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Radiation therapy-related ataxia associated with FDG-PET cerebellar hypometabolism

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Abstract

Brain FDG-PET after radiation therapy is classically used to differentiate between tumor recurrence and radiation-related tumor necrosis. Little is known about FDG-PET in patients with radiation-induced leukoencephalopathy without radiological aspect of necrosis. We present a 69-year-old woman who had preventive whole brain radiation after a diagnosis of paraneoplastic Lambert-Eaton syndrome related to small cell lung cancer. Five months after radiation therapy, she developed radiation-induced leukoencephalopathy manifested by ataxia. Profound cerebellar hypometabolism on FDG-PET was in contrast with the presence of only discrete cerebellar white matter changes on MRI. FDG-PET abnormalities seem to correlate better with clinical signs related to radiation-associated brain toxicity than MRI.

Key words: FDG-PET; MRI; leukoencephalopathy; radiation; chemotherapy; cancer; Lambert-Eaton.

Case report

A 69-year-old woman with a history of cigarette smoking presented with rapidly progressive bilateral proximal lower limb weakness associated with dry mouth and involuntary weight loss. Clinical examination revealed generalized proximal limb weakness and reduced deep tendon reflexes. Nerve conduction studies showed small compound muscle action potentials, a decremental response (42%) to 3-Hz repetitive nerve stimulation studies, and an incremental response (2700%) after voluntary muscle contraction. Voltage-gated calcium channel (VGCC) antibody levels were elevated. Whole body FDG-PET revealed hypermetabolism of mediastinal and left hilar lymph nodes, seen on thoracic CT scan. Brain MRI showed apart of some small periventrical T2-hyperintense lesions, probably vascular in origin, no abnormalities. Cognitive tests were normal. Lymph node biopsy revealed a small cell lung cancer. A diagnosis of paraneoplastic Lambert-Eaton syndrome was made. A symptomatic treatment with 3,4-diaminopyridine was started, and combined chemotherapy (cisplatin 100 mg/m^2 and etoposide 75 mg/m^2 2 courses every 4 weeks, lowered by 40% the following 4 courses because of neutropenia) and thoracic radiation was given, followed 6 months later by preventive whole brain radiation (26 Gy in 2 Gy fractions) started.

Five months later, the patient developed vertigo and gait unsteadiness progressively over a few weeks. Clinical examination showed gait and bilateral (left predominant) limb ataxia. Nerve conduction and repetitive nerve stimulation studies, VGCC antibodies, other paraneoplastic antibodies (anti-Hu, -Yo, -Ri, amphiphysin, -Ma1, -Ma2, -CV2), whole body FDG-PET scan, and lumbar puncture (including PCR for JC virus) were normal. Brain MRI FLAIR sequences showed diffuse supratentiorial posterior-dominant leukoencephalopathy and only very slight white matter changes in the cerebellum (Fig. 1), in absence of gadolinium-enhancement. Brain FDG-PET showed moderate frontal hypometabolism, and profound cerebellar hypometabolism with left-sided predominance (Fig. 2). Cognitive tests only showed slight abnormalities (i.e. executive and attentional deficits together with an amnestic syndrome). A diagnosis of brain radiation-induced leukoencephalopathy was made. High dosis of corticoid treatment was given followed by incomplete clinical improvement. Brain MRI 6 months later was unchanged, and slight cognitive deficit and ataxia persisted.

