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SARS-Cov-2 Omicron variant reinfections at the CHU Ibn Rochd in Casablanca: About 4 cases

Bouchra IFEGH[1],Ouiame ELFADEL[1],yasmine SAHEL[1] ,Hassna JABRI[2],Moulay Hicham AFIF[2], Maha SOUSSI ABDALLAOUI[1]
1-Microbiology Laboratory
2-Pneumology Department Ibn Rochd University Hospital in Casablanca
Faculty of Medicine and Pharmacy, Hassan II university of Casablanca

Abstract:- Since the emergence of the new Omicron B.1.1.529 variant of Severe Acute Respiratory Syndrome *Coronavirus* 2 (SARS-CoV-2) in November 2021, the number of positive cases has continued to increase. Due to its rapid spread, this new variant has become dominant worldwide. This is also the case in Morocco, where 95% of SARS-CoV-2 infections are secondary to this variant. In addition, the high number of mutations in the viral S protein has raised concerns about the possibility of escape of the virus from antibodies induced by previous infection or by vaccination. However, very few studies have reported the notion of reinfection with this new variant. We report four cases of Covid-19 reinfection with the Omicron variant, diagnosed at the Ibn Rochd University Hospital in Casablanca, in four vaccinated healthcare professionals.

Keywords:- *SARS-CoV-2, COVID-19, Reinfection, Vaccination, Mutation, SARS – CoV-2 variants.*

I. INTRODUCTION

SARS-CoV-2 is a virus that first appeared in December 2019 in Wuhan, China, and has caused more than 360 million cases and 5.6 million deaths to date [1]. Several variants have emerged during these 2 years and have been responsible for different epidemic waves. The main mutants that have appeared are : Alpha (B.1.1.7), Beta (B.1.351), Gamma (P.1) and Delta (B.1.617.2) [2]. The latter is characterized by high transmissibility, high viral load, long duration of infection and occurrence of severe forms [3]. As a result, Delta rapidly became the dominant variant worldwide until November 2021.

On November 26, 2021, 23 months after the first case of SARS-CoV-2, a new variant, SARS-CoV-2 B.1.1.529, was reported and named Omicron [4].

Several mutations have been identified particularly in the Spike (S) protein of the Omicron variant (e.g., 69-70del, T95I, G142D/143-145del, K417N, T478K, N501Y, N655Y, N679K, and P681H) explaining its high transmissibility and infectivity [5,6].

Despite the development of new vaccines, the problem of reinfection and appearance of new variants continues to proliferate making it difficult to limit the spread of this virus.

We report four cases of rapid reinfection with the Omicron variant, diagnosed at the Ibn Rochd University Hospital in Casablanca (Morocco), in four health professionals.

- *Observation 1*

This is a 25-year-old female patient, healthcare professional, with no specific pathological history, vaccinated with two doses of Sinopharm® vaccine against SARS-CoV-2, the last dose was in March 2021. On January 3, 2022, the patient presented with a fever, cough, pharyngitis, headache and myalgia.

The SARS-Cov-2 RT-PCR *(MASCIR 2.0 Kit)* on a nasopharyngeal sample came back positive with Cts at 18 and 20 respectively for the S and RdRp genes.

A Multiplex PCR (BioFire FilmArray Respiratory Panel-2.1 SARS-CoV-2; BioMérieux®) was performed on the same sample, and revealed a SARS-CoV-2 and Respiratory Syncytial Virus co-infection. The work-up was completed by an RT-PCR with the TaqPath COVID-19 RT-PCR KIT®, revealing the presence of the ORF1ab (Ct:18) and N (Ct:17) genes and an absence of detection of the S (Drop S) gene, pointing to an Omicron variant infection.

The patient received treatment based on: Azithromycin 500mg on the first day and 250mg for 6 days, vitamin C 1g twice a day and zinc 45mg once a day and paracetamol if necessary. The evolution was marked by the total regression of clinical signs after one week and the patient returned to work.

Three weeks later, the patient presented a second, more severe infectious episode with an influenza-like illness and a fever of 39.5°C, all evolving in a context of profound asthenia. A second RT-PCR was performed by the (Mascir® and TAqPath® kits) and came back positive for SARS-CoV-2 with no detection of the S gene suggesting an infection with the same Omicron variant. A multiplex PCR was performed to search for possible viral co-infections that could explain the clinical symptomatology; and that objectified an isolated SARS-COV-2 infection. A neutralizing anti-SARS-CoV-2 antibody assay (ABBOTT®/ARCHITECT®) was performed, showing the presence of anti-SARS-Cov-2 IgG AC at 24892.6 AU/ml.

