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Case Report

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Cerebral radionecrosis following skin epidermoid carcinoma's irradiation: A case report

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Abstract

Cerebral Radionecrosis is a rare but severe, iatrogenic complication, which occurs in a long period after the cerebral area's irradiation. Indeed, it usually affects radiotherapy-treated patients more than 6 months after the treatment. This phenomenon's pathophysiology is not entirely elucidated yet but radionecrosis is caused by vascular and glial lesions involving the immune system. It provokes different symptoms depending on the irradiated brain's volume. Because the radiation-induced brain damages can become irreversible and lead to a vital and functional prognosis' degradation, this complication needs to be prevented but also supervised by every physician. Usually, cerebral radionecrosis happens through the irradiation of an intracerebral lesion but not only. Here, we present the case of a 65 year-old French male who suffered histologically proven cerebral radionecrosis in 2019 after undergoing irradiation of a removed skin's epidermoid carcinoma in 2017, few years after irradiation of cerebral metastasis. The diagnosis was suspected through cerebral imaging (Magnetic resonance imaging/Computed tomography scan) and confirmed through cerebral biopsy. Afterwards, the patient was treated and clinically imporved by corticosteroids. This complication warns us about the risk of cumulative radiotherapy doses and the absolute necessity of targeted irradiation to avoid eventual side effects as much as possible.

Introduction

Radiotherapy is a major treatment of several tumors, allowing a statistically increased progression-free survival [1]. This treatment can be used alone but also associated with surgery, chemotherapy, immunotherapy. Like every treatment, it can have side effects [2], mainly depending on the irradiated zone. Among them, we will focus on radionecrosis, especially cerebral radionecrosis.

Cerebral radionecrosis is defined as the radiation-induced death of brain cells, due to immunological and vascular mechanisms, that often concerns the white matter [3,4]. This necrosis, radiologically whether revealed by a CT-Scan (Computed Tomogramphy Scan) or a MRI (Magnetic Resonance Imaging) usually appears between 6 to 12 months after the irradiation. This complication often happens after treating a cerebral tumor (glioblastoma, cerebral metastasis) [5,6] or after treating a tumor in the ENT area (such as Undifferenciated carcinoma of the nasopharynx) and might have non-negligible clinical consequences. The main described symptoms are the following ones : consciousness disorders, seizures, dizziness, memory loss and intracranial hypertension symptoms [2,7,8]. The complica-

tion's frequency varies from 5 to 22% according to the previous studies [9-11] but the incidence may be underrated because a surveillance after a cerebral irradiation by CT scan or by MRI has not always been systematical. Moreover, the risk can increase or decrease according to the irradiation site.

Here, we present a case of cerebral radionecrosis following skin irradiation of a surgically removed vertex epidermoid carcinoma.

Patient case

The present case concerns a 65-year-old patient who was followed in pneumology for a left inferior lobe suspicious lesion discovered in 2019.

Regarding his medical record, we notice acute B lymphoblastic leukemia since 2012 treated according to GRAALL 2005 guidelines and with allograft in April 2013, an obesity with gastroplasty in 2012, a Barrett's Esophagus and a dyslipidaemia.

A lobectomy was performed on the 19th June 2019 with hilar and mediastinal lymph node dissection through videothoracoscopy. No complications occured throughout the surgery and the patient went home after respiratory rehabilitation. The pathological examination revealed a epidermoid carcinoma PDL1- 5% with no lymph node invasion in the resected piece and in the dissected nodes. At the time of the surgery: the TNM classification is the following one: pT1c N0 (18N-) stade IA3. After the surgery, a simple monitoring was settled.

In parallel, the patient was seen by our fellow dermatologists for the removal of multiple epidermoid carcinomas, among which in the left ear, left and right forehead respectively in April and October 2018. Besides these locations, our colleagues removed in June 2017 an epidermoid carcinoma in the vertex, with secondary cerebral, skin and nodes localisations treated with occipital metastasectomies, left cervical lymph node dissection, followed by adjuvant radiotherapy located in left and right parieto-occipital area and in left cervical lymph node.

