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During the preparation of this manuscript the Authors used Claude (Anthropic) to English language and readability of the text, and to write a Python script to assemble the figure panels. No text content or images was generated by artificial intelligence. Figures were assembled from axial MR images exported unmodified from the hospital PACS. Processing was limited to cropping of the black background, uniform scaling of each panel to a common height and composition into a single panel.

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Introduction

Reports of diagnostic error often blame inattention. In this case, the failure was largely metacognitive, driven by a fixation and anchoring bias[1].

An unvaccinated 41-year-old man presented with subacute cortical visual loss, motor aphasia and ideomotor slowing. Despite an exhaustive diagnostic workup – including multiple MRIs, serial EEGs, repeated lumbar punctures and a brain biopsy – the clinical team remained stuck in an inherited radiological label. This anchoring and diagnostic momentum[2] prevented clinicians from reevaluating their own clinical reasoning.

In an era where measles is resurging[3-4], overcoming such cognitive fixation is critical to recognizing late complications like subacute sclerosing panencephalitis (SSPE).[5]

Case presentation

A 41-year-old man presented with three days of acute visual decline on a background of one year of anorexia with 7 kg weight loss and intermittent headache. He used cannabis heavily. He reported measles seven years earlier, requiring hospital admission for high fever, severe headache, bilateral conjunctivitis, and pneumonia. Initial computed tomography, laboratory studies and ophthalmological assessment were unremarkable, and he was discharged for elective MRI. That study showed focal T2/FLAIR hyperintensity of the left occipital pole with marked vasogenic oedema, sulcal effacement, mild midline shift and minimal enhancement, and was reported as highly suggestive of posterior reversible encephalopathy syndrome (PRES) (Fig. 1).

He re-presented on Day 0 with ideomotor slowing, word-finding difficulties and right upper limb dysaesthesia. He was normotensive. Examination showed motor aphasia, right homonymous hemianopia, apractic ocular pursuit, dyschromatopsia and right upper limb agraphaesthesia. Total-body computed tomography, a serum autoantibody panel and electroencephalography were non-contributory, and ophthalmology reported a severe bilateral visual deficit of neurological origin without primary ocular damage. Day 1 cerebrospinal fluid was clear, with protein 0.58 g/L, 4 leukocytes/µL, oligoclonal IgG bands and a Link index of 0.68; a twelve-pathogen virology panel – including rubella virus – was negative, and intrathecal antibody indices were measured for herpes simplex and varicella-zoster virus. The working diagnosis remained PRES, label reported also in MRI on Days 3 and 7.

Clinically he deteriorated to confusion, cortical blindness with bilateral threat extinction, and oculomotor and buccofacial apraxia. By the end of Day 10 he was in deep sopor (Glasgow Coma Scale 7) and was transferred to the neurocritical care unit. MRI on Day 13 showed progression with new involvement of the splenium of the corpus callosum and bilateral occipital cortical restricted diffusion; the report concluded that the findings suggested an evolving inflammatory process rather than typical PRES and urged urgent clinico-laboratory correlation. This written challenge was the point at which the working diagnosis was abandoned.

Lumbar puncture was repeated on Day 14 with measles-specific antibodies added. CSF measles PCR returned negative on Day 15. Given the rapid evolution and persisting diagnostic uncertainty, a left occipito-polar brain biopsy on Day 18 confirmed encephalitis, demonstrating a dense histiocytic and macrophagic infiltrate with perivascular lymphocytes, astrogliosis and spongiosis. On Day 20 the laboratory reported intrathecal measles IgG synthesis with an antibody index of 14.7 (pathological >1.5) on the stored Day 1 specimen, establishing SSPE on two major Dyken criteria[6]; the Day 14 index was 42.5. Interferon-alpha, lamivudine and inosine pranobex produced no response. A further MRI on Day 25 showed continued progression, with confluent bilateral posterior involvement extending to the splenium of the corpus callosum and to capsulo-mesencephalic and pontine structures, and with restricted diffusion in the affected territory

(Fig. 2); spectroscopy showed N-acetylaspartate depletion with elevated myo-inositol and lactate. Seizures and progressive dysautonomia supervened, and he was declared brain-dead on Day 30.

Discussion

Table 1 maps each diagnostic cue against the day it was documented and the day it was acted upon; the intervals are the substance of this report. We recognize that retrospective reconstruction inflates the salience of cues embedded at the time in a far larger volume of concurrent data.

