

of the 303 COPD patients, by the time of their recruitment, have been previously published,^{3,4} and some are presented in Table 1.

In the meantime, 61 patients (20.13%) died. Their median and mean age of death was, respectively, 77.00 and 77.02 (\pm 8.78) years, being 77.00 and 77.45 (\pm 8.51) years for male patients and 76.50 and 74.13 (\pm 10.6) years for female patients. The mean FEV₁% of the patients who died and those still alive was 43.36 and 54.40, respectively (P = 0.032), at the time of recruitment. However, we found no statistically significant association between death and the GOLD classification nor with a history of frequent exacerbations.

Thirty-two patients presented COPD exacerbation with acute-on-chronic respiratory failure by the time of death. Pneumonia, heart failure, advanced stage lung cancer and kidney failure were the other most important causes of

death. In 27 patients, two or more different disorders contributed and were present at the time of death.

COPD exacerbation with acute-on-chronic respiratory failure was the most important cause contributing to death, suggesting that most of these patients have died, in fact, because of COPD. Taking into account the current average life expectancy of the Portuguese population⁵ – 81.06 years, 78.07 for men and 83.67 for women – COPD was associated with a shorter life expectancy, particularly in female patients.

COMPETING INTERESTS

The authors have no competing interests to declare related to this study.

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A Case Report of Acute Hepatitis of Unknown Origin

Caso Clínico de Hepatite Aguda de Origem Desconhecida

Keywords: Biomarkers; Child; Disease Outbreaks; Hepatitis
Palavras-chave: Biomarcadores; Criança; Hepatite; Surtos de Doenças

Dear Editor,

Since the first international alert on the 5th April 2022 and the ongoing news, probable cases of hepatitis of unknown origin have been reported in children worldwide. The etiology and pathogenic mechanisms of the disease remain under investigation, and so far the evidence suggests adenovirus or SARS-CoV-2 as being the most likely infectious causes, although toxins, drugs or environmental exposures have been considered as well. Further hypotheses point out a novel pathogen or variant of adenovirus or SARS-CoV-2.¹

In Portugal, according to the most recent data from the European Centre for Disease Prevention and Control (ECDC), published on the 1st July there are only 19 suspected cases.²

We report, to the best of our knowledge, the very first suspected case of non-viral A-E hepatitis in Portugal.

The patient was a previously healthy 22-month-old female child, with a history of SARS-CoV-2 infection in January 2022. During April 2022, she presented with prolonged fever (maximum 40.2°C) that was managed with antipyretics, not exceeding therapeutic daily doses, with complete resolution after day-10. She also presented with anorexia and malaise, and on days four and five with non-bloody diarrhea. On day nine she had limited vomiting.

During the acute illness there were no signs of jaundice, choloria or acholic stools. A good general appearance was kept throughout the disease course.

With no relevant previous results, follow-up bloodwork

at day-11 showed elevation of serum aspartate and alanine aminotransferase (1163 U/L and 814 U/L respectively), lactate dehydrogenase (1003 U/L), alkaline phosphatase (358 U/L) and gamma-glutamyl transpeptidase (239 U/L), and hence a diagnosis of acute hepatitis was made. Abnormal results had nearly normalized by day-23 of symptom onset. Liver function tests, as well as bilirubin levels, remained normal throughout the rest of the disease course.

Microbiologic evaluation excluded hepatitis A-E virus. The serology for SARS-CoV-2 was IgG positive and IgM negative, suggesting a non-recent infection. A subspecies C adenovirus was isolated in the respiratory tract. No toxicology tests were performed. No relevant epidemiological link was found, including recent trips, or known contact with similar cases.

This case strengthens the role of adenovirus as a possible etiologic agent, identifying a similar enteric subtype when compared with both respiratory and fecal samples from children in the United Kingdom.³ It also emphasizes a possible consequence of adenovirus infection in children previously infected by SARS-CoV-2, supporting previous knowledge on the subject.⁴

The nonspecific clinical spectrum should be emphasized, suggesting that this entity can present even in the absence of more specific clinical signs of hepatitis. On another note, it is important to raise awareness that not all potential cases progress to acute liver failure or hospital admission, and that there are milder courses of disease as reported here.

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We recommend a systematic approach to all cases of acute hepatitis, highlighting the need for a thorough clinical and epidemiological characterization and reporting.

AUTHORS CONTRIBUTION

All authors contributed equally to this manuscript.

PROTECTION OF HUMANS AND ANIMALS

The authors have followed the protocols of their work center on the publication of data. The data was anonymized and none of the authors had access to patient identification. The study was conducted in accordance with the Helsinki Declaration updated in 2013.

DATA CONFIDENTIALITY

The authors declare having followed the protocols in use at their working center regarding patients' data publication.

INFORMED CONSENT OF THE PATIENT

Obtained.

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