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RESEARCH ARTICLE

NEUROLOGICAL MANIFESTATIONS IN ADULTS INFECTED WITH SARS-COV2 AND OTHER RESPIRATORY VIRUSES: A REVIEW

David Alberto Anguizola Tamayo, M.D.[1], Juan Carlos García Moncó, M.D.[2], María Ángeles Gómez Beldarraín, M.D.[3], Lucía Vidorreta Ballesteros, M.D.[3], Javier Jose Arranz Martínez, M.D.[3], Irene Sustatxa Zarraga, M.D.[3] and Adriana Barquin Toca, M.D[3]

[1]Pacífica Salud Affiliated with Johns Hopkins Medicine International, Panama City, Panama Republic
[2]Department of Neurology, Basurto University Hospital, Osakidetza Basque Health Service, Bilbao, Vizcaya, Spain
[3]Department of Neurology, Galdakao Hospital, Osakidetza Basque Health Service, Galdakao, Vizcaya, Spain

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ABSTRACT

The COVID-19 pandemic is a challenge to both public health and the clinicians who confront it. At the same time, other respiratory viruses remain on the clinical stage. It is a reality that COVID-19 affects various organs, including the nervous system, like other respiratory viruses. We have designed this review as a tool for the clinician to deal with the diagnosis and treatment of neurological manifestations in adults caused by COVID-19 and respiratory viruses.

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INTRODUCTION

The recent pandemic of SARS-CoV-2 virus infection known as COVID-19 disease has alerted the neurological community about a variety of neurological conditions that may appear as a consequence of infection by respiratory viruses. It is, therefore, important that neurologists be aware of these complications to establish a proper diagnosis and measures of management, including contagion prevention and isolation when indicated. Furthermore, co-infection between SARS-CoV-2 and other respiratory pathogens may be common; a recent study found that 20% of the specimens that tested positive for SARS-CoV-2 were also positive for 1 or more additional respiratory pathogens. This highlights the importance of recognizing the neurological disorders associated with the different pathogens that in turn may overlap. We have reviewed for the neurological complications of the most common respiratory viruses in adults, including influenza virus, respiratory syncytial virus, and human metapneumovirus. We have compared them with those recently associated with the SARS-CoV-2 virus as well as with previous Severe Acute Respiratory Syndrome (SARS) and Middle East Respiratory Syndrome (MERS).

***Corresponding author:* Dr. Juan Carlos García Moncó,**
Department of Neurology, Basurto University Hospital, Osakidetza Basque Health Service, Bilbao, Vizcaya, Spain.

METHODS – SEARCH STRATEGY

We searched PubMed for articles up to may 16th of the present year using the following criteria: ""Influenza" OR "Metapneumovirus" OR "Syncytial Respiratory Virus" OR "MERS" OR "SARS-CoV" AND "Neurol" OR "Encephalitis" OR "Meningitis" OR "Stroke" OR "Guillain-Barré" OR "Miller-Fisher" OR "Myelopathy" OR "Poly cranialis" AND "Adults". Due to the small results in PubMed for "COVID-19" at the time, we conducted this search also using Science Direct (figure 1). We defined adults as > 18 years. The neurological alterations correspond to those published in COVID-19. We restricted the search to articles in Spanish and English. Priority was given to case series and systematic reviews over case reports. Pediatric case report and series have been excluded, except for those that include also adults.

RESULTS

Table 1 summarizes the main neurological manifestations according to the different respiratory viruses, Table 2 compares their incubation and contagious periods, and Table 3 describes the available prevention methods. The neurological complications of these respiratory viruses are detailed below according to the specific virus.