Table 1 – Diagnostic cues: when they were documented and when they were acted upon

Diagnostic cue	First documented	Acted upon	Interval
Unvaccinated status and remote measles requiring hospital admission	Day −7 (first ED visit)	Day 14 (measles-specific CSF antibody requested)	21 days
Cortical visual syndrome: reduced acuity, right homonymous hemianopia, dyschromatopsia, ocular pursuit apraxia	Day 0	Day 14	14 days
Ophthalmology: severe bilateral visual deficit of neurological origin, no primary ocular damage	Day 1	Day 14	13 days
No identifiable PRES precipitant (normotensive throughout; no eclampsia, renal failure, cytotoxic or immunosuppressive exposure)	Day 0	Day 13	13 days
Progressive, non-remitting deterioration despite supportive care	Day 2	Day 13 (MRI report questioning PRES)	11 days
Oligoclonal IgG bands in CSF with a normal Link index (0.68)	Day 1	Day 14	13 days
Intrathecal antibody index performed for HSV 1-2 and VZV but not for measles	Day 1	Day 14	13 days
Twelve-pathogen CSF virology panel including rubella but not measles	Day 4–6	Day 14	8–10 days
Measles-specific antibody index 14.7 on the Day 1 CSF specimen	Not looked for (ideally	Reported Day 20	19 days

Diagnostic cue	First documented	Acted upon	Interval
	obtainable Day 1)		

CSF, cerebrospinal fluid; ED, emergency department; HSV, herpes simplex virus; PRES, posterior reversible encephalopathy syndrome; VZV, varicella-zoster virus. Day 0 denotes the second emergency department presentation; the first occurred approximately seven days earlier.

PRES without a precipitant is not PRES, and reversibility cannot be asserted prospectively

PRES occurs in a defined context: abrupt hypertension, pre-eclampsia or eclampsia, renal failure, autoimmune disease, or exposure to cytotoxic or immunosuppressive agents[7]. Our patient was normotensive, with normal renal function and no relevant medication; chronic cannabis use is not an established cause. The absence of a precipitant was documented on Day 0 and was not treated as a problem until Day 13. Reversibility is a retrospective attribute, established by observing resolution once the precipitant is removed[7], yet our patient deteriorated for 30 days, with no interval of radiological or clinical improvement at any point (Figs. 1, 2). By Day 2 the trajectory was already incompatible with the diagnosis. The diagnosis was nonetheless re-examined only when imaging contradicted it eleven days later, inverting the appropriate hierarchy: the clinical course was both the more informative and the more timely datum. Table 2 summarises the bedside discriminators.

Table 2 – Distinguishing PRES from adult-onset subacute sclerosing panencephalitis

Feature	PRES	Adult-onset SSPE
Precipitant	Required: abrupt hypertension, pre-eclampsia or eclampsia, renal failure, autoimmune disease, cytotoxic or immunosuppressive drugs	None
Course	Evolves over hours to days; resolves over days to weeks once the precipitant is removed	Progressive over weeks to years; death within 6 months in the acute fulminant variant
Visual findings	Cortical visual loss, common and reversible	Cortical visual loss, often the presenting syndrome; also chorioretinitis and optic atrophy
MRI	Posterior-predominant vasogenic oedema, regressing on follow-up; diffusion usually facilitated, restriction atypical	Parieto-occipital subcortical T2/FLAIR hyperintensity extending to corpus callosum, thalami and brainstem on follow-up; cortical diffusion restriction; low N-acetylaspartate with high myo-inositol and lactate

Feature	PRES	Adult-onset SSPE
EEG	Normal or non-specific slowing	Periodic (Radermecker) complexes in 65–83%, but absent in fulminant and in some adult-onset cases
CSF	Normal	Normal routine parameters; oligoclonal bands; measles-specific antibody index >1.5 (frequently >4); measles PCR negative
Decisive test	Identification of a precipitant and documented reversibility	Measles-specific intrathecal antibody index

CSF, cerebrospinal fluid; EEG, electroencephalogram; MRI, magnetic resonance imaging; PCR, polymerase chain reaction; PRES, posterior reversible encephalopathy syndrome; SSPE, subacute sclerosing panencephalitis

The cortical visual syndrome was localising

The presentation was not “visual loss” but a bi-occipital and parieto-occipital cortical syndrome: reduced acuity, homonymous hemianopia, dyschromatopsia and apractic ocular pursuit, progressing within days to cortical blindness with bilateral threat extinction and buccofacial apraxia. Ophthalmology confirmed on Day 1 that the deficit was neurological, without primary ocular damage. Ophthalmological involvement occurs in up to 42% of SSPE and may precede neurological signs by weeks to years[5]; in adult-onset disease it dominates, with 8 of 13 virologically confirmed adult cases presenting with purely ophthalmological symptoms against 2 opening with behavioural change, the classic paediatric first stage[8]. The diagnostic weight of this syndrome was lost precisely because it was congruent with the working hypothesis: cortical visual loss is compatible with PRES, so a finding that should have narrowed the differential instead reinforced the anchor[1].

