


Rare Diseases and COVID-19: How are the Patients?

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Dear Editor,

When searching the scientific literature COVID-19-associated syndromes in addition to syndromes middle eastern respiratory syndrome (MERS), severe acute respiratory syndrome (SARS), some cardiovascular syndromes and post intensive care syndrome [1,2], we found the syndromes of Guillain-Barré, Miller Fisher, polyneuritis cranialis, Kawasaki, Inflammatory multisystem syndrome, and syndrome of inappropriate antidiuretic hormone secretion [3-29]. Of these, only Guillain-Barré syndrome and Miller Fisher syndrome, Kawasaki diseases and Inflammatory multisystem syndrome have currently present cranio-facial manifestation (Table 1), but possibly others will become know when the damage of COVID-19 becomes known.

Although there is no standardized definition of rare diseases, the classification of rare diseases is closely related to a definition according to point prevalence in the current political and legislative context, and such definitions are based on a prevalence threshold directly or implied. According to the World Health Organization (WOS) and adopted by the Ministry of Health of Brazil, a rare disease affects up to 65 per 100,000 individuals [30]. Each rare disease, taken separately, affects a limited number of people. Considering, however, that there are up to 8,000 types of rare diseases worldwide, when grouped under a single category, their epidemiological impact may become quite significant. About 80% of those are caused by genetic factors, and the rest by other factors, such as environmental, infectious and immunologicalones [31]. Thus, rare diseases are a global challenge that must be overcome. A multi-professional and interdisciplinary team, including pediatric dentistry, oral medicine and pathology, is essential for success throughout the process.

Approaches involving rare diseases have been a constant concern by WHO. On 21 February 2019 - Nata Menabde, Executive Director, WHO office at the United Nations moderated a session to commemorate Rare Diseases Day. She highlighted the importance of including efficient and equitable health care systems in order to reduce inequalities to ensure no one is left behind, including persons with rare diseases, as we strive to achieve the 2030 Agenda for Sustainable Development (<https://www.who.int/news-room/feature-stories/detail/rare-diseases>).

Table 1. Characteristics of the patients with COVID-19-associated syndromes.

Syndrome	Number of Cases	Systemic Manifestations	Cranio-Facial Manifestations	PCR Assay for COVID-19	References
Guillain-Barré Syndrome (#139393)	37	Acute weakness in both legs; lower-limb weakness; lower-limb and upper-limb paresthesia; generalized areflexia; ataxia; flaccid areflexic paraplegia; severe fatigue; and respiratory failure.	Flaccid areflexic tetraplegia; facial weakness; facial diplegia; ataxia; and paresthesia.	Positive	Caress et al., 2020 [3]
Kawasaki Disease	26	Polymorphous maculopapular rash, and swelling of the hands and lower extremities	Limbic-sparing conjunctivitis; dry cracked lips, prominent tongue papilla	Positive	Jones et al., 2020 [4]; Labé et al., 2020 [5]; Toubiana et al., 2020 [6]; Whittaker et al., 2020 [7]
Inflammatory Multisystem Syndrome	534	Polymorphic rash, swelling (palms and soles), conjunctivitis, decreased appetite, diarrhea, dysuria, abdominal pain, hypotension or shock, severe cardiac illness, or severe end-organ illness	Dry, cracked, erythematous lips	Positive and Negative	Toubiana et al., 2020 [6]; Whittaker et al., 2020 [7]; Belot et al., 2020 [8]; Capone et al., 2020 [9]; Cheung et al., 2020 [10]; Chiotos et al., 2020 [11]; Dasgupta and Finch, 2020 [12]; Davies et al., 2020 [13]; Dufort et al., 2020 [14]; Greene et al., 2020 [15]; Lee et al., 2020 [16]; Perez-Toledo et al., 2020 [17]; Pouletty et al., 2020 [18]; Ramcharan et al., 2020 [19]; Regev et al., 2020 [20]; Rivera-Figuerosa et al., 2020 [21]; Riollano-Cruz et al., 2020 [22]; Sokolovsky et al., 2020 [23]; Verdoni et al., 2020 [24];
Miller Fisher Syndrome and Miller Fisher-like Syndrome	4	Anosmia; ageusia; ataxia; areflexia; albuminocytologic dissociation.	Right internuclear ophthalmoparesis, right fascicular oculomotor palsy	Positive	Gutiérrez-Ortiz et al., 2020 [25]; Fernández-Domínguez et al., 2020 [26]; Lantos et al., 2020 [27]; Reyes-Bueno et al., 2020 [28]
Syndrome of Inappropriate Antidiuretic Hormone Secretion	3	Fever; evidence of pneumonia (abnormal chest X-ray depicting bilateral infiltrates); euvolemic hyponatremia (< 135 mmol/L) with concurrent low serum and high urine osmolality (< 280 and >100 osmol/kgH ₂ O, respectively) and high urine sodium (>40 mmol/L).	-	Positive	Yousaf et al., 2020 [29]
Polyneuritis Cranialis	1	Ageusia; bilateral abducens palsy; areflexia and albuminocytologic dissociation.	-	Positive	Gutiérrez-Ortiz et al., 2020 [25]

Wakap et al. [32] found that the evidence-based population prevalence estimate of 3.5-5.9%, which is equivalent to 263-446 million people affected globally at any point in time, is still conservative. Many of these diseases still have limited understanding of their pathogenesis and/or limited efforts towards targeted therapy development. Due to the unusual existence of such diseases, it remains a long-recognized challenge for physicians, scientists and patient advocacy organizations to convince government agencies and businesses to provide the requisite funding to research them and to establish efficient and accessible therapies [32].

In this period of pandemic, with the numerous limitations and performance of health services, particularly dental clinics, oral medicine services and clinical genetics, we have a reflection and concern about these millions of patients with rare diseases and how they are being systematically monitored. Successful experiences have been presented with actions directed to patients and professionals remotely in three main lines: (1) care and treatment aspects directly related to rare diseases; (2) psychological aspects that the emergency itself produces or amplifies; and (3) social and legal aspects that influence the life of the individual concerned at work and in relationships [33-35].

Thus, an intense collaboration between services, telemedicine groups and also the opening of communication and monitoring channels for these patients is fundamental, particularly with regard to dentistry.

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