LETTER TO THE EDITOR

Management guidelines in triplidemia due to respiratory viruses and the social importance of the clinical-genetic diagnosis algorithm of SARS-COV2

Estrategias de manejo en la triplidemia por virus respiratorios y la importancia social del algoritmo de diagnóstico clínico-genético de SARS-COV2

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To the Editor,

We revisit the recently published article by Ramírez-García[1], which demonstrates how to detect different types of SARS-CoV-2 variants without molecular testing (Table 1) through examination of the oral cavity. From a social perspective, this is crucial because it enables a faster response to a global health issue like the "tripledemic" caused by the simultaneous infection with SARS-CoV-2 Omicron variant BQ.1.1, influenza virus H2N3, and respiratory syncytial virus (RSV). This approach facilitates differential diagnosis and the early initiation of treatment, potentially reducing mortality. In this context, one target is to strengthen trained immunity, for which the use of OM-85 may be reconsidered as it promotes the production of alpha-defensins that opsonize respiratory pathogens such as SARS-CoV-2, RSV, and influenza virus, among others[2]. Additionally, OM-85 has an antiviral effect vs SARS-CoV-2, reducing RNA from open reading frames and other genes. Other adjuvants worth reconsidering in addressing the tripledemic include extended-release pirfenidone, Vita Deyun®, and S-adenosylmethionine[3,4], as they have anti-inflammatory, antioxidant, and antiviral properties effective vs COVID-19. By silencing ACE2 expression, these agents prevent SARS-CoV-2 entry and simultaneously block the cytokine storm. S-adenosylmethionine, in particular, seems to have an effect on controlling mitochondrial oxidative stress during respiratory infections, especially in managing the accumulation of circulating mutated mitochondrial DNA, which has recently been reported in COVID-19[5]. Lastly, calcium dobesilate, which blocks the APOE-heparan sulfate system binding to ACE2 and prevents SARS-CoV-2 entry, should also be reconsidered; it is especially useful in Omicron variants that show significant genetic variability in the spike protein. In managing the tripledemic within both private and public hospital settings, it is essential to clinically identify the COVID-19 variant and initiate specific treatment within the first 2 to 4 days to reduce mortality and morbidity, along with specific antivirals for influenza and RSV. Therefore, it is proposed to consider as alternatives the viral fusion membrane inhibitors such as OM-85, calcium dobesilate, extended-release pirfenidone, and Vita

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Table 1. Clinical-Genetic Algorithm for Identifying SARS-CoV-2 Variants

SARS-CoV-2 Genetic Lineage or Variant	Oral Cavity Characteristics	Reason for Consultation
Omicron (lineages BQ.1.1), known as "Hellhound"	Diffuse palatopharyngeal enanthem with petechiae, telangiectasia, increased blood vessels in the palate, exudative posterior palate and violet anterior palate	Maculopapular rash on the chest, back, and plantar area
Omicron (lineage BA2.75, p.G446S and p.R493Q in the spike protein gene), known as "Centaur"	Erythematous palate with hyperproliferation of blood vessels	Peripheral neuropathy with moderate respiratory symptoms
Omicron (lineages BA.5, BA.4, BA.1)	Palatal vasculitis with ephelides, serpentiform enanthem on the posterior palate	Proximal and distal peripheral neuropathy
Delta AY.4/Omicron BA.1 lineage (deltacron)	Palatopharyngeal vesicular enanthem in a cluster pattern, hyperproliferation of blood vessels and micro-ephelides, salmon-colored palate	Neuropathy, venous insufficiency, ocular and skin telangiectasia
Omicron (lineages BA.2.12 and BA.2.9)	Palate with exudative ulcerative oropharynx and petechiae	Macroangiopathy
Omicron (lineages BA.2 and BA.2.12.1)	Petechiae in the oropharynx accompanied by diffuse vesicular enanthem on the pharyngeal arch and base of the tongue	Mild flu-like symptoms
Omicron (lineages BA.2, BA.3, BA.4, and BA.5)	Violet posterior palate, diffuse palatopharyngeal vesicular enanthem, hyperproliferation of blood vessels	Peripheral neuropathy
Omicron (lineages B.1.1.529)	Single telangiectasia and vasculitis in the form of micro-ephelides, pale pink or salmon-colored anterior palate	Peripheral neuropathy
Omicron (lineages B.1.1.529)	Single telangiectasia and vasculitis in the form of micro-ephelides, pale pink or salmon-colored anterior palate	Peripheral neuropathy
Omicron (lineages B.1.1.529)	Single telangiectasia and vasculitis in the form of micro-ephelides, pale pink or salmon-colored anterior palate	Peripheral neuropathy
Omicron (lineages BA.1, BA.1.1)	Hyperproliferation of blood vessels, micro-ephelides, salmon-colored or pale pink palate	Peripheral neuropathy and diarrhea
Alpha lineage Q Beta lineage B1.1351 Gamma (lineages P.1) Epsilon (B.1.43 and B.1.43)	Vesicular palatopharyngeal enanthem, posterior palate mucosa salmon or yellow in color, hypertrophy of gustatory corpuscles	Severe respiratory symptoms
Alpha (lineage B.1.1.7, GR clade)	Salmon or yellow-colored palatal mucosa, no enanthem	Severe respiratory symptoms
Delta (lineage B1.617.2)	Palatopharyngeal vesicular enanthem in a racemose and diffuse pattern, palatal hematomas	Spontaneous epistaxis
Delta (lineages AY)	Palatopharyngeal enanthem in a racemose and/or diffuse pattern, exudative oropharynx with cracks	Spontaneous epistaxis
Mu (B.1.621, B.1.621.1)	Posterior pharynx with herpetiform vesicular enanthem and palatopharyngeal hematomas	Moderate respiratory symptoms
Prolonged COVID-19, Subacute COVID-19	Central palatal fibrosis, pale pink, light violet, or salmon-colored anterior and posterior palate	Peripheral neuropathy

Deyun®, as well as free radical antagonists like S-adenosylmethionine. In private health care settings in Mexico, medications are available to tackle the tripledemic, making it a proposal for public policy consideration.

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Conflicts of interest

None declared.

Ethical disclosures

Protection of human and animal subjects. The authors declare that the procedures followed were in accordance with the regulations of the relevant clinical research ethics committee and with those of the Code of Ethics of the World Medical Association (Declaration of Helsinki).

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author is in possession of this document.

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