Influenza virus: Influenza viruses (IV; family Orthomyxoviridae) are negative-stranded RNA viruses classified into 4 groups (A-D). They contain an envelope with two main surface proteins: hemagglutinin (H1-H18) and neuraminidase (N1-N11). Human influenza A and B viruses cause seasonal epidemics of disease almost every winter. Influenza A is classified according to these 2 proteins, with H1N1, H1N2, H2N2 y H3N2 representing the subtypes associated with a higher risk[1]. Seasonal influenza A is caused by H3N2 and H1N1 subtypes. Antigen variations and point mutations in influenza A genome may result in worldwide pandemics every 10-40 years**.** It has been proposed that most of the neurological manifestations are consequence of a virus-mediated systemic inflammatory activity.

In addition to the classical respiratory symptoms with fever, headache and myalgias lasting 1 to 5 days, influenza infection may cause diarrhea, vomiting, conjunctivitis, and otitis. Involvement of the CNS in influenza virus infection is infrequent, particularly in adults, and usually appears after 3 days of flu symptoms. In an Austrian series of 21 patients (age 4-78 years) with influenza A virus-associated neurological complications, the final diagnoses were acute encephalopathy (2 patients), encephalitis (13 patients), meningitis (5 patients), and transverse myelitis (1 patient)[2]. The virus could be detected in the cerebrospinal fluid (CSF) only in one patient of 18. Six patients experienced influenza encephalopathy during the course of the respiratory illness, and 14 patients experienced post-influenza encephalopathy within 3 weeks after the resolution of respiratory symptoms. Brain MRI showed focal areas T2 of high signal intensity in 6 patients with postinfectious encephalopathy. In 2 patients, there were large areas of increased signal intensity in the temporal and parietal regions of the brain associated with significant cerebral edema, while in the remaining 4 multiple foci of high–signal intensity lesions were distributed asymmetrically throughout the brain. The authors concluded that influenza encephalopathy is frequently associated with metabolic disorders related to systemic inflammation due to infection and respiratory alterations and liver function abnormalities, whereas post-influenza encephalopathy appears to have an autoimmune mechanism triggered by viral particles, considering the lesions in brain MRI and the neurological sequalae found in these patients. CSF examination in cases of encephalopathy-encephalitis may be normal or show a lymphocytic pleocytosis (50-100 cells/mm^3) and increased proteins with normal glucose levels.

Bilateral thalamic necrosis on neuroimaging has been described in Influenza-associated encephalopathy[3]. Interestingly, one similar case has been described in COVID-19[4]. Other findings include reversible splenial lesions[5] and acute hemorrhagic leukoencephalitis[6]. During the influenza A (N1H1) pandemic of 2009 several cases of CNS involvement were described.

In a retrospective study of 55 patients admitted to an Iranian hospital with laboratory confirmed H1N1 virus infection, 23 (42%) had neurological signs and/or symptoms that were severe in 9%[7]. The most common neurological manifestations were headache (34%), numbness and paresthesia (18.2%), drowsiness (9.1%), and coma (9.1%). Other symptoms were focal weakness in 4 patients, generalized weakness in 1, vertigo in 4, ataxia in 2, myoclonus in 1, and seizures (focal status epilepticus and encephalopathy) in 1 patient. One 22-year-old patient had a Guillain-Barre syndrome-like illnessand died from respiratory failure in a few days. The association of influenza with stroke, in contrast with COVID-19 disease, is less frequent. In an Austrian series of 37 patients with influenza A and B during 2017-2018, 5 patients had a stroke, 24 had an influenza encephalopathy (associated with status epilepticus in 2 patients), 6 had seizures with normal brain MRI, 1 had a GBS, and another had a Miller-Fisher syndrome[6]**.** None of the patients had been vaccinated. Seizures may occur in otherwise healthy adults during Influenza A and B; neuroimaging is normal, and they tend not to recur[8]. Similar to SARS-CoV-2, a few reports of transverse myelitis have been described[9,10] as well as rhabdomyolysis with CK elevations > 1000 U/L[11].

