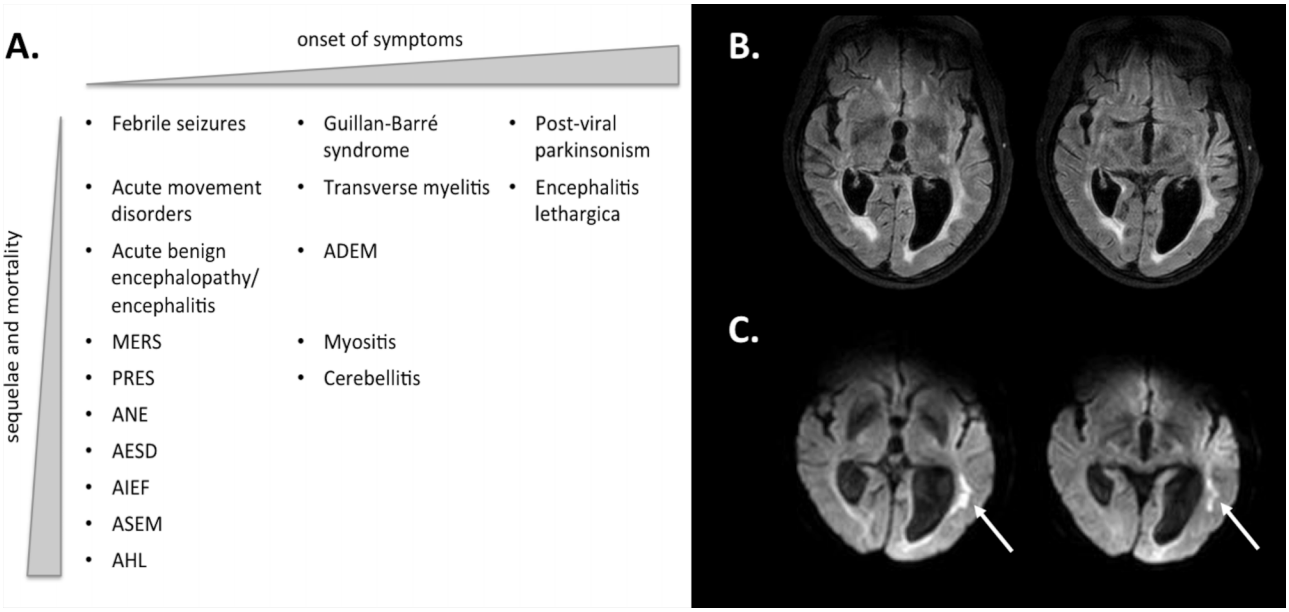

Figure 1. **Clinical Syndromes and MRI Findings Associated with Influenza A Mediated Encephalopathy.** Overview of possible neurological manifestations of influenza infections (adapted from Goenka et al.[1]) (A) and magnetic resonance imaging (MRI) findings in the present case of influenza-A mediated encephalitis (B,C). Transversal fluid-attenuated inversion recovery sequence (B) and diffusion-weighted imaging (C) MRI scans revealed an elongated pattern confluent periventricular lesion at the left upper temporal lobe (arrowheads). Additionally, aspects of normal pressure hydrocephalus with signs of transependymal liquor diapedesis adjacent to the ventricles are present; MERS, Mild Encephalitis/Encephalopathy with Reversible Splenial Lesions; PRES, Posterior Reversible Encephalopathy Syndrome; ANE, Acute Necrotizing Encephalopathy; AESD, Acute Encephalopathy with Biphasic Seizures and Late Reduced Diffusion; AIEF, Acute Infantile Encephalopathy Predominantly Affecting the Frontal Lobes; ASEM, Acute Shock with Encephalopathy and Multiple Organ Failure; AHL, Acute Hemorrhagic Leukencephalopathy; ADEM, Acute Disseminated Encephalomyelitis.

