CASE REPORT

Posterior fossa progressive multifocal leukoencephalopathy: first presentation of an unknown autoimmune disease

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SUMMARY

We present a case of a 57-year-old man who presented with progressive cerebellar ataxia and cerebellar ataxia. Additional investigations confirmed the diagnosis of progressive multifocal leukoencephalopathy (PML) in the posterior fossa. This is a demyelinating disease of the central nervous system, caused by an opportunistic infection with John Cunningham virus. PML has previously been considered a lethal condition, but because of careful monitoring of patients with HIV and of patients using immunosuppressive drugs, it is discovered in earlier stages and prognosis can be improved. Our patient had no known immune-compromising state, but further work-up revealed that the PML was most likely the first presentation of a previous untreated autoimmune disorder: sarcoidosis.

BACKGROUND

Progressive multifocal leukoencephalopathy (PML) is a life-threatening demyelinating disease of the central nervous system (CNS) caused by a viral infection, usually encountered in immune-compromised patients.1 With this case, we illustrate that physicians should also be aware of PML in supposedly immune-competent patients.

CASE PRESENTATION

A 57-year-old man presented at a regional hospital with a 3-month history of gradually worsening of articulation and right-sided coordination problems. His medical history mentioned Raynaud phenomenon and transient muscle complaints with spontaneous normalised positive antinuclear antibodies (ANA) 15 years ago. Neurological examination revealed a cerebellar dysarthria and ataxia of his right arm and leg.

INVESTIGATIONS

MRI scanning of the brain showed non-specific white matter lesions in both cerebellar hemispheres, without contrast enhancement or diffusion restriction. Routine blood serum and cerebrospinal fluid (CSF) examinations were normal. ANA and extractable nuclear antigens (ENA) were increased; the antineutrophil cytoplasmic antibodies were negative. The patient clinically deteriorated during the following week and was referred to our university hospital for further work-up. Repeated CSF examination showed a mild mononuclear pleocytosis of 19 cells/mm³. Repeated brain MRI (figure 1) showed progressive white matter lesions (hyperintense on fluid-attenuated inversion recovery (FLAIR) and T2-weighted images and hypointense on T1-weighted images) displaying subtle peripheral diffusion restriction. Serum serological tests for Lyme disease, syphilis and HIV were negative. Additional laboratory findings showed a low CD4 count (0.24×10⁹/L) and the angiotensin-converting enzyme (ACE) in serum was minimally increased (54 U/L). CSF cytology and PCR for cytomegalovirus, herpes zoster and herpes simplex virus 1 and 2 were negative. Paraneoplastic antibodies were also negative. Eventually, PCR for John Cunningham virus (JC virus) was positive in the CSF. Finally, a whole-body [¹⁸F]fluorodeoxyglucose positron emission tomography (PET)–CT showed symmetric mediastinal and hilar lymphadenopathy with increased tracer uptake, consistent with sarcoidosis.

DIFFERENTIAL DIAGNOSIS

Initial differential diagnostic thoughts were among others opportunistic viral infections, acute disseminated encephalomyelitis (ADEM) and neurosarcoidosis. But imaging findings were not fully consistent with both ADEM and neurosarcoidosis.

Finally, the positive PCR for JC virus, combined with clinical and radiological features, made a clear diagnosis: PML.2 Further work-up made an underlying autoimmune disease plausible.

OUTCOME AND FOLLOW-UP

Our patient deteriorated fast suffering from progressive ataxia of both arms and legs, severe dysarthria, swallowing difficulties, behavioural changes and depression. He declined any further diagnostic work-up; therefore, histopathological evidence of a suspected underlying immune-suppressive disease is not available. Treatment with mirtazapine was started, unfortunately without any measurable clinical improvement. The patient died about 2 months after first presentation. We obtained no obduction.

DISCUSSION

PML is a demyelinating disease and a rare complication of an opportunistic JC virus infection; a polyomavirus that infects >50% of the world’s population.1 Clinical symptoms depend on the location of demyelination of the CNS. Most common locations are the frontal or parieto-occipital
Progressive multifocal leukoencephalopathy (PML) can be diagnosed with the triad of compatible clinical features, compatible imaging findings and positive cerebrospinal fluid PCR for John Cunningham virus; a brain biopsy is not necessary.

Although relatively rare, PML can present in the posterior fossa structures.

Consider PML in your differential diagnosis, even when there is no known immune-compromising state.

When PML is diagnosed search for an underlying cause: typical causes (untreated HIV) or the use of immune-suppressive drugs or atypical causes (unknown or untreated inflammatory/autoimmune disease).

Unusual presentation of more common disease/injury

Figure 1 Follow-up MRI of the brain. Transverse T2-weighted image, diffusion-weighted image (DWI) and corresponding apparent diffusion coefficient (ADC) map (left to right). Transverse T2-weighted image of the posterior fossa shows confluent hyperintense white matter changes in both cerebellar hemispheres. On the right more than left side, there is extension through the middle cerebellar peduncle into the brainstem. DWI depicts high signal in the periphery of the white matter lesions left more than right (arrowheads) with corresponding low signal on the ADC map (arrowheads), consistent with restricted diffusion. There was no contrast enhancement (not shown).

Learning points

- Progressive multifocal leukoencephalopathy (PML) can be diagnosed with the triad of compatible clinical features, compatible imaging findings and positive cerebrospinal fluid PCR for John Cunningham virus; a brain biopsy is not necessary.
- Although relatively rare, PML can present in the posterior fossa structures.
- Consider PML in your differential diagnosis, even when there is no known immune-compromising state.
- When PML is diagnosed search for an underlying cause: typical causes (untreated HIV) or the use of immune-suppressive drugs or atypical causes (unknown or untreated inflammatory/autoimmune disease).

Contributors  PS: main contributor, manuscript concept and design. PK: contributor of the radiological data and conclusions, revision of the manuscript. BJ: supervisor, critical revision of the manuscript.

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