The confirmatory diagnosis of influenza infection is achieved by RT-PCR of anasopharyngeal swab or retrospectively by showing a 4-fold increase in serum specific antibodies. The treatment of influenza is aimed at controlling the associated systemic inflammatory with corticosteroids, intravenous immunoglobulins, plasmapheresis, and interferon together with antivirals (neuraminidase inhibitors), but their effectiveness is not well established, particularly in patients with neurological complications. Oseltamivir is the current drug of choice for influenza but has poor CNS penetration. A randomized trial showed that a combination of oseltamivir, amantadine, and ribavirin was not superior to oseltamivir alone in terms of clinical benefit[12], nor was intravenous zanamivir superior to oral oseltamivir[13]. Resistances to oseltamivir have been reported in Japan. Intravenous peramivir was successfully employed in one patient with influenza meningoencephalitis[14], but data on CSN penetration are lacking and additional studies are needed. Malignant edema may require external ventricular drainage. There is no epidemiological data available regarding morbidity and mortality in adults with encephalitis or encephalopathy. In a series of 44 cases, 61% had a good recovery, 20% had a sequel and the remaining 19% died[15].

Respiratory syncytial virus: The human Respiratory Syncytial Virus (RSV) belongs to the family Pneumoviridae, genus Othopneumovirus and is the main responsible for lower respiratory tract infections in children. In adults, respiratory symptoms can be mild or severe, mainly in immunocompromised patients and the elderly. Neurological manifestations occur mainly in children, in the form of encephalopathy, seizures, and esotropia. In adults, only a few cases have been reported. In 1979, a series of 25 cases detected 4 patients with CSF antibodies against RSV (1 meningitis, 3 myelitis), but their age was not specified[16]. In 1982, a 59-year-old woman developed a polyneuritis cranialis and ataxia during a feverish respiratory tract infection; anti-RSV antibodies were detected in blood and CSF[17]. In 1996, a 28-year-old man developed meningitis and a polio-like syndrome with respiratory compromise and very slow recovery; CSF had inflammatory changes and was positive for RSV by culture, which was negative after treatment with ribavirin, intravenous immunoglobulins, and dexamethasone[18]. Finally, in 2010, a 22-year-old man developed encephalitis (seizures and loss of consciousness) with symmetrical cortical lesions; the CSF revealed lymphocytic pleocytosis and had positive anti-RSV antibody; he was treated with ribavirin and dexamethasone and regained consciousness 3 weeks later[19]. These diverse neurological presentations suggest that RSV may be responsible for many more cases than those reported in the literature. Therefore, RSV should be included in the differential in patients who develop neurological disturbances following respiratory tract infection.

Human *metapneumovirus:* *Human metapneumovirus* is a negative-sense single-stranded RNA virus (family: Pneumoviridae) that was first isolated in the Netherlands in 2001. It is closely related phylogenetically to the syncytial respiratory virus. Its infection results in an influenza-like syndrome with dyspnea and occasional conjunctivitis that involve healthy and immunocompromised individuals. The diagnosis is made by RT-PCR in a nasopharyngeal swab. Neurological complications may occur, particularly in children, and include febrile and afebrile seizures, brain edema, and ADEM. As with the other respiratory viruses, the CSF RT-PCR is usually negative in these patients. Encephalitis has been reported in 4 adults and one girl. The first case was a 47-year-old male that went into a coma 2 days after an upper respiratory infection. Brain MRI showed high signal intensities with restricted diffusion in the perirolandic area and external capsule that resolved in 3 months[20]. His CSF did not contain cells and had a moderate protein increase (77 mg/dl); RT-PCR was not performed. A similar clinical and radiological picture occurred in A 10-year-old girl with encephalitis presented an Abrupt clinical deterioration was associated with the presence of multiple areas of demyelination and cortical abnormalities on MRI; the CSF contained 52 cells/mm3 with normal glucose and proteins and the viral RT-PCR was positive[21]. Two additional patients presented seizures with normal bran MRI and benign evolution[22,23]; in one of them, specific IgG against the virus in the CSF was demonstrated[22]. Finally, a 32-year-old man with encephalitis had multiple hyperintense foci on his brain MRI; although the CSF biochemistry was normal, the RT-PCR in the CSF was positive for the virus[24]. Treatment in these patients has included methylprednisolone[20], intravenous immunoglobulins and plasmapheresis[21]. One patient received oral ribavirine[24].

