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Overview on the Neuropsychiatric Manifestations of COVID-19: Experience of a Third Level Hospital

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Summary

In 2020, the world experienced the outbreak of Sars-cov 2, a virus that emerged in China and then spread rapidly around the world. In Morocco, the first case of sars-cov 2 was confirmed in March 2020. The sars-cov 2 infection affects almost the entire immune system of the body. In this short communication we report the different neurological and psychiatric manifestations secondary to sars-cov 2 infection observed in the neurology department at the University Hospital of Marrakech over a 3-month period. Headache was the dominant manifestation with a prevalence of 94.28% followed by anosmia/hypoagueusia with a prevalence of 80% of patients, as well as the depressive syndrome represented in the majority of our patients. Cases of polyradiculoneuritis, strokes, decompensations of epileptic patients, meningo-encephalitis and other manifestations were also observed.

Keywords: *Covid 19, neurological manifestations, anosmia, headache, psychiatric manifestations.*

Introduction

Since mid-December 2019, a new strain of coronavirus called SARS-Cov2 has been detected in the Chinese city of Wuhan, Hubei province, and has spread worldwide.More than 56 million cases and 1.3 million deaths worldwide have been confirmed, and the numbers continue to rise [1].

The most frequently reported symptoms of COVID-19 are fever, and respiratory symptoms such as cough and dyspnea. However, an increasing number of observations describe the existence of extra pulmonary symptoms, including gastrointestinal, thromboembolic, cardiac, dermatological, renal and also neurological manifestations [2],

The majority of the population had a mild or uncomplicated course [3]. Cases of suspected neurological involvement in patients with COVID-19 have been reported mainly in cohorts in Wuhan, China, and Strasbourg, France [4]. A first retrospective study on 214 hospitalized patients reported the existence of neurological symptoms in 36% of cases [5] such as stroke, encephalopathy or acute polyradiculoneuritis [6].

More recently, attention is being paid to the persistence or appearance of chronic symptoms several weeks after the initial infection, including headache, mood disorders and cognitive impairment [7].

Objective

In this manuscript, we describe the different neurological and psychiatric manifestations of this pandemic through our experience in the neurology department at the Marrakech University Hospital.

Methods

1- Study design and patient population

This is a prospective and observational study at the University Hospital of Marrakech. We exploited the medical records of Covid positive patients confirmed by PCR, admitted in the neurology department over a period of 3 months from October to the end of December 2020. Our series contains 35 patients, 23 males and 12 females, hospitalized in the neurology department for inaugural neurological manifestations or secondary to a complication of SARS cov 2 infection.

2- Data collection:

Demographic data including age, gender, pre-existing comorbidities, were extracted from the medical record. Records were reviewed for neurological symptoms or signs affecting the central or peripheral nervous system.

Statistical analyses were carried out with the software Microsoft Excel for Windows version 2007.

Results

A total of 35 patients with confirmed COVID-19 were included in this study. The average age is 44 years, with predominance of two age categories: [20-30] and [41-50]. (Figure 1).

