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Abnormal growth of Virchow-Robin spaces secondary to radiotherapy☆

Crecimiento anormal de espacios de Virchow-Robin secundario a radioterapia

Dear Editor:

The terms perivascular space or Virchow-Robin space (VRS) refer to the spaces surrounding the vessels supplying the brain parenchyma, and constitute a separate structure from the subarachnoid space. In MRI studies, dilated VRS typically appear as round or linear shapes and are isointense to cerebrospinal fluid (CSF) on all sequences. Generally, the parenchyma surrounding these spaces presents normal signal intensity. While they usually appear in typical locations (basal ganglia, subcortical white matter, midbrain), dilated VRS may occur in practically any location.[1]

Dilated VRS are a frequent neuroimaging finding, and their prevalence is greater in elderly individuals or patients with small-vessel disease, associated with lacunar stroke and vascular leukoencephalopathy.[2,3] Despite this, the mechanism by which these spaces become dilated remains unclear; multiple theories have been proposed, including increased arterial wall permeability, alterations in CSF drainage, spiral elongation of blood vessels, and brain atrophy. A correlation has been described between dilated VRS and neuropsychiatric disorders, multiple sclerosis, traumatic brain injuries, and microvascular diseases.[1,4] Some of these situations are equivalent in pathological terms to the effects of radiotherapy, such as white matter oedema, demyelination, fibrinoid changes in blood vessels, coagulative necrosis, and cysts with liquefied centres and peripheral gliosis.[5] Recently, brain radiotherapy has been proposed as a likely cause of dilated VRS.[6,7]

We present the case of a 63-year-old man who attended the emergency department due to a seizure in 2012, reporting similar episodes of absence seizures in the previous months, with no other relevant personal history. An emergency head CT scan revealed an intra-axial lesion in the right frontal lobe. The study was subsequently expanded with an MRI scan and a biopsy study, which confirmed the diagnosis of diffuse astrocytoma with foci of anaplastic transformation. Four months later, the patient started chemotherapy (temozolomide) and radiotherapy, with a total dose of 60 Gy in fractions of 2 Gy/day between October and November 2012. The patient subsequently underwent clinical and neuroimaging (MRI) follow-up by the oncology department.

The follow-up brain MRI scan performed in 2017 detected a new cystic lesion in the right corona radiata, which displayed progressive growth in subsequent studies (Fig. 1). Clinical examination identified no new neurological alterations or deficits. The lesion was cystic and septated, isointense to CSF on all sequences, was not surrounded by oedema or gliosis, and presented no diffusion restriction or contrast enhancement. It was located in the radiation field and surrounded by multiple punctiform haemorrhagic foci, visible on magnetic susceptibility sequences, in the adjacent white matter (Fig. 2).[8]

In the light of these findings, differential diagnosis may include cystic neoplasm, infectious lesions, or ischaemic lesions. Purely cystic brain neoplasms are extremely rare, and the absence of oedema or contrast uptake makes this diagnosis highly unlikely. The lack of associated symptoms or diffusion restriction allows us to rule out such infectious lesions as abscesses. The absence of adjacent or distant white matter alterations and the progressive growth of the lesion favoured a diagnosis of dilated VRS, rather than a lacunar ischaemic lesion.

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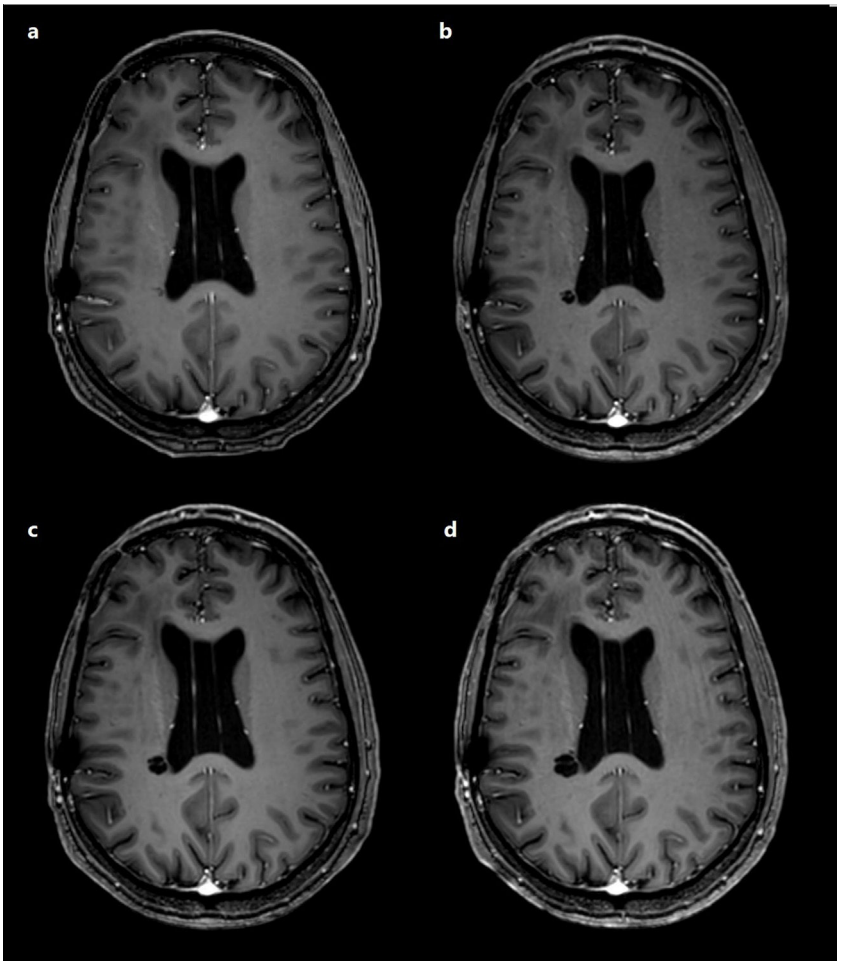

