May 10, 2014

Dear Editor,

Please find enclosed the edited manuscript in Word format (file name: Answers to reviewers).

Title: Rare large homozygous *CFTR* gene deletion in an Iranian patient with cystic fibrosis

Author: Shirin Farjadian, Mozhgan Moghtaderi, Roberta Zuntini, Simona Ferrari

Name of Journal: *World Journal of Clinical Cases*

ESPS Manuscript NO: 10604

The manuscript has been improved according to the suggestions of reviewers which are highlighted in YELLOW:

Reviewed by 00029421

Straightforward focussed and relatively well written Ms describing a patient with CF among a population where this condition is not common. A rare but not unprecedented large gene deletion was identified - the unusual nature of the case is partially related to the fact that this deletion was homozygous due to parental consanguinity which resulted in unusual results (no delta F508 allele) on initial testing. Minor text changes needed It might be interesting to know what frequency and the spectrum of CF mutations are in this population.

Answer: As reported before, CF is not rare in Iran and the most frequent mutation is ΔF508. However, it is not as common as in Europe. We added this point in the revised ms with the related reference.

Reviewed by 00403513

The manuscript “Rare large homozygous CFTR gene deletion in an Iranian patient with Cystic Fibrosis” by Farjadian and colleagues reports a patient with homozygous exon 4-10 CFTR gene deletion mutation. Overall, this manuscript is well written and suitable as a case-report. Some minor issues might be considered previous to publication

1) General: Please proof-read English grammar.
   Answer: Proofreading was done by an experienced native English speaking editor.

2) The reported patient has parents with first-degree consanguinity.

Are there any further symptoms which might not be related to CF?
Answer: Parents and living siblings seem to be normal and with no particular problems diagnosed to date.

Could a syndrome i.e. due to multiple gene mutations be ruled out?
Answer: No, because we did not analyze other parts of their genomes.

3) Did the heterozygous parents/sister/brother show abnormal sweat tests or any sign of mild CF disease?
Answer: The results of their sweat tests were normal, which we have now noted in the revised ms.

4) Was genetic counseling performed for the family and the patient?
Answer: Genetic counseling is routinely performed for all CF patients referred to our center. We are aware that in this family, both parents, the patient's brother and one of the patient's sisters are carriers of del 4-10. We recommended that the carrier siblings should request genetic counseling again when they decide to get married, especially if they plan to marry one of their relatives.