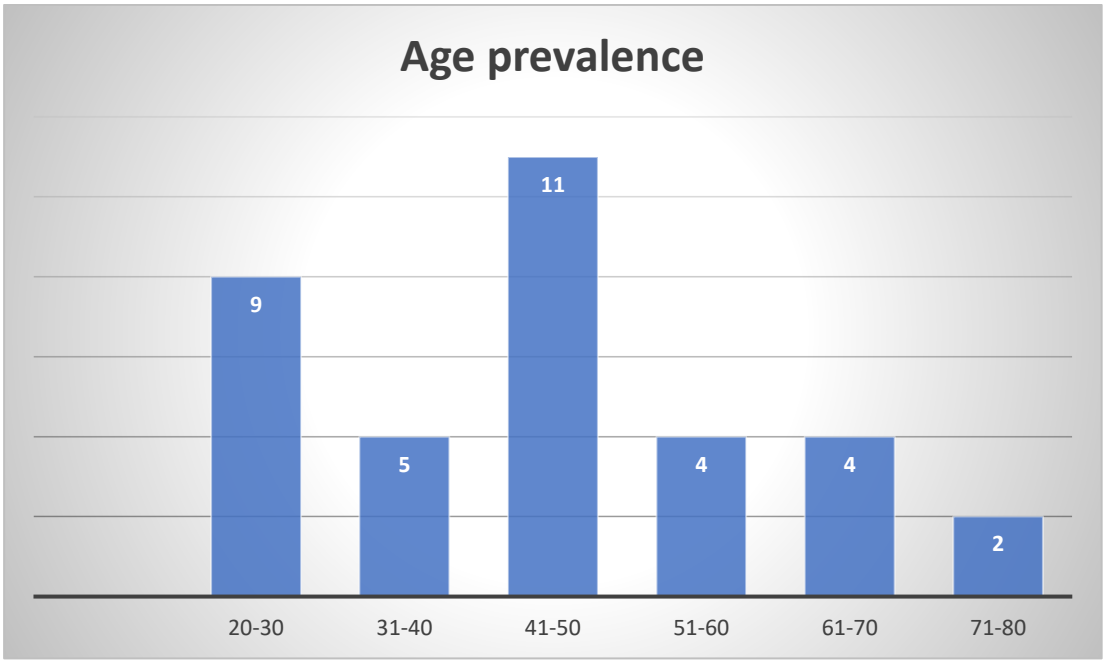

Figure 1: Age distribution of the study cases.

Overall, 20% of patients were hypertensive, 11.42% had diabetes, while the majority of patients 48.57% had no specific pathological history. (Table 1)

Table 1: Patients comorbidities.

Medical history	N°	%
None	17	48,57
HTA	7	20
Diabetes	4	11,42
Asthma	3	8,57
Migraine	2	5,71
Epilepsy	2	5,71
Psychiatric illness	0	0

A multitude of neurological manifestations were observed. It should be noted that some patients had more than one neurological manifestation. The most frequently observed symptom was headache with a prevalence of 94.28%. Anosmia and/or hypoagueusia come in second place with a prevalence of 80% followed by anxiety-depressive disorders 74.28% and insomnia 14.28%. Four patients had ischemic stroke, two had cerebral venous thrombosis. Acute polyradiculoneuritis was found in 4 cases. Only one case presented meningoencephalitis. The rest of the symptoms will be presented in the graph and table below (Figure 2).

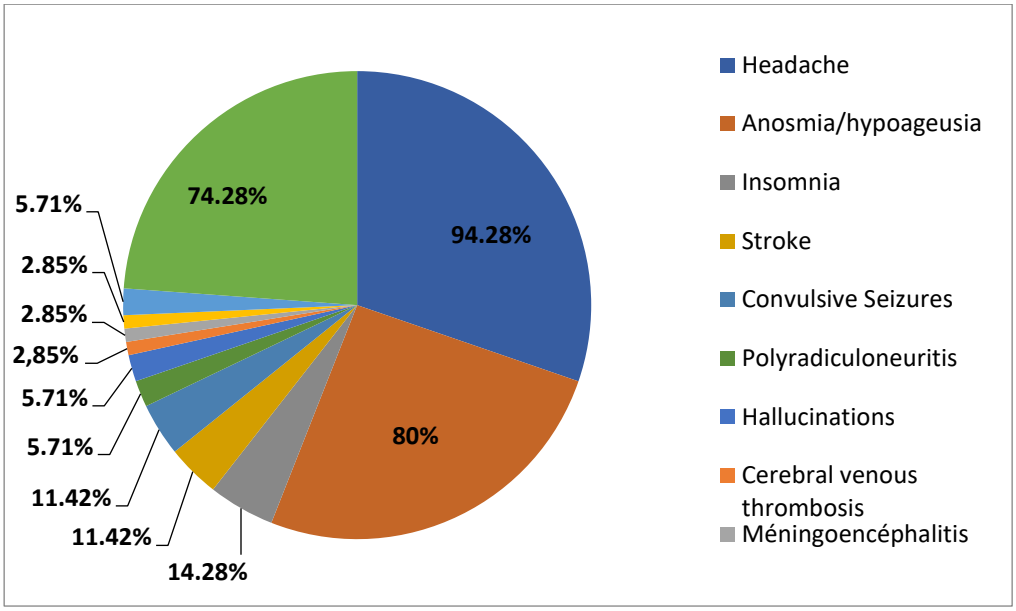

Figure 2: Neuropsychiatric manifestations.

