HGG Advances

LETTER TO THE EDITOR

Letter to editor: Orofacial overgrowth with peripheral nerve enlargement and perineuriomatous pseudo-onion bulb proliferations is part of the PIK3CA-related overgrowth spectrum

We read with interest the recent article by Koutlas et al.,[1] "Orofacial overgrowth with peripheral nerve enlargement and perineuriomatous pseudo-onion bulb proliferations is part of the *PIK3CA*-related overgrowth spectrum." All three cases exhibit the phenotypic characteristics of hemifacial overgrowth, polypoid lesions on the tongue/buccal commissure, and segmental arrested development of the roots of teeth. All three cases showed similar histopathological features including "perineuriomatous pseudo-onion bulbs" and had *PIK3CA* mutations identical to those previously described in *PIK3CA*-related overgrowth syndrome (PROS).[2] Given the nerve enlargement and perineuriomatous pseudo-onion bulbs in these cases—features that show some histologic overlap with perineurial tumors—at the encouragement of the primary author of the original article, we examined exome sequencing data from our previously published series of 16 patients with intraneural perineuriomas (in which we identified frequent *TRAF7* mutations)[3] and 14 patients with soft tissue perineuriomas (in which we found frequent deletions in the *NF2* and *NF1* loci but no *TRAF7* mutations).[3,4] Reexamination revealed no evidence of a pathogenic *PIK3CA* mutation in any of these cases. These data provide further evidence that the pathogenic mechanism underlying peripheral nerve enlargement as a phenotypic manifestation in PROS (as described by Koutlas et al.[1]) is genetically distinct from that of intraneural perineuriomas or soft tissue perineuriomas. Accordingly, it would be of interest to determine whether *TRAF7* mutations or large gene rearrangements are present in the three cases described by the authors. Continued efforts to examine somatic mutations broadly with perineurial pathological features will be important with *PIK3CA, TRAF7,* and deletions of *NF2*, *NF1* currently established as associated.

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Declaration of interests

The authors declare no competing interests.

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