Figure 1 Contrast-enhanced T1-weighted 3D-SPGR MRI studies: follow-up studies performed in 2017, 2018, 2019, and 2020 (images a-d, respectively). The images show progressive growth of a round lesion in the right corona radiata, isointense to CSF and without enhancement.

Table 1 Similar cases from the literature.

Article	N.° cases	Time between RT and appearance (years)	Localisation	Total dose (Gy)
Gopinath et al.[6]	1	5	Basal ganglia, bilateral	Not reported
Mark et al.[7]	2	6	Basal ganglia, unilateral	54
		8	Basal ganglia, unilateral	54

RT: radiotherapy.

All these findings further support the diagnosis of a benign process, such as new dilated VRS in a patient undergoing radiotherapy. Its localisation, within the radiation field, and the delay between radiotherapy and detection of the lesion (approximately 5 years) are consistent with the findings reported in similar cases by Gopinath et al.[6] and Mark et al.[7] (Table 1); we therefore consider that radiotherapy probably caused the dilation of the VRS.

In conclusion, understanding of the mechanisms by which radiotherapy acts on the central nervous system and the evidence discussed above lead us to suspect radiation as the cause of the dilated VRS. Although this finding is not pathologically significant, it should be taken into account in the differential diagnosis of patients receiving radiotherapy, in order to prevent misdiagnosis as conditions that may require other courses of action, with potentially harmful consequences.