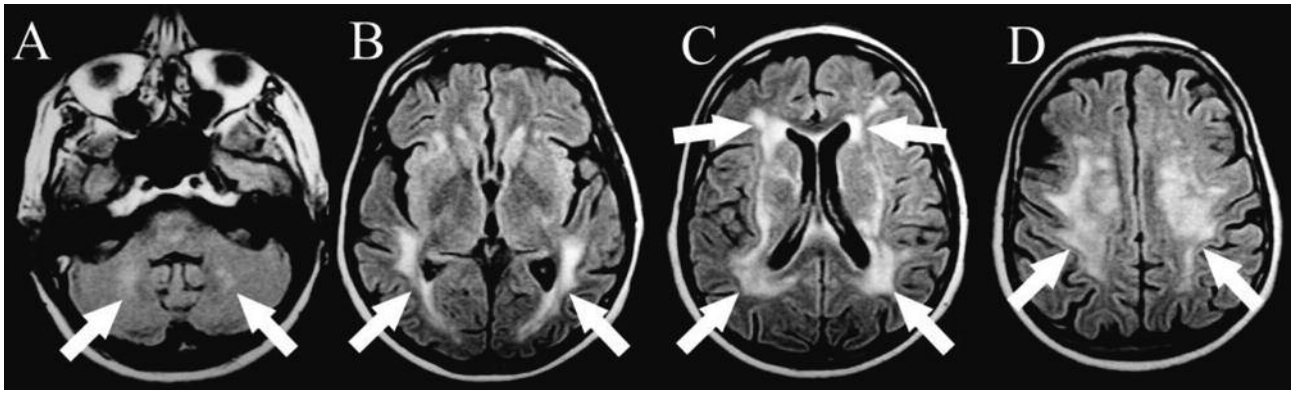

FIG. 1. — Brain MRI showing very slight bilateral white matter changes in the cerebellum (A) and diffuse supratentiorial posterior-dominant leukoencephalopathy on FLAIR sequences (B-D).

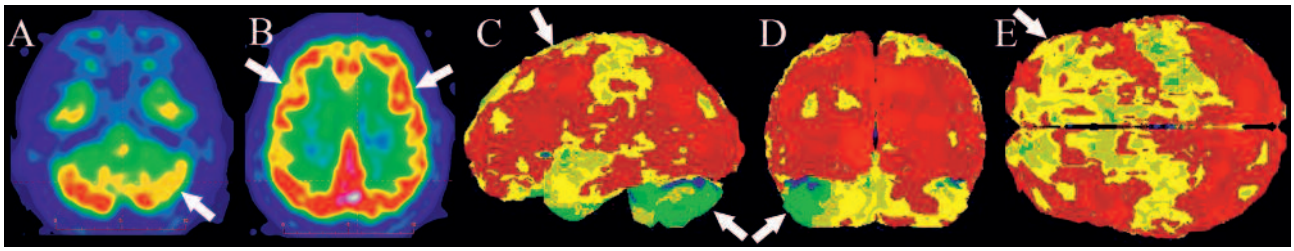

FIG. 2. — Brain FDG-PET (A and B are axial images; C, D, and E are 3D reconstruction images with respectively lateral view, posterior view, and superior view) showing profound left predominant cerebellar hypometabolism (A, C, D) and moderate frontal hypometabolism (B, C, E).

Discussion

FDG-PET after radiation therapy is classically used to differentiate between tumor recurrence and radiation-related tumor necrosis. However, FDG-PET metabolism patterns (hypometabolism in tumor necrosis and hypermetabolism in tumor recurrence) are not specific (Ricci *et al.*, 1998). In our patient, favourable clinical outcome was against a diagnosis of progressive multifocal leukoencephalopathy (and PCR for JC virus was negative), brain lymphoma (and there was no gadolinium enhancement on MRI), and paraneoplastic cerebellar syndrome (and paraneoplastic antibodies were negative). Simultaneous occurrence of diffuse leukoencephalopathy, cognitive decline, and ataxia (and clinical improvement after corticoid treatment) was in favour of radiation-related cerebellar toxicity. The distribution of FDG-PET abnormalities (profound left predominant cerebellar hypometabolism) corresponded better than MRI changes with the clinical symptoms (left dominant ataxia). Radiation-related brain toxicity is most often characterized by dementia, gait abnormalities, and urinary incontinence. Ataxia is a rare manifestation of radiation-related brain toxicity. Few data exist on FDG-PET in patients with radiation-induced leukoencephalopathy without radiological aspect of necrosis (Miyatake *et al.*, 1992; Herholz *et al.*, 2007). Risk factors for developing radiation therapy-related leukoencephalopathy include older age, high doses of radiation, higher daily fractions of radiation, and associated chemotherapy (as in our patient). Frontal FDG-PET hypometabolism in our patient was in contrast with the posterior predominance of the leukoencephalopathy on MRI. Therefore, this frontal hypometabolism might be (at least partially) related to frontal diaschisis secondary to profound cerebellar hypometabolism.

Profound cerebellar hypometabolism on FDG-PET was in contrast with the presence of only discrete cerebellar white matter changes on MRI. FDG-PET abnormalities seem to correlate better with clinical signs related to radiation-associated brain toxicity than MRI.

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