Coronavirus: Coronaviruses (CoV; family Coronaviridae), are enveloped, positive-stranded RNA viruses. CoV are zoonotic and are further divided by host preference. Alpha and beta CoV infect mammals including humans, whereas gamma and delta CoV infect birds. Six different CoVs have been identified in humans. The earliest CoV were discovered in the 1960's.Since then, two additional betaCoVs have emerged in human epidemics of severe acute respiratory syndromes (SARS), and their discoveries changed the nomenclature of these viruses. SARS-CoV 1 was responsible for an outbreak of viral pneumonia in 2002/2003 that started in China and infected nearly 10,000 patients with close to a 10% mortality rate[25]. The other highly pathogenic and epidemic CoV infecting humans was discovered in Saudi Arabia in 2012, hence, the middle eastern respiratory syndrome- MERS CoV[26].

SARS-CoV-2 virus infection (COVID-19): The infection with SARS-CoV-2 may have a nonspecific prodrome of respiratory and/or gastrointestinal infection that overlaps with other respiratory viruses. Patients most often have fever, cough, and shortness of breath. COVID-19 may also associate a number of neurological disturbances. The analysis of the data of the initial series of respiratory patients of this pandemic[27] revealed the presence of myalgias in a median of 27.5% (range, 11%-44%) of patients and headache in 8% (6.5-23.1%). Dizziness was reported in 9% of patients, confusion in 8%, and seizures in 1 patient (5%) of 1 series each. The fact that they were respiratory patients attended by non-neurologists may have resulted in under-recognition of the real spectrum.

Afterwards, Mao et al analyzed retrospectively a series of 214 patients hospitalized with a laboratory confirmed diagnosis of severe acute respiratory syndrome from coronavirus 2 (SARS-CoV-2) infection over a one-month periodand found neurological problems in 36.4% of patients[28]. Data were collected by other specialists, but 2 neurologists checked the neurological symptoms that were divided into central nervous system (CNS) (24.8%), peripheral nervous system (PNS) (8.9%), and musculoskeletal symptoms (10.7%). Among CNS disorders, dizziness (16.8%) and headache (13.1%) were most common, whereas the most common PNS problems were dysgeusia (5.6%) and hyposmia (5.1%). A series of 58 patients admitted to the ICU for severe disease found neurological problems in 8 patients (14%) on admission and in 39 (67 %) when medication was withheld. Agitation, confusion, corticospinal tract signs, and a dysexecutive syndrome were most commonly encountered[29].

Guillain-Barré syndrome was initially described in one patient and then followed a series of 5 Italian patients with a seemingly axonal variant of the disease that appeared 5-10 days after COVID-19 disease onset[30]. Other case reports have followed to the date of this review (may 16, 2020)[31]. The median time to presentation was 10 days (range, 3-24), 5 patients presented with bilateral facial palsy, most patients had CSF albumin-cytological dissociation, and RT-PCR in the CSF was negative in the 10 patients in whom it was performed. Most patients responded favorably to therapy with intravenous immunoglobulins, although follow-up to this time is insufficient. Two Spanish patients with Miller-Fisher and favorable recovery (one of them after IVIGs, the second with no specific therapy) have been reported[32]. Encephalitis has been described in a few patients[33,34]. Half of the cases had a mild lymphocytic pleocytosis in the CSF and RT-PCR for SARS-CoV-2 virus was positive in 3. Most presented with headache, confusion and seizures, and 1 had MRI evidence of rhombencephalitis[35]. All recovered completely.Also, single case reports have described cases of necrotizing encephalopathy[36], myelitis[37], and one encephalitis with CSF pleocytosis and positive RT-PCR in the CSF[34]. Encephalopathy manifested as disorientation, confusion, and agitation in different combinations is frequent in COVID-19 and has a multifactorial origin, including the viral infection as well as the secondary inflammatory response and multiorgan failure.