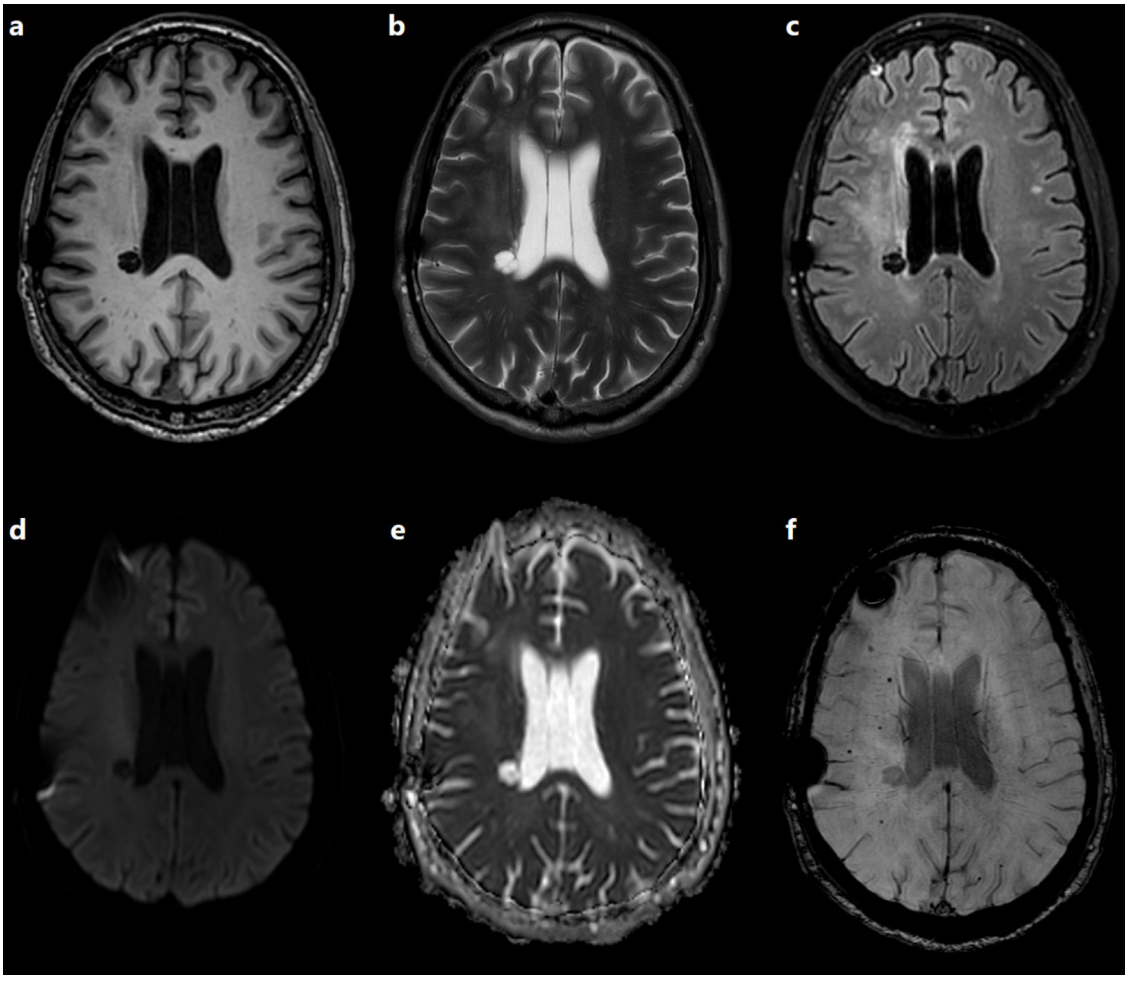

Fig. 2 Status of the lesion in an MRI study performed in 2020. a) Non-contrast T1-weighted 3D-SPGR sequence; b) T2-weighted TSE sequence; c) 3D T2-FLAIR sequence; d) diffusion sequence (b = 1000); e) ADC map; f) magnetic susceptibility sequence. The lesion is isointense to CSF on T1- and T2-weighted sequences (a, b), and presents signal suppression on T2-FLAIR sequences (c), which suggests free water in the centre and absence of peripheral oedema or gliosis; it also presents facilitated diffusion (d, e). The magnetic susceptibility sequence shows hypointense haemorrhagic foci near the lesion, within the radiation field (f).

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Reply to: Factors related to immediate response to symptoms in patients with stroke or transient ischaemic attack☆

Respuesta a: Factores relacionados con una respuesta inmediata a los síntomas en pacientes con ictus o accidente isquémico transitorio

Dear Editor:

It was with great interest that we read the article by García Ruiz et al.[1] published in your journal under the title ''Factors related to immediate response to symptoms in patients with stroke or transient ischaemic attack.'' This study demonstrates that when stroke is witnessed by a patient's daughter/son and presents greater severity, the delay in seeking help for stroke symptoms is reduced; emergency departments of hospitals in the Spanish national healthcare system are the main medical contacts in these cases[1]. We observed the same findings in our sample of 425 patients from Northern Spain,[2] and similar factors have been associated with earlier hospital arrival in other countries[3]; therefore, these findings are robust and can be generalised. Another recurrent finding is that the number of patients contacting emergency services to seek help is much higher among patients seeking help in the first 15 minutes than among those seeking help later.[2,3] Unexpectedly, the reason for later hospital arrivals in cases in which emergency services were not contacted is not the transport time, but rather longer delays in seeking help.[2] The reduced delay when stroke is witnessed by a patient's daughter/son may be explained by 2 facts: the witness may better identify the need for help; and witnesses are more easily able to seek assistance than a patient who is alone at stroke onset. However, the fact that greater stroke severity, regardless of the presence of a daughter/son, decreases the delay in seeking help suggests that the perception of the need for help reduces this delay more than stroke-derived motor impairment increases it. As extended families with grandparents, parents, and grandchildren living together continue to be replaced by nuclear families, help-seeking by a witnessing daughter/son will become less frequent. In stroke care protocols, time to hospital arrival is the longest; as has been observed in many countries during the COVID-19 epidemic, it is also the most likely to be affected by external circumstances[4] and shows the most room for improvement. Therefore, we concur with García Ruiz et al.[1] that public awareness campaigns on emergency responses to stroke should stress the importance of immediate action in the event of mild symptoms, and focus on individuals presenting vascular risk factors or living alone.

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