Response to: 'Mutation in MMP2 gene may result in scleroderma-like skin thickening' by Bader-Meunier *et al*

MMP2 related disease (Multicentric osteolysis, nodulosis and arthropathy—MONA syndrome—OMIM #259600) consists of a continuous clinical spectrum in terms of severity.[1] Even in the same affected individual, different features may present with varying severity (eg, nodulosis may be absent even with severe osteolysis). Till date less than 15 families with *MMP2* mutations have been reported[2 3] and, therefore, it is likely that the full phenotypical spectrum of *MMP2*-associated conditions has not yet been realised.

In this context, this report from Bader-Meunier *et al*[4] of a patient with biallelic *MMP2* mutation and scleroderma-like skin thickening in addition to the other known features of MONA syndrome is instructive. Notably, most previous reports of individuals with *MMP2* mutations are of young children and skin thickening can be a progressive feature. In future it will be interesting to learn about evolution of the phenotype in previously reported cases or the adult phenotype of this group of conditions.

We reported two families with 8q22.1 duplications and Leri's pleonostoesis (LP) and provided evidence that LP could also be considered as a transforming growth factor (TGF)-betapathy.[5] Interestingly, skin thickening was seen in one of our families with LP but was absent in all the members of the other family. Our previous work and the report of Bader-Meunier *et al* provides further support that presence of skin thickening can be a clue towards monogenic TGF-betapathies. However, skin thickening may be a more variable feature of those TGF-betapathies where it is not part of the core phenotype (cf Stiff skin syndrome—OMIM #184900).[6]

Recognising additional monogenic causes of scleroderma due to alterations in the TGF-beta pathway strengthens the possibility that rare variants in genes encoding members of this pathway as being causally linked with more common forms of scleroderma.

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