He was then regularly followed in consultation by his dermatologist with control images.

Through his medical process, the patient received two radiotherapy protocols : he was first taken care of by radiotherapists for the treatment of his leukemia where cerebral prophylactic irradiation was performed in April 2013 (10 fractions of 1.5 Gy for a total body irradiation of 15 Gy). Few years later, in 2017, he received 54 Gy divided in 30 fractions of 1,8 Gy in the precedent paragraph mentionned territory for his skin epidermoid carcinoma.

On a control CT Scan of lung cancer in September 2019 an asymptomatic left cerebellum's leptomeningeal enhancement was observed with intracerebral oedema which could be related with a meningeal dissemination. There was no evidence of a thoracic or abdominal recurrence of lung cancer. Clinical and radiological monitoring was decided.

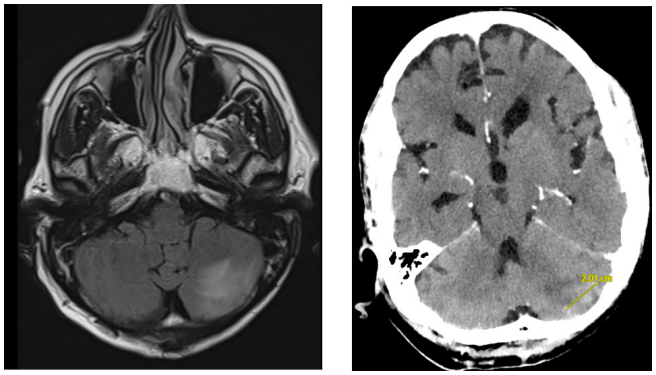

Figure 1: T2 Flair Cerebral Magnetic Resonance Imaging (left) and Injected Cerebral computed Tomography (right) showing the radiological signs of cerebral radionecrosis in the left cerebellus area.

On the 21st November 2019, the patient was hospitalized in neurology with a control MRI showing stable images in comparison to the September CT Scan, which meant the left cerebellum lesion didn't grow. The patient underwent a lumbar puncture to exclude the carcinomatous meningitis hypothesis. The results showed elevated proteins (0.6 g/L) without reduced glycorachy. No abnormal cells were noticed in the pathological examination. The spinal MRI as well didn't show any abnormalities. This hospitalization didn't gather enough evidence to conclude to carcinomatous meningitis

The patient is then followed by control MRI's and his record is discussed in multidisciplinary consultation meeting, in which an indication of cerebral biopsy is retained.

The biopsy was performed in July 2020 an found superficials necrosis areas with leptomeningeal thickening. The homogenous necrosis' aspect with vascular sclerohyalinosis make us evoke radionecrosis' foci. No argument was found for a metastasis, an infection or another tumor.

After this radionecrosis diagnosis, the patient was followed by his neurologist who performed regular MRI's. In June 2020, the MRI showed a growth of the left cerebellum lesion with appearance of cortical bilateral occipital and left parietal lesions.

Regarding the clinical symptoms, our patient described disabling anterograde amnesia, and balance loss when standing still or walking. However, our patient didn't show any clinical static or kinetic right cerebellum syndrome.

Afterwards, the patient was treated during 3 months with corticosteroids 1 mg/kg. After the treatment, the patient didn't evoke any neurological clinical symptoms, particularly no balance loss, no signs of intracranial hypertension, no seizures, no cerebellum syndrome's signs.

His last CT Scan was performed on 23rd December 2021, where we objectified this left cerebellum hypodense lesion, which was stable in comparison with the last cerebral CT Scans realized. Moreover, the cortical contrast enhancement was also stable, measuring 25 mm. No new lesion and no other contrast enhancement was observed.