The exposure was in the chart; the latency lay outside the window we search

The remote measles infection and the absence of any vaccination were both recorded at the first emergency department contact, and neither generated a hypothesis for three weeks. The reason is structural: clinical histories are searched backwards over days to months, whereas SSPE has a median latency of 9.5 years[5]. Our patient's seven-year interval sat squarely within the canonical 7–10 year window[3,9], and the primary infection had been severe enough to require hospital admission. Adult-onset cases compound the difficulty, presenting at a mean age of 25.4 years with latencies of up to 25 years[8]. The remedy is a question rather than a reflex: in adults with a progressive cortical syndrome of unclear cause we would ask directly about measles history and vaccination status.

Measles was not on the panel, and PCR was the wrong test

Two findings in this case seem to us the most generalisable. First, the Day 1 CSF virology panel interrogated twelve agents, although omitting measles. Second, intrathecal antibody indices were performed on that same specimen, for herpes simplex and varicella-zoster virus. The assay was run, the sample was adequate and the result was reportable; only the measles target was absent from the request. When measles was added on Day 14 and applied retrospectively to the stored Day 1 aliquot, the antibody index was already 14.7.

The test that was eventually requested first was also the wrong one. A negative CSF measles PCR is the expected result in SSPE: biased hypermutation concentrated in the

matrix (M) gene yields a matrix protein that can no longer support virion assembly, so spread occurs trans-synaptically rather than by release of free virus[5,10]. SSPE is a non-productive infection, and the literature warns explicitly that when PCR is the only CSF investigation performed the result misleads and delays diagnosis[9]. Nor does a normal global index exclude the diagnosis: our Day 1 Link index was 0.68 despite oligoclonal bands, and a markedly elevated pathogen-specific index alongside a normal total index is the signature of a microorganism-driven rather than polyspecific response, which in SSPE exceeds even that of multiple sclerosis[11]. Electroencephalography was never going to resolve the question either: periodic (Radermecker) complexes and periodic myoclonus were absent throughout, as in three of the thirteen reviewed adult-onset patients[8] and as described in the acute fulminant variant, in which the shortest reported interval from diagnosis to death is 19 days[5,12]. The diagnosis was always going to be serological.

Conclusion

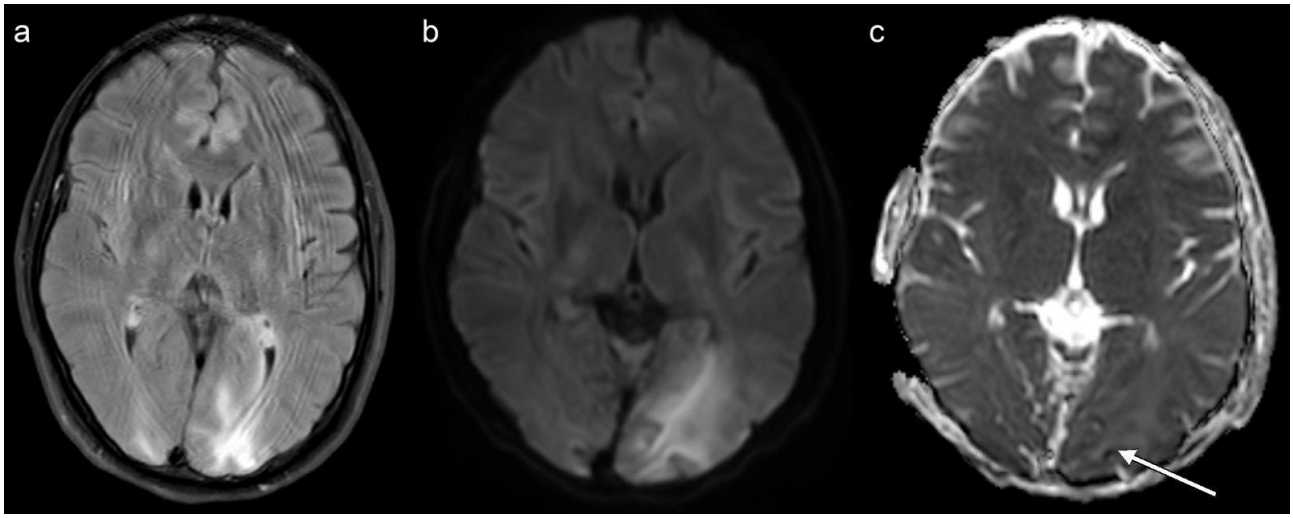
A 41-year-old unvaccinated man died of a late complication of a vaccine-preventable infection, carried for 13 days under a diagnosis that the bedside findings had already refuted. The workup was thorough; the architecture of the reasoning, and the composition of the panels that framed it, were not. Earlier recognition would probably not have altered survival – there is no disease-modifying therapy for SSPE[13] and the patient had reached the equivalent of Dyken stages III–IV before treatment began – but it would have avoided empirical immunotherapy, under consideration while autoimmune encephalitis remained in the differential, and allowed accurate prognostication and earlier palliative support. Where measles is resurgent, measles-related central nervous system disease must re-enter both the differential diagnosis of progressive cortical syndromes and the panels we order. No improvement in our reasoning, however, would have saved this patient: the incidence of SSPE tracks vaccination coverage[5,14], and the only intervention that would have changed this outcome preceded his admission by four decades.