Discussion

In our study, the average age of the patients was 44 years, which is consistent with the literature where the average age of the hospitalized patients was between 47 and 56 years in these 2 studies (46 to 67 years in the study of Zhou et al, 35 to 58 years in the study of Guan et al) respectively [8,9]. 23 of our patients were men, which corresponds to 65.71%, which is similar to the results of the literature marked by a clear male predominance represented by 63.7% and 62% in the studies of Guan et al. and Zhou et al. This difference is possibly explained by the higher frequency of risk factors for disease severity in the male sex. [10].

The main comorbidities found in our patients were hypertension in 20%, diabetes in 11.42% of cases, which is consistent with the results of the literature where the main risk factors in the hospitalized population were arterial hypertension (15 to 30%), diabetes (7.4-19%) and vascular pathologies (2.5-8%) [8,9]. On the other hand, the percentage of smoking patients in our population was much higher than that reported in other studies with a percentage of 37.14% versus 6-12.6% [8]. In a retrospective analysis on Asian population by Mao et al [4].The prevalence of neurological manifestations in COVID-19 was 36.4%, Mao's study, finds 14.8% of cases of altered mental status, followed by headache 13% [11].

The mechanisms of neurological damage of COVID-19 are diverse, involving hypoxia, immune system and the angiotensin converting enzyme (ACE2) [12]. Li et al, proposes that the neurological tropism of Sars-Cov-2 may be responsible for anosmia/hypoagueusia, neuromuscular damage that would decrease the efficiency of coughing, as well as damage to the medullary respiratory center that would explain the absence of spontaneous breathing observed in several patients, and would favor acute respiratory distress [13]. It has been assumed that nervous system manifestations may occur due to the spread of the virus via peripheral nerves, the hematogenous route, direct endothelial injury, or as a result of a hypercoagulable state [13] .

Figures *3* and 4 explain the Pathophysiological Mechanism of SARS-COV-2 and the Pathogenesis of Nervous System Injury Caused by Coronaviruses [14].

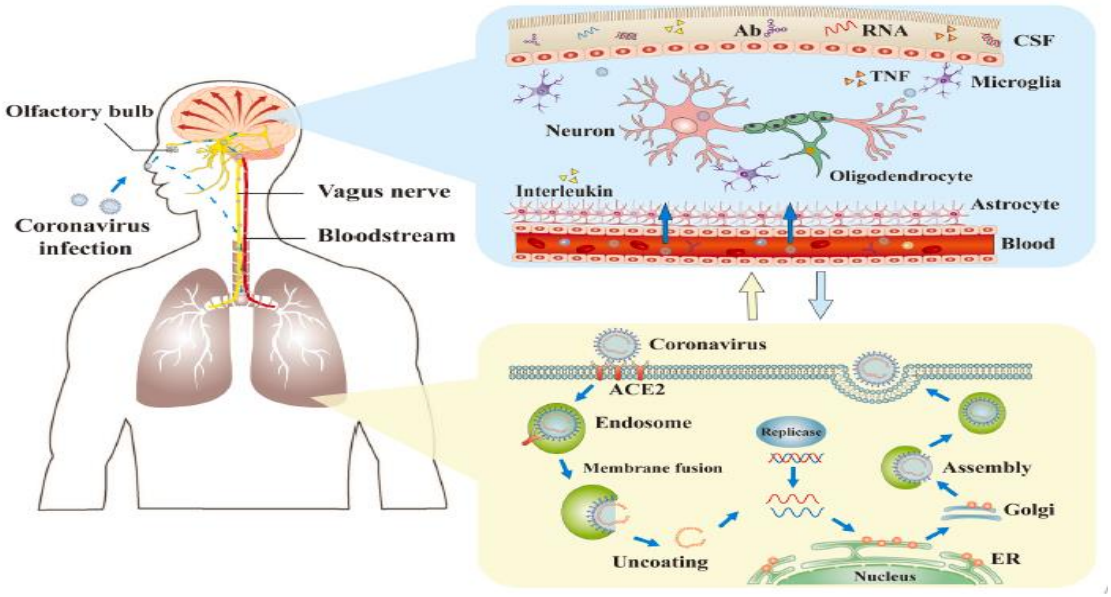

Figure 3: Pathophysiological mechanism of SARS-COV-2. Y. Wu, et al. [14].