Table 1. Neurological manifestations and viral infections: main pathogens involved

Neurological manifestation	Viruses involved	Comments	References
Meningitis (aseptic)	•Influenza	•5 patients in a series of 21 with influenza A	2
	•RSV	•Rare •1 patient	16
	•Parainfluenza-3	•Rare	50
Encephalopathy	•Influenza	•2 patients in a series of 21 with influenza A and 6 with post-influenza encephalopathy	2
	•SARS-CoV-2	•Frequent in COVID-19 of multifactorial origin	29
Encephalitis	•Influenza	•13 patients in a series of 21 with influenza A	2
	•*Human metapneumovirus*	•Reported in 4 adults and 1 girl	20,21
	•*RSV*	•Very rare •A 22-year old patient •A 28-year-old patient	18,19
	•*Adenovirus*	•Very rare •Mostly Immunocompromised patients	46,47,48
	•*Hendra Virus*	•7 cases since 1994 to 2009.	64
	•*Nipah Virus*	•643 cases since 1998 to 2018.	65
Necrotic encephalitis	•*Influenza*	•Bilateral thalamic necrosis •RESLES •Acute hemorrhagic leukoencephalitis	3,5,6
	•*SARS-COV2*	•Bilateral thalamic necrosis	4
Myelitis	•Influenza	•Rare •One case associated with Anti-MOG antibodies	9,10
	•SARS-CoV-2	•A 66-year-old man with COVID-19 with acute flaccid paralysis of lower limbs	37
	•RSV	•3 patients	16
Stroke	•SARS-CoV-2	•Multifocal •Younger patients •Large infarcts •Coagulation abnormalities	29,43,44
	•*Influenza*	•Infrequent	6
Seizures	•*Human metapneumovirus*	•2 patients with normal brain MRI	22,23
	•*Influenza*	•Influenza A and B, normal MRI and CSF, infrequent	6,8
	•SARS-CoV-2	•Tonic-clonic seizures •Some focal-onset seizues •Occasional status •Non-specific MRI findings	40,41, 34,42
	•RSV	•Rare	19
Guillain Barré syndrome	•SARS-CoV-2	•Classical demyelinating and atypical locked-in presentations •Ten days (3-24) after infection •Viral PCR in the CSF negative •Improvement on IVIGs	30,31
	•RSV	•A 59-year-old woman developed a polyneuritis cranialis and ataxia	17
Miller-Fisher syndrome	•SARS-CoV-2	•One patient •50-year-old male •Ophtalmoparesis and ataxia •5 days after infection	32
Creatin Kinase elevations	•SARS-CoV-2	•Frequent, with associated myalgias, reported in 27% (11-44) in pooled series	27
	•*Influenza*	•Frequent; occasional rhabdomyolysis	11
Anosmia	•SARS-CoV-2	•Frequent; between 6% and 86%, depending on the reporting tool	39
	•Rinovirus	•Most frequent cause of anosmia post common cold.	49

Table 2. Respiratory viruses with their incubations and infectious period*

Virus	Incubation Period*	Contagious Period**	References
Influenza	1 to 4 days	From -1 to 7 days (1).	61
RSV	3-7 days	Symptomatic days.	61
Metapneumovirus	3-6 days	Unknown	62
SARS-COV2	Median 5 days 99th percentile: 14 days	From -3 to 7 days. (3,4).	63
Adenovirus	5-6 days	+ 14 days (9)	61
Rinovirus	2-4 days	About -2 days until end of symptoms.	61
Parainfluenza	2-6 days	Not clear. Highest the first days of illness.	61
Hendra Virus	7-12 days	No person to person transmission. Virus shed in human nasopharyngeal secretions and urine	64
Nipah Virus	Mostly < 15 days	Unclear. Transmission risk highest in > 45 years old and respiratory symptoms	65