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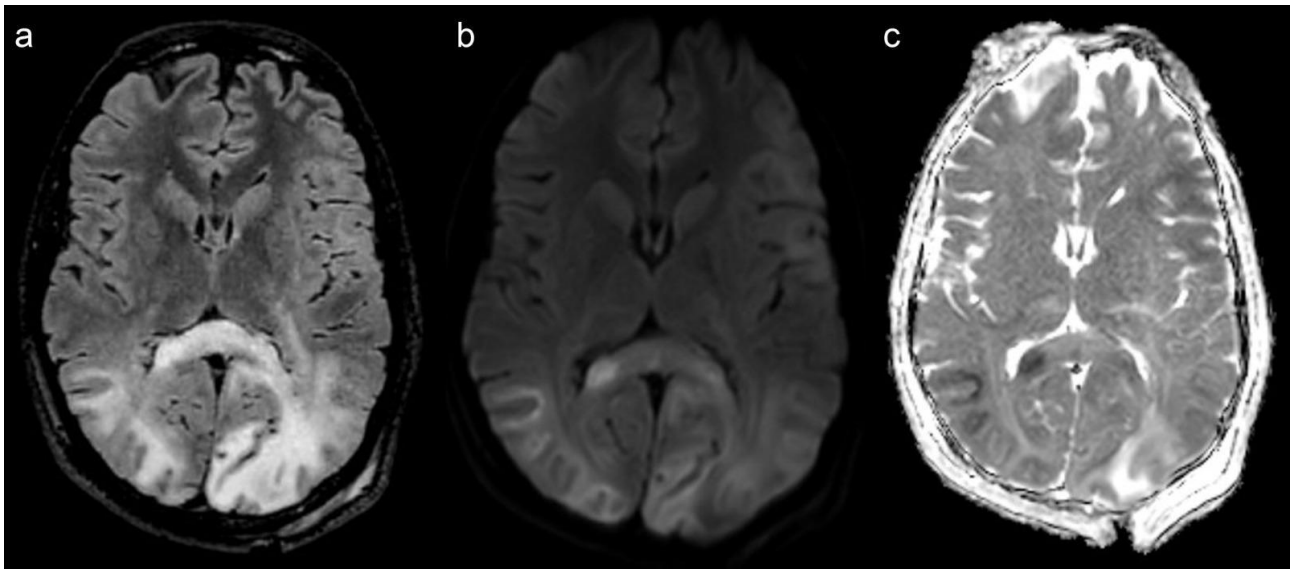
Figure legends

Fig. 1 Magnetic resonance imaging at presentation: the study that generated the diagnosis of PRES



Axial images from the presentation study at comparable levels; c is the apparent diffusion coefficient map derived from the acquisition shown in b, so the two are directly comparable. a FLAIR shows occipital hyperintensity, more marked on the left, with vasogenic oedema and sulcal effacement. b Diffusion-weighted imaging shows high signal in the same territory. c The apparent diffusion coefficient map shows, at the left occipital pole (arrow), iso- to faintly hyperintense rather than hypointense signal, indicating facilitated diffusion: the high signal in b therefore represents T2 shine-through and not true restriction. This combination – posterior-predominant distribution, vasogenic oedema and absence of true diffusion restriction – is radiologically compatible with posterior reversible encephalopathy syndrome, and the study was reported as highly suggestive of it. Nothing in this examination refuted the diagnosis; the discriminating change appears only on follow-up (Fig. 2).

Fig. 2 Day 25, after brain biopsy: progression of parenchymal involvement and conversion to cytotoxic oedema



Same three sequences as Fig. 1, acquired on Day 25, seven days after the left occipito-polar biopsy; post-surgical changes are visible at the left occiput and should not be read as disease. a FLAIR shows marked progression of parenchymal involvement, now confluent and bilateral in the posterior white matter, with extension to the splenium of the corpus callosum. b Diffusion-weighted imaging of the same study. c The corresponding apparent diffusion coefficient map. Cortical diffusion restriction had appeared by Day 13; read

against Fig. 1c, in which the apparent diffusion coefficient was iso- to faintly hyperintense, this documents the conversion from vasogenic to cytotoxic oedema over the course of the admission. That conversion, in a patient with no identifiable precipitant and no interval of clinical or radiological improvement, is the single most discriminating radiological observation in this case and is incompatible with posterior reversible encephalopathy syndrome.