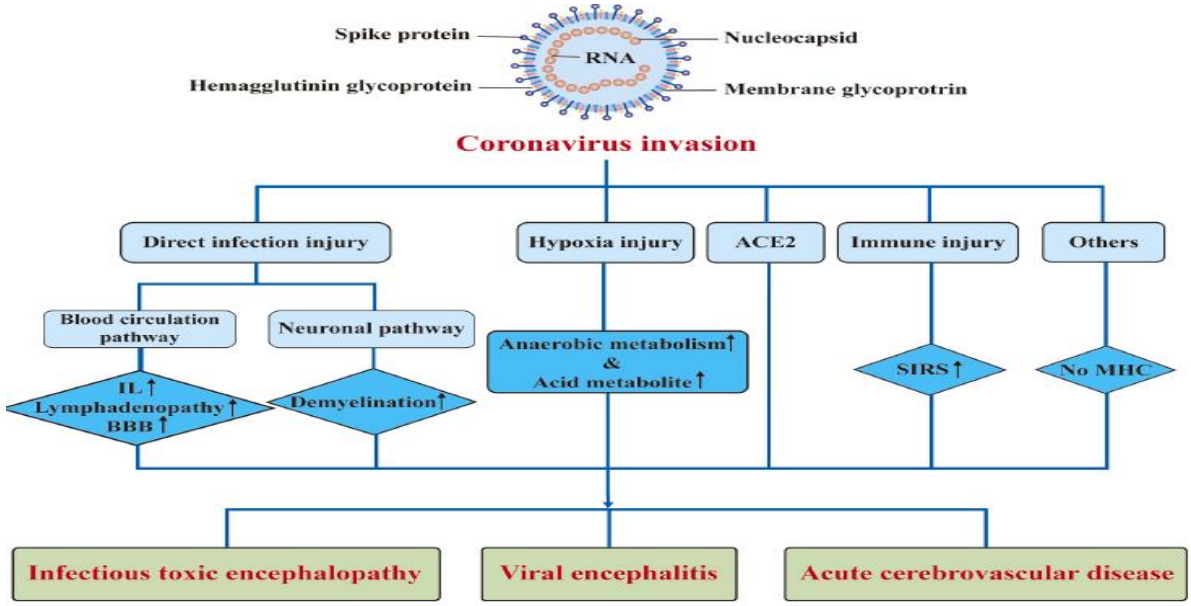

Figure 4: Pathogenesis of nervous system injury caused by coronaviruses (ACE2: angotensin-converting enzyme2; BBB: blood-brain barrier; IL: interleukins; MHC: major histocompatibility complex; SIRS: systemic inflammatory response syndrome) [14].

The different acute neurological impairments occurring during SARS-CoV-2 infection have been classified according to our study results:

1- Headache:

In our study headache represents the most frequently encountered neurological sign with a prevalence of 94.28% while it presented only 13% of cases in a retrospective study on 214 patients conducted in Wuhan (China), The lack of specificity and the poverty of the semiological description of this symptom does not make it a very discriminating clinical character [4].

2- Anosmia and/or hypoagueusia:

These 2 signs represented the most frequently found clinical symptoms in our population after headache with a prevalence of 80% which is close to the results of a recent European study [4] with a percentage of 85.6% for anosmia and 88% for dysgeusia while their prevalence was 19.4% in Italy [15] and much more diminished in Chinese studies, where these complaints were noted only in, respectively, 5.1% and 5.6% of patients [4].

3- Neurovascular features:

In our study, 4 patients had a cerebral infarction, which corresponds to a prevalence of 11.42% and which remains lower than the results of the literature or Cerebral infarctions are classified among the most frequently reported disorders with a prevalence of 26 to 62% [16], The pathophysiology of cerebral infarction could be related to a disturbance of coagulation phenomena, due to the inflammatory syndrome, but also to a state of hypercoagulability specific to COVID-19, as evidenced by

higher levels of D-dimer, as already reported in MERS [17]. This hypercoagulability would account for the fact that many cerebral infarctions occurred in the absence of a pre-existing pathological condition and were of particular severity [18]. COVID-19 thus appears to be an independent risk factor for cerebral infarction [19].