* In immunosuppressed patients, the incubation period may be shorter than indicated and the infectivity period longer.
** Negative numbers denote pre-symptomatic days. RSV: Respiratory syncytial virus

Table 3. Respiratory viruses and last updates in their vaccination investigation

Virus	Vaccination	Reference
Influenza	Influenza vaccination, with an effectiveness of 59-83% is recommended, although its effect on neurological manifestations are unknown.	66
RSV	A phase 2b trial in the elderly proved immunogenicity but not protection. Three formulations provided neutralizing antibodies in nonpregnant women.	67,68
Metapneumovirus	9 of 21 patients generate neutralizing antibodies when a recombinant MPV was inoculated. Many candidate molecules are on preclinical research.	69
SARS-CoV-2	Partial or complete protection in macaques using an inactivated vaccine. Dozens of vaccines are in development, with 8 currently in phase 1 trials.	70,71
Adenovirus	Bivalent vaccine against Adenovirus-5 and influenza induced full protection for both viruses in a mouse model.	72
Rhinovirus	At least 160 serotypes discovered. Serotype cross-reactivity was found in mice and rabbits using common capsid regions.	73
Parainfluenza	A bivalent vaccine (PIV3 + hRSV) induced neutralizing antibodies in newborn lambs by maternal vaccination.	74
Hendra virus and Nipah virus	A recombinant rabies-based vaccine showed a cross-reactivity protection to Hendra and Nipah Virus in a mice model.	75

RSV: respiratory syncytial virus.

