In 1971, the JC virus (JCV) was isolated from the brain of a patient with Hodgkin’s disease who died of progressive multifocal leukoencephalopathy (PML). In that moment, the disease was named “JC virus” after the patient’s initials, and classical PML was described as a condition presenting in patients with neurological symptoms associated with nonenhancing focal lesions, preferentially in white matter, with a positive result for JCV detected in brain tissue by polymerase chain reaction (PCR).

Before 1980, PML was a very rare disease, a “back of the textbooks” condition. With immunosuppression caused by HIV infection, JCV reactivation occurred, and with AIDS epidemics, an increased frequency of classic PML was seen. Not only more patients presented with classic PML, but novel manifestations of PML were described in patients presenting with AIDS-related PML, such as gray matter involvement and symmetrical lesions in brain magnetic resonance imaging (MRI). With the development of highly active antiretroviral therapy (HAART), an additional new form of PML was described, named “inflammatory PML”, as a part of immune reconstitution inflammatory syndrome (IRIS). In this new description, different from classic PML (where brain lesions are demyelinating nonenhancing after contrast infusion), patients experience worsening of neurological condition after initiating HAART, a consequence of inflammation and edema of cerebral parenchyma. This can be radiologically translated as brain edema, mass effect and contrast enhancement. Despite the improvement in immunological recovery consequent to the spreading HAART use, PML frequency has not decreased to the extent of other opportunistic infections.

Finally, more recently, JCV was linked with cerebellar syndrome in HIV infected patients. Besides the fact that, traditionally, JCV causes supratentorial disease, some patients presented with cerebellar syndrome with image showing isolated atrophy. In 1998, a syndrome of degeneration of the cerebellum in HIV-infected patients was described, one of whom had JCV detected by PCR in cerebellar tissue biopsy. The authors proposed the possibility of latent JCV infection of cerebellar granular cells in HIV-infected patients with cerebellar atrophy, lacking further evidence of other features of PML.

Later, in 2005, Koralnik et al. described a case of JCV granule cell neuronopathy in a patient with JCV-associated cerebellar degeneration with isolated cerebellar symptoms. MRI showed diffuse cerebellar atrophy and occasional white matter abnormalities within the cerebellum. The disease was confirmed when immunohistochemistry demonstrated preservation of Purkinje cells, and in situ PCR revealed selective depletion of cerebellar granule cells and JCV infection of granule cell neurons. Thus, the third form of JCV encephalic disease was described as JCV granule cell neuronopathy.

In this issue of BJID, Piza et al. analysed retrospectively patients presenting with PML over a five-year period of admissions at the Emilio Ribas Institute (São Paulo – Brazil). Forty-seven cases were described and the newer forms of PML were observed, such as inflammatory PML (three patients, 6%) and JCV granule cell neuronopathy (four patients, 9%). Mortality of patients presenting PML was also studied. In one year of follow-up, with available data from 39 of the 47 patients, the study showed 54% mortality, mostly in-hospital deaths. Overall mortality was high (54% of 39 patients with available data within 1 year of follow-up).

This article shows that newer (or unveiled?) forms of JCV infection also occur in Brazil, and there is a need for high suspicion by infectious diseases specialists to detect these syndromes and order specific tests. Unfortunately, JCV news are not all good. More than 40 years later, treatment of AIDS-related PML relies only on optimized HAART, and there is no specific treatment showing good results. Diagnostic criteria for PML must be reviewed now that novel syndromes and more cases of clinically defined PML lacking JCV positive PCR have been described, a fact that may be related to less severe immunosuppression seen in many HIV patients nowadays.

More than 40 years later, PML is still a hit, with newer related syndromes and continuing debate of proper treatment and best way of diagnosis.

REFERENCES

