Letter to the Editor

Gigantism Remains a Clinical Challenge

To the Editor,

We read with interest the profile of Dr. Ghorban and in particular, the care of his patient with gigantism, Mr. Siah Khan in Shiraz published by Dr. Najjari.[1] The clinical history of Mr. Siah Khan is an interesting one for a number of reasons and was detailed by Dr. Ghorban in 1966.[2] Mr. Siah Khan, it was noted, was born in 1912 into humble circumstances and was apparently normal until about the age of 6. Thereafter, he began to grow extremely rapidly, attaining adult height at the age of 9, and thereafter growing further to an exceptional height during his life (he died aged 38). From existing photographs in late adolescence and adulthood, Mr. Siah Khan can be seen to have a profoundly disfiguring form of acro-gigantism, with bony overgrowth affecting the head, upper arms and other sites.[2] Dr. Ghorban illustrated these pathological findings in his description of the skeleton of Mr. Siah Khan, and Dr. Najjari provides a clear modern photograph of the assembled skeleton in his recent article.[1,2]

The pathological findings in this case of aggressive acromegalic gigantism, multiple sites of deforming bony overgrowth particularly affecting the skull, and suggestions of gonadal hyperfunction in this case are highly suggestive of McCune-Albright syndrome (MAS). MAS results from mosaicism for an activating mutation in the *GNAS1* gene and causes a variable pattern of bone (polyostotic fibrous dysplasia), endocrine (precocious puberty, pituitary adenomas, testicular tumors), skin (*café-au-lait* spots) and other disorders.[3] The bony overgrowth in Mr. Siah Khan, therefore, likely represents polyostotic fibrous dysplasia, one of the archetypical features of MAS. In patients with growth hormone excess in the setting of MAS, pituitary fossa deformation may not be very marked (as noted in Mr. Siah Khan's case). However, the cranial bony deformation that occurs in acromegalic MAS patients can cause distortion of important structures, notably the optic nerves.[4] In Mr. Siah Khan's case, Dr. Ghorban also noted poor vision in adulthood.

MAS is a rare cause of gigantism, accounting for 5% of cases in our recent series.[5] This case brings to mind other MAS related acrogigantism cases, including one from our group.[6] That patient exemplified the severity that acrogigantism can reach in the setting of MAS, and the involvement of both classical and novel sites of MAS-related genetic and clinical pathology.[6] Writing nearly 50 years ago, Dr. Ghorban suggested that the case of Mr. Siah Khan might represent one of the last such cases to develop to such a severe extent.[2] While options have improved, acrogigantism remains quite difficult to treat. Early onset and aggressive pituitary tumorigenesis is frequent in several genetic types, like X-linked acro-gigantism or *AIP* mutations (in addition to MAS) and this is complicated by relatively poor therapeutic response rates and a heavy disease burden.[7,8] The timely article by Dr. Najjari reminds us that experience with such rare cases, like that of Dr. Ghorban with Mr. Siah Khan, remains highly relevant to medical science today.

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