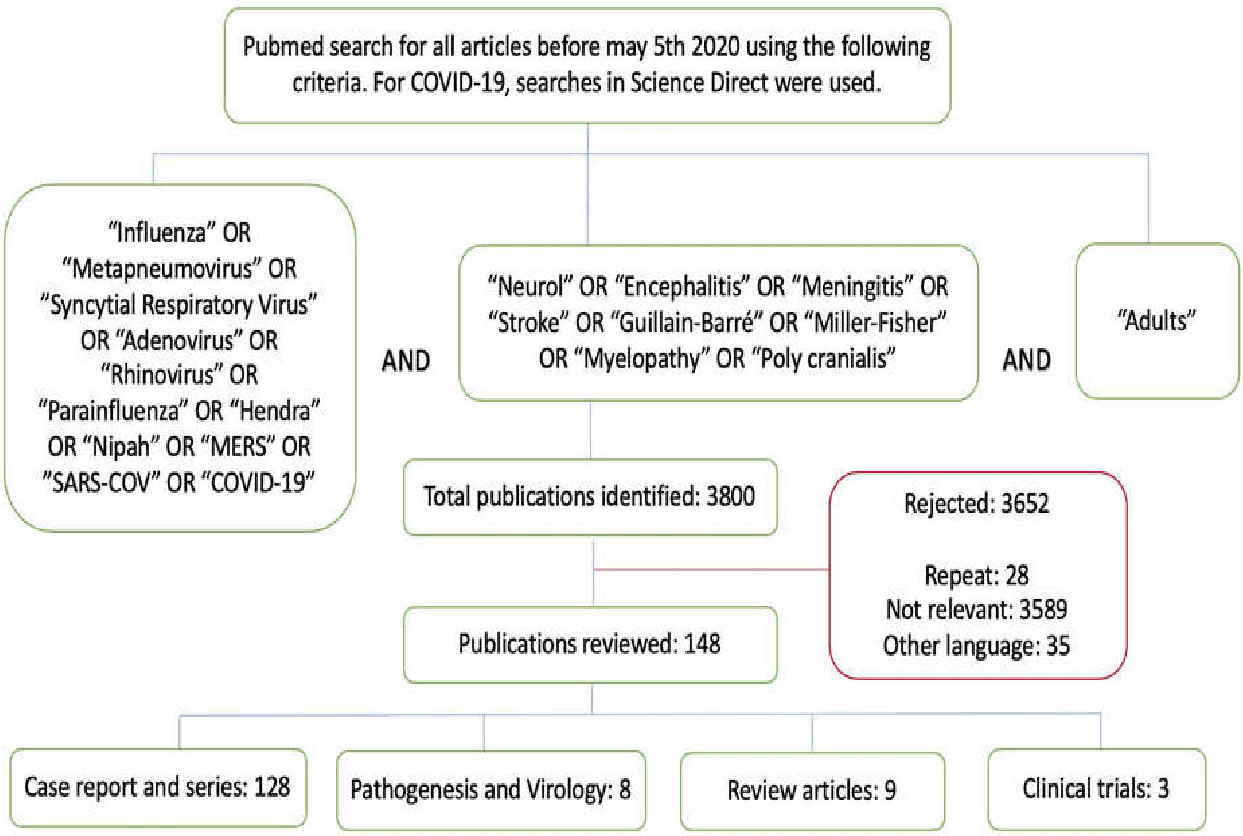

Figure 1. Search strategy employed for the study

Five patients with exacerbation of myasthenia gravis due to concomitant COVID-19 have been described[38]. Anosmia or some degree of smell dysfunction has been reported in a wide range of 59% of positive PCR COVID-19 patients compared to 19% negative patients, but the method of detection is critical, as it ranged from self-report to a standardized specific questionnaire; moreover, a combination of other symptoms in addition to anosmia, is predictive of COVID-19 positive (S: 54%, E: 86%)[39]. Seizures were described in one patient (4.8%) of a series of 21 critically ill patients in Washington state, US[40] A retrospective multicentric evaluation of 304 patients with COVID-19 admitted in Hubei province did not find any seizures or status epilepticus, despite the fact that 108 of them had a severe infection[41]. However, several additional cases have been reported, many of them with associated features of encephalopathy or encephalitis and focal status epilepticus [34,41,42].

Stroke has been reported in several case reports [29,43,44] and in fact COVID-19 infection itself has also been described as a risk factor for stroke. Patients tend to have severe, ischemic strokes, and some of them are strikingly young (under 40). The coagulation abnormalities together with the cardiac problems of these patients predispose them to stroke. The presence of pre-existing cerebrovascular disease resulting in intracranial stenosis with hypoperfused brain regions may be at increased risk for ischemic stroke while in a state of severe infection and systemic inflammation. The possibility of coinfection Between SARS-CoV-2 and Other Respiratory Pathogens should also be borne in mind. In a recent study on 1217 specimens, 116 (9.5%) of patients tested positive for SARS-CoV-2 infection, of which 24 (20.7%) were positive for 1 or more additional pathogens, including rhinovirus/enterovirus (6.9%), respiratory syncytial virus (5.2%), and non–SARS-CoV-2 Coronaviridae (4.3%)[45].

Other Respiratory Viruses (Adenovirus and Paramixovirus): Adenoviruses are large, non-enveloped double-stranded DNA viruses that frequently cause upper respiratory tract symptoms, gastroenteritis and conjunctivitis. Occasionally, adenovirus cause severe meningoencephalitis and encephalomyeloradiculitis in immunocompromised patients[46,47] and in healthy individuals[48]. Encephalitis may associate confluent periventricular lesions[46] and brainstem (rhombencephalitis)[47]. Therapy withcidofovir and brincidofovir has been used off-label in some cases. Adenoviruses have been also implicated in post-influenza encephalopathy[2]. Rhinovirus, the most common cause of the common cold, has been associated with anosmia, along with the Parainfluenza virus[49]. This virus belongs to the Paramyxoviridae family and causes laryngotracheobronchitis and bronchopneumonia. The Parainfluenza-3 subtype has been rarely implicated in adults with aseptic meningitis[50] and Guillain-Barré syndrome[51]. Finally, two other viruses from the Paramyxoviridae family, the Hendra Virus and the Nipah Virus, have been associated with neurological manifestations during zoonotic outbreaks. The first, with cases of equine-associated encephalitis in Australia[64], and the second with meningoencephalitis in relation to pigs in a slaughterhouse in Malaysia, Singapore, and Bangladesh[65]. Brain MRI showedbrain white matter involvement in Hendra Virus whereas gray matter involvement was observed in Nipah Virus[52]. The use of ribavirin in Nipah Virus encephalitis was associated with a 36% reduction in mortality[53].

