The new syndrome is not really a new syndrome. *Al-Aqeel Sewairi syndrome, a new autosomal recessive disorder with multicentric osteolysis, nodulosis, and arthropathy*

To the Editor

I have read with great interest the article by Al-Aqeel,[1] wherein the authors described a new syndrome, I went through the scientific content of this manuscript in detail and was surprised to find this manuscript to be a replication of another manuscript recently published**,** which has been co-authored by the author of the current manuscript.

I would brief my comments on the following: 1. This syndrome has been described under the name of Nodulosis-Arthropathy-Osteolysis (NAO) syndrome (OMIM # 605156) and was published in the American Journal of Medical Genetics.[2] 2. Though the author described another family member, it does not mean it is a different syndrome. The author and Al-Mayouf et al[3] shared with Martignetti[3] the mapping of the disease gene to 16q12-q21, which means all included patients have the same disease. 3. Unfortunately, the author was trying to show that the new name (MONA/ Al-Aqeel-Sewairi syndrome) is recognized by OMIM and they gave the same number of NAO syndrome but in reality the name is not found (please see Table 1).[1] 4. The author was not accurate in delivering the information from other references: The author said that Al-Mayouf reported 5 affected members (page 25), apparently it was 10 affected members. In addition, the author used figures that have been published previously without citing the reference (Figure 1, 2).

I am sorry to be firm in my critique. However, this is purely based on scientific bases and I feel that for any publication to be credible it needs to be in comfort with known scientific and ethical principles of our medical profession.

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To the Editor

I have read with great interest the above mentioned article by Al-Aqeel,[1] where the author describes this syndrome. I reviewed the manuscript and its scientific contents. I believe this syndrome should be called Nodulosis-Arthropathy-Osteolysis (NAO) and not Al-Aqeel-Sewairi syndrome for the following reasons: 1. This syndrome was described as Nodulosis-Arthropathy-Osteolysis (NAO) syndrome and published in the American Journal of Medical Genetics.[2] The only accepted alternative symbols are NAO Syndrome and Osteolysis, idiopathic, Saudi type. Al-Aqeel-Sewairi syndrome is the synonym for the NAO syndrome and it was described in the same issue of American Journal of Medical Genetics.[4] 2. Following collaborative work between the 2 groups, the Riyadh Military Hospital (one family with 2 sibs affected), King Faisal Specialist Hospital and Research Centre (6 unrelated families with 10 affected) and Dr. Desnick and Martignetti from the Department of Human Genetics, Mount Sinai School of Medicine, resulted in mapping the disease gene to 16q 12-q21 and eventually identifying matrix metalloproteinase 2 (MMP2) a disease candidate gene. Mutation of the matrix metalloproteinase 2 gene (MMP2) causes a multicentric osteolysis and arthritis syndrome.[3]

In conclusion, to avoid clinical confusion in the future, in the event that the author may wish to publish other manuscripts using additional data or has further findings relating to this topic, the above syndrome should be referred to by its internationally accepted name "Nodulosis-arthropathy-osteolysis syndrome".

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Reply from the Author

In response to their comments, I would like to thank them for reading the article with great interest. But I wonder, which recent publication Dr. Al-Mayouf is referring to, as the publications I had on the syndrome were in 1999 (reference 13); 2000 (reference 14); 2001 (reference 16, 17, 18).[1] None of these are a replication of the present manuscript, as reference 13, 14 were mainly clinical and reference 16, 17, 18 were molecular.[1] However, the present manuscript is a complete description of the syndrome starting from phenotype to genotype (exact molecular and protein defect) with elucidation of the pathogenesis of the syndrome and the pathophysiological role of the matrix metalloproteinase 2 (MMP-2) protein in the syndrome and in other pathologies.

In response to their comments: 1. The syndrome was first described by myself at the American Society of Human Genetics (ASHG) Meeting in October 1999 and published at the American Journal of Human Genetics (AJHG) in 1999 under Al Aqeel-Sewairi Syndrome (see reference 13).[1] The syndrome was then described by 2 independent groups in the same issue of the American Journal of Medical Genetics (AJMG) (reference 14 and 15).[1] I have described it as multicentric osteolysis resembling Torq syndrome (Saudi type), that is why in OMIM, they referred to both references as OMIM # 605156. I did not name it on my AJMG manuscript (reference 14), as Al-Aqeel-Sewairi syndrome, as I was suspicious that it could be Torq syndrome.

In my original manuscript submission, I put all the names for the syndrome including nodulosis, arthropathy, osteolysis (NAO). However, (NAO) was deleted on editing, to fit the journal formatting, but the spell out is still there. 2. I was the principal investigator who collaborated with Martignetti et al[3] to try to clone the gene for this new syndrome. Then the reader joined us with their patients (reference 16,17,18), so I am not reporting a different syndrome, but reporting a detailed review of the syndrome. 3. After we found the exact molecular defect of the syndrome, and we have studied Torq syndrome patients, we are now sure it is a new syndrome with a novel molecular defect. We also know more about the clinical features and the progress of the disease. So using the exact description of the clinical features (multicentric osteolysis, nodulosis, arthropathy (MONA) / Al –Aqeel Sewairi syndrome) is appropriate (see reference 17, 19).[1] As it was first described as Al-Aqeel Sewairi in AJHG, then multicentric osteolysis (Torq like) – Saudi type, NAO in AJMG and OMIM. So it is appropriate to give it the same OMIM number, so OMIM could be updated according to the medical literature, as the name first given in OMIM was referred to my article in AJMG (reference 14), and the reader's article (reference 15). 4. The reader was not accurate on the figures, as Figure 1 is a combination of photos on 2 patients. Figure 2 is a combination of the x-rays of 2 patients and their MRI. However, in my previous manuscripts, there were separate figures for each.

I was accurate in delivering the information as when we studied the syndrome at the molecular level and then the reader joined us with their patients, we only studied 11 affected patients, as there was an overlap between our patients and their patients (see Methods page 24-25) and I am reporting these 11 patients in this manuscript.

In conclusion, this syndrome "Al Aqeel Sewairi Syndrome: a new autosomal recessive disorder with multicentric osteolysis, nodulosis, arthropathy. The first genetic defect of matrix metalloproteinase 2 gene" was first reported in 1999, and is a detailed description of it from phenotype to genotype (exact molecular and protein defect), with elucidation of the pathophysiological role of matrix metalloproteinase-2 (MMP-2), in health and disease.[1]

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