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➢ *Observation 2*

This is a 56-year-old patient, healthcare professional, with risk factors of obesity with a BMI of 30 and high blood pressure, vaccinated with two doses of Sinopharm® vaccine against SARS-CoV-2, the last dose being in February 2021 . The patient presented on December 30, 2021 with a symptomatology consisting of cough, pharyngitis, headache and myalgia. The SARS-Cov-2 RT-PCR *(MASCIR 2.0 Kit)* on a nasopharyngeal sample came back positive with Cts at 29 and 31 respectively for the S and RdRp genes. RT-PCR using the TaqPath COVID-19 RT-PCR KIT®, showed the presence of the ORF1ab and N genes (Cts: 31) and an absence of detection of the S gene (Drop S), pointing to an Omicron variant infection.

Multiplex PCR (BioFire FilmArray Respiratory Panel-2.1 SARS-CoV-2; BioMérieux®) performed on the same sample did not detect other viral targets associated with SARS-CoV-2. The patient received treatment based on: Azithromycin 500mg on the first day and 250mg for 6 days, vitamin C 1g twice a day and Zinc 45mg once a day and paracetamol if necessary. The evolution was marked by the total regression of clinical signs and the patient returned to work.

Twenty-two days later, the patient presented a second flu-like episode with a fever of 38.7°C, all evolving in a context of conservation of the general state. The RT-PCR confirmed the Covid-19 infection (by Mascir® and Taq-Path® kits) with the Omicron variant (Drop S) with Cts at 19 and 17 for the ORF1ab and N genes respectively. Multiplex PCR confirmed an isolated SARS-CoV-2 infection. An anti-SARS-CoV-2 neutralizing antibody assay (ABBOTT®/ARCHITECT®) was performed, showing the presence of anti-SARS-CoV-2 IgG AC at 4983.1 AU/ml.

➢ *Observation 3*

This is a 29-year-old female patient, healthcare professional, with a history of chronic respiratory disease, vaccinated with three doses of SARS-CoV-2 vaccine, two doses of Sinopharm® vaccine and a third with Pfizer® vaccine received in October 2021. On January 5, 2022, the patient presented with fever, cough, pharyngitis, headache and myalgia. The SARS-Cov-2 RT-PCR *(MASCIR 2.0 Kit)* on a nasopharyngeal sample came back positive with Cts at 16 and 17 respectively for the S and RdRp genes. RT-PCR using the TaqPath COVID-19 RT-PCR KIT®, showed the presence of the ORF1ab and N genes (Cts: 18 and 17) and an absence of detection of the S gene (Drop S), pointing to an Omicron variant infection. Multiplex PCR (BioFire FilmArray Respiratory Panel-2.1 SARS-CoV-2; BioMérieux®) performed on the same sample did not reveal any other viral targets associated with SARS-CoV-2.

The patient received treatment based on: Azithromycin 500 mg on the first day and then 250 mg for 6 days, vitamin C 1g twice a day and Zinc 45 mg once a day and paracetamol if necessary. The evolution was marked by the total regression of clinical signs after one week and the patient returned to work.

One month later, the patient presented a second infectious episode with similar signs. RT-PCR on February 03, 2022 confirmed infection with SARS-CoV-2 variant Omicron (Drop S) (by Mascir® and Taq-Path® kits) with Cts at 33 for the different genes. Multiplex PCR confirmed an isolated SARS-CoV-2 infection. An anti-SARS-CoV-2 neutralizing antibody assay (ABBOTT®/ARCHITECT®) was performed, showing the presence of anti-SARS-CoV-2 IgG AC at 28367.1 AU/ml.

➢ *Observation 4*

This is a 30-year-old female patient, healthcare professional, with no specific pathological history, not vaccinated against SARS CoV-2. The patient presented on January 3, 2022 with a symptomatology of respiratory difficulty, cough, pharyngitis and headache. The SARS-Cov-2 RT-PCR *(MASCIR 2.0 Kit)* on a nasopharyngeal sample came back positive with Cts at 30 and 32 respectively for the S and RdRp genes.

The work-up was completed by an RT-PCR using the TaqPath COVID-19 RT-PCR KIT®, revealing the presence of the ORF1ab (Ct:29) and N (Ct:30) genes and an absence of detection of the S (Drop S) gene, pointing to an Omicron variant infection.

The patient received treatment based on: Azithromycin 500mg on the first day and 250mg for 6 days, vitamin C 1g twice a day and zinc 45mg once a day and paracetamol if necessary. The evolution was marked by the total regression of clinical signs after ten days and the patient returned to work.

