in a patient with cerebral metastasis. A case report and review of literature

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Keywords
basal ganglia calcification, post irradiation, computed tomography

ABSTRACT

Background: Basal Ganglia calcification is now being diagnosed with increasing frequency with the widespread application of computed tomography (CT) scan in clinical practice. One of the rare causes of bilateral basal ganglia calcification is post-irradiation sequelae. So far, there are a total of 11 reported cases of post-radiotherapy basal ganglia calcification.

Case report: Here, we report another case of bilateral basal ganglia calcification following radiotherapy for cerebral metastasis from Ca- ovary along with a review of the other reported cases. The exact pathogenesis of this condition is not clear. It appears, however, to be related to radiation vasculitis of the small vessels of the brain with resultant hyalinization and calcification. Conclusions: A long-term follow-up study would be necessary to evaluate the significance and implication of post-irradiation calcification of the grey matter.

INTRODUCTION

Basal ganglia calcification is seen in approximately 1% of all CT scans of the brain (3). It is seen more frequently in older patients and is considered a normal incidental and idiopathic finding in an elderly patient but should be considered pathological in persons younger than 40 years unless proved otherwise (2). There are many pathological causes e.g. toxic, infectious, metabolic, hypoxic, inherited and idiopathic. The pathogenesis though exactly unknown, is assumed to be deposition of a colloid material in and around the finer cerebral blood vessels, with subsequent hyalinization and calcification of this colloid (1). Many patients are found to be asymptomatic; while others present with seizure, weakness, movement symptoms e.g. unsteadiness, walking difficulties, tremors, rigidity and others

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ISSN online 2344-4959
© Romanian Society of Neurosurgery

First published
September 2023 by
London Academic Publishing
www.lapub.co.uk

demonstrate psychiatric symptoms e.g. psychosis, mood disorders or dementia (6). CT scan is considered the gold standard for diagnosis which identifies calcifications as hyperdense lesions typically bilateral and symmetrical, most frequently involving basal ganglia, but also dentate nuclei, thalamus and subcortical white matter (4). In the basal ganglia region, the most common site of calcification is globus pallidus followed by putamen and caudate nucleus (21,5,17,19,20).

CASE REPORT

A 35 years old, non-diabetic, normotensive, non-asthmatic lady (para 2+0) presented to our department with the complaints of recurrent attacks of generalized tonic clonic seizure, occasional headache and vomiting for last 4 months. She had a history of total abdominal hysterectomy with bilateral salpingo-oophorectomy with omentectomy with appendicectomy due to papillary serous cystadenocarcinoma of ovary with multiple hepatic metastases 4 years back. Following surgery, she received 6 cycles of adjuvant chemotherapy (Carboplatin+Paclitaxel) within the next 6 months. After that, she didn't have regular follow up and again presented with the afore mentioned complaints. On examination, she was conscious (GCS 15) with intact higher psychic function and intact cranial nerves.

There was right sided hemiparesis with muscle power MRC grade 4 in all groups; with normal tone and jerks. She underwent an MRI(figure 1 and figure 2) of brain with contrast and it revealed ring enhancing irregular mass in the left frontal lobe with perilesional edema and was diagnosed as a case of cerebral metastasis from recurrence of the Ca-ovary. At that time, tumor marker CA 125 was markedly elevated: 127 U/mL (Normal upto 0-35U/Ml) (12). After initial resuscitation with injectable anticonvulsants and steroids, she was referred to the clinical oncology department and there she was treated with palliative radiotherapy to whole brain; 3DCRT (Photon, 6 MV LINAC), 300 cGy per fraction. She received ten fractions equating to 3000 cGy of total radiation exposure within 14 days.

She had an uneventful recovery (with persistence of hemiparesis) after completing scheduled doses of radiotherapy and was discharged to home with advice for follow up CT scans at every 6 months interval. During her first follow up (after 6 months), she complained of occasional headache. Muscle power of left upper and lower limb was as before (MRC grade 4) with no new neurological deficit and no constitutional symptom. CT scan of brain with contrast was done and it revealed hypodense area indicating radiation necrosis in the previous tumor bed. Moreover, there was calcification in the Globus pallidus of both basal ganglia region which was not evident in previous imaging studies(figure 3).