PREVENTION

Prevention of respiratory infections is accomplished by 2 methods: avoiding exposure to and modifying the immune status of the individual. Both for health professionals, the general population and public health strategies, it is necessary to know both the incubation periods and infectivity of pathogens (Table 2). Methods that avoid exposure to pathogens have been scientifically studied. Using an epidemic simulation model of influenza, researchers from Singapore were able to demonstrate a progressive decrease in SARS-COV2 R_0 by implementing measures of social distancing (closure of schools and events, teleworking and others)[54]. Hand hygiene is indisputably one of the best methods for the prevention of infectious diseases, however, adherence to this practice is low. Japanese researchers measured the adherence of handwashing before and after following the WHO recommendations, obtaining an increase in adherence [55]. When hand washing is added to the use of masks, it is possible to reduce the transmission of the influenza virus in households[56]. Also, the use of masks prevents respiratory infections in mass gatherings[57]. Vaccination is one of the pillars of public health. There are on-going efforts to obtain vaccines for respiratory viruses (Table 3). In addition, there are other ways to strengthen the immune system. An individual participant data meta-analysis of 25 studies has shown that vitamin D reduces the risk of acute respiratory infections (OR: 0.88, IC: 0.81-0.96)[58]. Moreover, probiotic supplements have also shown a protective effect, but the evidence is of low quality[59]. Finally, both meditation and exercise have a statistically significant beneficial effect[60].

Diagnostic and treatments recommendations: Taking into account our experience, such as the review carried out, we make the following recommendations for clinical practice.

- Perform the first nasopharyngeal RT-PCR searching for every respiratory virus and then, do specific studies in CSF. Consider RSV and metapneumovirus in parents (because of children contagion) and in young people. Consider too, the season (winter is related to Influenza infections) and your local epidemiological data. We strongly recommend extracting enough CSF to be able to carry out subsequent analyzes. Although not essential for diagnosis, detection of pathogenic particles in CSF could be useful in epidemiological and pathophysiological research.
- Consider other pathogens listed in this review that may manifest with respiratory symptoms, flu-like symptoms, and also neurological abnormalities.Among them, we have Mycoplasma pneumoniae, Chlamydia pneumoniae and arboviruses such as Dengue Virus, Chikungunya, Zika Virus and other flaviviruses. Their neurological manifestations are out of scope of this review.
- Apparently, opportunistic infections have not been reported after immunomodular treatment with corticosteroids or immunoglobulins. We recommend the latter for its better safety profile and because it does not limit the action of cellular immunity; consider that its rapid administration could cause headache. Treat promptly to avoid neurological sequalae.

- Despite the experiences described in different reports and case series, no conclusions can be drawn regarding the efficacy and safety of the treatments described in this review. However, due to the high morbidity and mortality of these pathologies, it is recommended to individualize each case and give treatment as soon as possible.

- Finally, consider the use of masks and protective equipment for both the patient and close relatives until the infectivity period ends. We recommend perform vitamin D (25-OH) levels and give supplementation if necessary. Provide advice to maintain an active and healthy life.

Conclusions

SARS-COV2 also neurological symptoms and it overlap both in its prodrome of respiratory and/or gastrointestinal infection and in the neurological manifestations of other pathogens, which may result in misdiagnosis. Post-infectious neurological disorders occur in adults following respiratory infection with a variety of viruses. Although there are no clear epidemiological data, the case series indicate that these conditions may convey a somber prognosis. The knowledge of these neurological conditions by the attending neurologist and internist is important, because the identification of the specific pathogen will allow for the proper treatment and preventive measures to be taken.

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