One month later, the patient presented a second infectious episode with a fever of 40°C, chills and pharyngitis, all evolving in a context of profound asthenia. A second RT-PCR was performed with the Mascir® kit and came back positive for SARS-CoV-2 with Cts at 32 and 32 respectively for the S and RdRp genes. A quantitative serology of SARS-CoV-2 was performed showing the absence of IgM type antibodies and the presence of IgG type antibodies at a titre of 40.475 (positive if > 1.6).

II. DISCUSSION

The rapid spread and international dissemination of the highly mutated variant, Omicron has raised concerns that this variant is dominant worldwide and that many therapeutic or preventive interventions are ineffective. This is the case in Morocco where 95% of Covid-19 infections are currently due to the Omicron variant [7].

Many of these concerns are justified since the Omicron variant S protein has escaped antibody-mediated neutralization. Indeed, the escape capacity of the variant is higher than those of any previously analyzed S proteins of the other variants [8].

Other studies conducted prior to the emergence of the Omicron variant have indicated that patients recovering from COVID-19 infection are effectively protected against

reinfection and that antibody responses play an important role in protection [9,10]. This is probably not the case for the Omicron variant since all four of our patients developed reinfection with the same variant during their convalescence period.

The new Omicron variant is characterized by a few deletions and more than 30 mutations, several of which (e.g., 69-70del, T95I, G142D/143-145del, K417N, T478K, N501Y, N655Y, N679K, and P681H) overlap with those of the Alpha, Beta, Gamma, or Delta variants [6]. These mutations are known to result in increased transmissibility, higher viral binding affinity, and greater escape from antibody response [11].

The absence of detection of S protein on so-called screening PCRs reflects the presence of the 60-70 deletion of S protein. This deletion exists in both the Alpha and Omicron variants. Therefore, given the current state of the pandemic and the disappearance of the Alpha variant, the non-detection of the S gene (Drop S) suggests a strong presumption of infection with the new Omicron variant in our patients.

Several studies suggest that neutralizing antibodies secondary to vaccination are essential for protection against SARS-CoV-2 [12,13]. For example, according to Hoffmann et al, antibodies obtained after two doses of vaccine neutralized the Omicron variant S protein with a 34-fold reduced efficacy compared to the Delta variant [8]. This is the case for three of our patients who, despite vaccination with at least two doses of the SARS-CoV-2 vaccine and the presence of a high level of neutralizing antibodies (above 10 times the threshold for patient 2 and 400 times the threshold value for patients 1 and 3), were reinfected with the Omicron variant.

Moreover, the protective role of antibodies produced following a previous infection with SARS-CoV-2, remains to be discussed concerning the Omicron variant. According to Hoffmann et al, results obtained after the study of serum samples collected in Germany during the first wave of the pandemic indicate that this high level of protection may not apply to reinfection with the new Omicron variant [8]. For example, neutralization of Omicron variant S protein was 80-fold less efficient compared to controls and several sera did not exert neutralizing activity. Although neutralization by sera from patients infected with the Delta variant remains to be studied, it is likely that convalescent patients are not sufficiently protected against symptomatic reinfection with the Omicron variant, according to recent data [8]. This is the case for patient 4, who developed anti-SARS-CoV-2 antibodies at a significant titer following a Covid-19 infection one month earlier. This would suggest an escape of the new mutated variant from neutralization by post-vaccination and post-infection antibodies.

In South Africa, current data suggest an increase in reinfection, although the increased use of rapid antigenic tests makes it difficult to assess the rate of reinfection with this new variant [14]. Nevertheless, these data could be explained by immune escape mutations present in the Omicron variant.

III. CONCLUSION

Reinfection with the Omicron variant remains poorly documented. The analysis of the data in the literature and the four cases in this study suggest several hypotheses that may explain reinfection by this same variant. First, the large number of mutations present on the Omicron variant S protein allows it to escape the immune system.

Secondly, the laxity observed in the general population regarding the application of barrier and protective measures, particularly after a first infection, thus giving a "false sense of protection", could increase the risk of reinfection. Finally, the absence of vaccination or the non-administration of booster doses of SARS-CoV-2 vaccines could also be factors favoring reinfection with the new variant.

Competing interests

The authors declare that they have no competing interests

Authors' contributions

All authors have contributed to conception and design, acquisition of data, analysis and interpretation of data, drafting the article and revising it critically for important intellectual content they also have approved the final version to be published.

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