Biochemical parameters were evaluated and it revealed normal renal function and normal serum calcium, inorganic phosphate and parathyroid hormone. On the basis of above findings, post radiotherapy bilateral basal ganglia calcification was diagnosed.

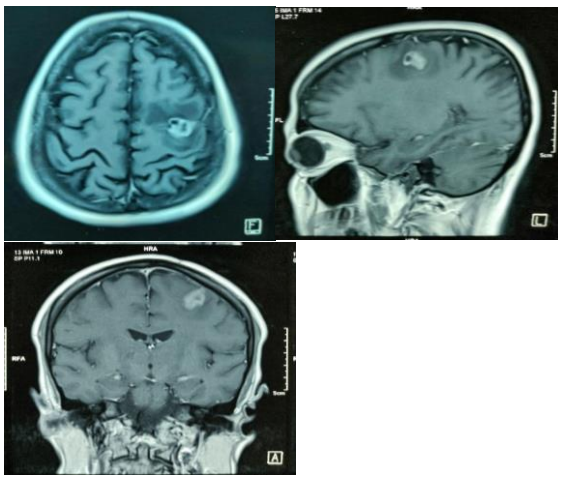

Figure 1. MRI of brain with contrast showing left frontal metastatic SOL with peri lesional edema with no other significant abnormality (before radiotherapy).

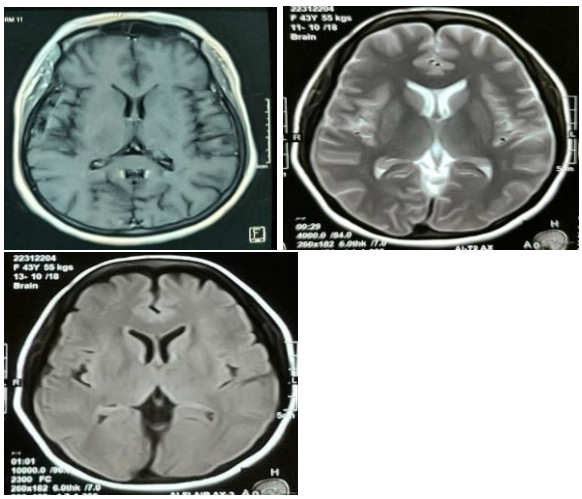

Figure 2. T1,T2, FLAIR sequences of MRI showing no significant abnormality of the basal ganglia region in the same patient (before Radiotherapy).

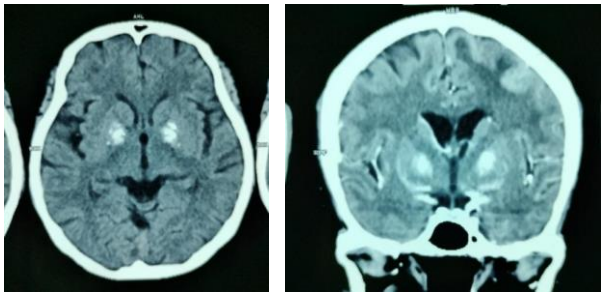

Figure 3. Post radiotherapy CT scan of brain showing symmetrical irregular hyperdensities in both Globus pallidus indicating bilateral basal ganglia calcification.

Discussion

Microscopic description of bilateral basal ganglia calcification was first made by Virchow (10) In 1935 Fritzsche (14) was the first to report roentgenologic appearance of basal ganglia calcification in 3 siblings. Its occurrence in idiopathic hypoparathyroidism was described by Eaton, Camp and Love in 1939 (13).

