Reviewer's report

Title: Early acute pancreatitis in a child with compound heterozygosis F508-del/R1438W/Y1032C cystic fibrosis: a case report.

Version: 4 Date: 12 May 2013

Reviewer: W. Edward E Highsmith

Which of the following best describes what type of case report this is?: Unexpected or unusual presentations of a disease

Has the case been reported coherently?: Yes

Is the case report authentic?: Yes

Is the case report ethical?: Yes

Is there any missing information that you think must be added before publication?: No

Is this case worth reporting?: Yes

Is the case report persuasive?: Yes

Does the case report have explanatory value?: Yes

Does the case report have diagnostic value?: Yes

Will the case report make a difference to clinical practice?: Yes

Is the anonymity of the patient protected?: Yes

Comments to authors:

The report by Leonardi et al. describes a pediatric patient who presented with an abnormal IRT newborn screen, abnormal sweat electrolytes, pancreatic sufficiency, absence of detectable pulmonary disease, and an episode of acute pancreatitis.

Reports of unusual genotypes are always welcome, as it is thru compilation of reports such as this that, ultimately, we may gain further insights into genotype/phenotype correlations and gene structure/function relationships.

There are a few items that need to be addressed prior to publication.

In the Abstract, Introduction, last sentence: That the patient was without
pancreatic involvement is not strictly true – as the authors are reporting acute pancreatitis. Perhaps phrasing the last sentence as either “….without pancreatic insufficiency nor respiratory involvement.” Or “…with pancreatic sufficiency and no detectable respiratory involvement.” would better capture what the authors are communicating.

Abstract, Conclusion, last sentence. Compound heterozygosity for deltaF508/R1438/Y1032C is not a mutation, it is a genotype. Recommend changing …a “CF-causing mutation’… to …a “CF-causing genotype. In addition, as the deltaF508 and R1438W were shown to be in cis, the genotype should be written as deltaF508-R1438/Y1032C (applies throughout the manuscript).

Introduction, 1st sentence. CF is not the most common autosomal recessive disorder in western countries (for example, hemochromatosis is several times more common). Recommend changing to …most common, potentially lethal, autosomal….

Introduction, 3rd sentence. This is a little confusing. Pancreatitis does not occur in 20% of CF patients. However, approximately 20% of CF patients are pancreatic sufficient; and, pancreatitis typically occurs in this subgroup. I believe that is what the authors are saying. Suggest rephrasing this sentence.

Discussion, 1st sentence. I am not sure that exocrine pancreatic function is the most reliable barometer of CFTR function (for example, the vas defrens is more sensitive to CFTR dysfunction). However, it is a reliable predictor of overall disease severity. Suggest rephrasing.

Discussion, 2nd sentence. Should read “…patients who carry a mild mutation on at least one allele…”

Discussion, 3rd & 4th paragraphs. 50% of Italian CF patients are not homozygous for deltaF508. The frequency of deltaF508 is approximately 50% on CF chromosomes (which gives q² = 0.5 x 0.5 = 0.25, or 25% of Italian CF patients being homozygous). Similarly, the frequency of deltaF 508 is 70% on Northern European CF chromosomes.

Discussion, 6th paragraph. There is a typographic error in several places where Y1032C is written as Y032C.

Quality of written English: Needs some language corrections before being published