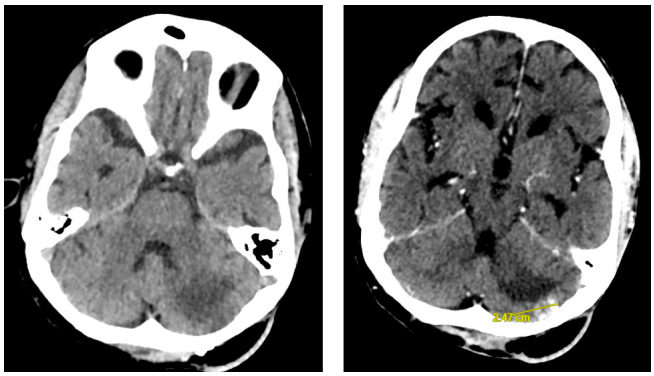

Figure 2: Non Injected (Left) and Injected (right) Cerebral computed Tomography showing the radiological signs of cerebral radionecrosis in the left cerebellus area.

Discussion

Radiotherapy is a major treatment of many different tumors, who proved his efficacy in increasing the progression-free survival. Besides her positive impacts, many sides effects may be explained by radiation-induced damages, some being acute side effects and some being chronic ones happening few months after the treatment's end [1,4].

Cerebral radionecrosis represents a challenging situation for many reasons.

First, the risk factors of this complication remain unpredictable. Various risk factors [4] have been found to help increasing the complication's incidence. Among them, we can mention a dose higher than 60 Grays [13], a split dose higher than 2 Grays, low number of fractions' dose [12,14], an important irradiations' volume, a neurotoxic associated chemotherapy (platinum salts, doxorubicin) [15] and preexistant cardiovascular risk factors (hypertension, diabetes, hyperlipidemia…).

Secondly, the radiological signs (CT scan hypodense lesions, oedema around the lesion observed in MRI) are not specific at all [16], and can be confused with a carcinomatous meningitis or with a tumor reccurence [17,18]. In parallel, the diagnosis needs to be accurately made as fast as possible because it influences our therapeutic strategy. Thereby, as it happened for our patient, we often need to realize the lesion's biopsy so that we perform a pathological examination in order to affirm the diagnosis and to deliver appropriate treatment. Indeed, treatments like Corticosteroids [19] or Bevacizumab [20,21] can be delivered to lower the radionecrosis' clinical consequences and a clear diagnosis avoid using radiotherapy to treat a carcinomatous meningitis which turns out to be a radionecrosis.

Lastly, because the differential diagnosis can be difficult, our patients can suffer a delayed diagnosis with clinical repercussions and worse prognosis. This challenge needs to be known by every physician taking care of oncology patients in order to carefully watch the control images and to, if applicable, deliver the optimal radionecrosis' treatment according to the most recent recommandations .

Thus, this case brings us to emphasize the major contribution of pathological's examination in order to affirm ou refute diagnosis. Indeed, even though the MRI or CT Scan are massively evolving [22] to help for the differential diagnosis between radionecrosis and tumor recurrence, the pathological examination enabled us to entirely define the patient's evolutive lesion as radionecrosis [23]. For instance, lesions such as fibrinoid necrosis with occlusion of the lumina, and inflammatory areas with focal perivascular lymphocytes and inflammatory ghost cells are some pathological specificities of late cerebral radionecrosis nd make us evoke this diagnosis as soon as they are found in histological tissues.

Therefore, the pathological examination help physicians avoid analyzing a radionecrosis lesion as a cerebral metastatic progression, which would have had major and possibly unwanted impacts on therapeutic strategies. Instead, we managed to treat it as recommended [24] and with an efficacy which stabilized the radionecrosis' lesion and overall the clinical state of our patient, especially regarding the neurological symptoms.

Conclusion

The intention of this case report was to increase awareness about monitoring one of the radiotherapy's adverse effects. Up to our knowledge, this might be the first case of cerebral radionecrosis induced by skin radiotherapy. We also wanted to emphasize the importance of an accurate diagnosis of this entity, that can be confused with other etiologies, because it strongly affects the resulting therapeutic perspectives.

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