Basal ganglia calcification in pseudohypoparathyroidism was first reported by Sprague, Hains, and Power in 1945 (15). Its occurrence subsequent to radiation therapy was first described by Harwood-Nash and Reilly in 1970 (12). Intrathecal administration of Methotrexate may produce intracranial calcification (18). Kramer and Lee described a case with diffuse calcification in the basal ganglia and cerebral cortex subsequent to irradiation and methotrexate (intrathecal) treatment for acute lymphocytic leukemia (9). Nakagaki et al. (16) described monkey brain damage from radiation in the therapeutic range. At six months after 6,000 rad, widely scattered punctate necrotic lesions, 1 mm or less, were demonstrated, whereas, 1 year later almost complete mineralization of necrotic lesions with innumerable minute deposits of calcium and iron were observed. Vasculitis and telangiectasia were also present.

Table 1. Previously reported cases of post irradiation basal ganglia calcification (5, 17, 19,20).

Case No	Author	Age (yrs.)	Sex	Pathology & site	Radiotherapy: source, field, site & dose	Duration following radiotherapy	S calcium and PO4
1	Harwood-Nash, Reilly. 1970	9	F	Glioblastoma multiforme in suprasellar region	External cobalt 60. 5 X 5 cm^2 4500 rad/4wks	3 yrs	Normal
2	Harwood-Nash, Reilly. 1970	3	M	Histiocytosis involving multiple areas of the calvarium	200 kV X ray various ports 300 rad X 3 1250 next yr, 1750 following yr	9 yrs	Normal
3	Kramer and Lee 1974	10	M	CNS involvement of lymphocytic leukaemia	External cobalt 60 550 rad Methotrexate	10 months	Normal
4	Numaguchi et al. 1974	9	F	Astrocytoma in Thalamic region	Supervoltage 2 MeV resonant transformer 7 X 7 cm^2 6000 rad/6 wks	6 yrs	Normal
5	Lee and Suh 1976	12	F	Spongioblastoma polare, Right optic nerve	External cobalt 60. 5 X 5 cm^2 5500 rad/5wks	10 yr	Normal
6	Lee and Suh 1976	16	M	Medulloblastoma cerebellar vermis	Total brain and spine axis 4000 rad. 4700 rad to vermis/ 4 wks	14 yrs	Normal
7	A D J Pearson, Campbell et al. 1983	2	-	Medulloblastoma	8 MeV Lateral 18 X 18 cm; 36 doses	5 yrs	-
8	A D J Pearson, Campbell et al. 1983	3	-	Medulloblastoma	8 MeV Lateral 18 X 19 cm; 39 doses	5 yrs	-

9	A D J Pearson, Campbell et al. 1983	4	-	Medulloblastoma	4.2 MeV Lateral 19 X 15 cm; 30 doses	5 yrs	-
10	Terry Lichtor, Robert L. Wollmann et al. 1984	14	-	Medulloblastoma	Total brain 4000 rads and 4000 rads to spine; 27 doses	12 yrs	Normal
11*	P Sanchetee, S Venkataraman et al. 1999						

The pathogenesis of calcification in the grey matter is not clear. Microscopically, vasculitis, fibroblastic process, hyalinization, and calcification were observed in the brains of both humans and animals following irradiation to the heads (17). The possibility of an autoimmune reaction localized to the irradiated demyelinated tissue with subsequent accumulation of abnormal metabolites was suggested by Lampert et al. (7). Babbitt et al. (8) proposed that the ferrocalcinosis is the end result of a process of circulatory disturbance resulting in local anoxia and necrosis. Harwood-Nash and Reilly (12) postulate that hypersensitivity of small vessels of the basal ganglia to radiation produces vascular damage with hypoxia resulting in calcification. A long term follow-up study would be necessary in order to assess the significance and implication of post-irradiation calcification in the grey matter.

Our reported case of post radiotherapy bilateral basal ganglia calcification is about a middle aged female with secondary brain tumor while previously reported cases were children or adolescents with primary brain tumors. Among the previously reported cases (table 1), three of the patients had poor attention and hyperactivity disorders with endocrine abnormalities (5) while our patient did not have any specific sign or symptom.

Conclusion

Basal ganglia calcification may lead to various motor and psychiatric symptoms. While treating any patient with neuraxial radiotherapy, possibility of basal ganglia calcification might be kept in mind. Whether the incidence of basal ganglia calcification is radiation dose related or not, needs to be further studied. All of such patients should be kept under close follow up regimen to ensure quality of life.

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