scan, no acute ischemia in perfusion-weighted CT, and no abnormalities of the supra-aortal vasculature in CT angiography. Cranial magnetic resonance imaging (MRI) performed one day later (see Figure 1) showed subcortical fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI) lesions in the left temporal region. The longish pattern of these lesions with transversal extension into the vascular territories of middle cerebral artery (MCA) and posterior cerebral artery (PCA) are not typical for an ischemic etiology. Viral encephalitis was considered in the differential diagnosis, and, thus, an empiric therapy with aciclovir was initiated. On her first day after admission the patient developed generalized chorea, including in the head, neck, trunk, and extremities, which she was unable to suppress. The chorea resolved spontaneously within 1 day. A subsequent cerebrospinal fluid (CSF) study showed an unremarkable cell count (4 leucocytes/μL; <5). Upon microbiological work-up there was no evidence for acute herpes simplex, varicella, or rubeola infection. An extensive work-up for autoimmunological or paraneoplastic disorders remained unremarkable (including autoantibodies against amphiphysin, CV2 (CRMP-5), GAD, Hu, Jo1, NMDA, PNMA2 (Ma-2), recoverin, LGI1, Ri, SOX1, titin, and Yo). There was also no clinical or laboratory-based indication of other underlying autoimmune and metabolic disorders, including dysglycemia, renal failure, hepatic dysfunction, electrolyte imbalance, hypoparathyroidism, or hyperthyroidism. Finally, a naso-pharyngeal swab for influenza A revealed a positive result. The influenza A infection was considered to be the underlying cause for the presented symptoms, although irrevocably proving a causal relationship is not possible. The neuropsychiatric symptoms remitted gradually although a tendency for perseveration and mild acalculia remained for days. The patient had no insight into her illness and was discharged against medical advice at her fourth day after admission.

Discussion

We have presented the case of a 74-year-old female with a complex neuropsychiatric syndrome and transient chorea. An acute influenza A-mediated encephalitis/encephalopathy (IAEE) was considered as the underlying cause of her medical condition. Radiographic findings with a left-sided periventricular FLAIR and DWI lesion support the diagnosis of an IAEE, and an extensive work-up for alternative infectious and autoimmunologic causes yielded negative results aside from influenza A. However, our patient displayed a rather benign disease course and showed spontaneous improvement of her symptoms without any treatment. Indeed, the subcortical MRI changes observed might be related to excessive immune response and present symptoms due to cytokine-mediated encephalopathy rather than to a direct cytotoxic effect of the virus.[6,7] This might explain the spontaneous remission and the discrepancy of the clinical syndrome and the lack of involvement of basal ganglia upon MRI. The most common clinical features of acute IAEE are seizures, delirium, altered vigilance, and speech abnormalities, of which only the last symptom was present in our patient.[8] For the corresponding year, 329/1,354 influenza swabs

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performed in our hospital were positive for influenza A (about 24%), with only this patient revealing neurological complications. To our knowledge, only two adult patients with acute IAEE and subsequent movement disorders have been published so far: one 26-year-old female patient with fever, headache, irritability, intermittent resting tremor of the right hand, and upper limb rigidity and a 42-year-old male patient with fever, headache, bilateral upper limb tremor, rigidity, and orofacial bradykinesia. No abnormalities in cranial CT scans or MRI (the latter only performed on the 26-year-old patient) were reported in these cases.[1] Consistent with our case, CSF findings in acute IAEE are usually non-inflammatory (as it was also in this case) and the virus itself can only rarely be detected in CSF or in brain tissue.[9,10] Given the spontaneous remission and the lack of CSF pleocytosis, we consider our patient to have had influenza A encephalopathy rather than encephalitis. Unfortunately, no follow-up imaging was performed and we missed the opportunity to take a video in time as the chorea was only transiently present. The efficacy of immune-modulatory therapies has been demonstrated in anecdotal reports.[6] Therefore, as the aforementioned case report from 1892 suggested, we would like to conclude that the treatment of these patients with "Liquor arsenicalis ..., milk, liquor carnis, peptonoids, peptonised cocoa ... brandy, and port wine" might no longer be applicable.

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