Cerebral venous thrombosis remains among the rare neurological manifestations described in Cov 2 sars involvement with a prevalence <0.5% of all COVID patients according to the literature [1] in our population we had 2 cases of cerebral venous thrombosis which corresponds to 5.71% of cases.

4- Critical phenomena:

Epileptic seizures were present in 4 patients of our series which represent about 11.42% of cases, 2 of them have convulsive seizures due to a destabilization of their already known epilepsy. In a Chinese series of 304 patients suffering from COVID-19, only 2 patients presented "epileptic-like" episodes in a context of ionic disorders [20] and in another French series of 222 patients, only 8 patients had an isolated epileptic seizure. It is therefore unlikely that the genesis of the disorders of consciousness is due to comital seizures [21].

5- Meningoencephalitis:

Meningoencephalitis directly associated with SARS-CoV-2 is rare, ranging from 6 to 9.5% depending on the series [1-18]. Only 1 case of meningoencephalitis was observed in our population 2,85% and we notably did not have isolated meningitis in our series which is the case for the majority of studies done, which is explained by the fact that the direct neurological tropism of sars-cov 2 remains uncertain. [22]

In different studies encephalopathies represented a significant percentage ranging from 31 to 38%, followed by encephalitis 4 to 10% [23] and in a recent English series of 43 neuro COVID patients found a surprisingly high number of acute disseminated encephalomyelopathies (ADEM) the CSF analysis did not show specific antibodies and the patients were treated with corticosteroids or polyvalent immunoglobulins, with variable but rather favorable responses [24].

There were no cases of metabolic or toxic encephalopathy in the patients of our study and in the different registers of COVID patients with neurological manifestations cited in the literature the frequency of these manifestations was difficult to estimate, due to probable under-reporting. [1]

6- Peripheral nervous system involvement:

It is very largely dominated by Guillain Barré syndrome, occurring 5 to 10 days (with a range of 7 to 24 days) after the onset of signs of viral infection. We described 4 cases of PRNA in our series corresponding to the classic form of Guillain-Barré syndrome (11.42%) which is in agreement with the literature where this syndrome represents (7 to 12%) [17,21]. In the literature only three patients had associated diarrhea [21]. While other variants of the syndrome were exceptional such as Miller Fisher syndrome [21], isolated involvement of the cranial nerves and the fibular nerve [17,21].

7- Psychiatric manifestations:

The majority of our patients presented a depressive syndrome during their hospitalization with a prevalence of 74.28% as well as insomnia described in 5 patients of our series 14.28% which exceeds the results of the literature, a retrospective study of more than 60,000 cases of Covid-19 in the United States indicate an incidence of 18, 1% of psychiatric diagnoses only (including depressive syndromes, anxiety disorders and insomnia) within two weeks or three months of a Covid-19 diagnosis, of which 5.8% were new psychiatric diagnoses [25].

In our study there was only 1 case of behavioral alteration and 2 patients who presented hallucinations which corresponds to 2.85% and 5.71% respectively, while in other retrospective studies the prevalence of mental status alteration (defined as acute alteration of personality, behavior, cognition or consciousness) was higher ranging from 8-21% [1] On the other hand, our resuscitation colleagues have observed many behavioral disorders in subjects with severe forms of the virus, especially in young patients, during intubation, which is described in the literature with the presence even of resistance to extubation, confusion and agitation, as well as hallucinations [5].

There were other rare neurological manifestations in our series such as vertigo discovered in 2 of our patients 5.71% which corresponds to the literature that describes the presence of vertigo in 1 to 17% of cases [1]. A study conducted in Strasbourg, France, reported several other neurological symptoms and signs in patients with COVID-19, such as pyramidal irritation (67%) and a dysexecutive syndrome (36%), these findings were not specific to the underlying disease mechanism [4].

Conclusions

Despite the fact that COVID 19 infection presents with respiratory manifestations first, neuropsychiatric complications are frequent and their great heterogeneity suggest that different pathophysiological mechanisms are involved, ranging from direct neuronal aggression by the virus to dysimmune or general mechanisms.A better understanding of the pathophysiology of these neuropsychiatric disorders will allow for better preventive and curative management.

Possible neurological consequences in the longer term are to be monitored, particularly in the context of "long COVID", an association of extremely varied symptoms, the description and exploration of which is the subject of numerous ongoing studies.

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