Autosomal dominant inheritance of Weaver syndrome

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Abstract
Most reports of Weaver syndrome have been sporadic cases and the genetic basis of the syndrome is uncertain. This report of an affected father and daughter provides evidence for autosomal dominant inheritance.

Keywords: Weaver syndrome; autosomal dominant inheritance

Weaver syndrome (WSS) was first described in 1974 and is characterised by accelerated growth, advanced bone age, typical facial appearance, digital abnormalities, and developmental delay. The syndrome has been recently reviewed by Cole et al. Most reports have been sporadic and the published familial cases have been difficult to interpret owing to paucity of clinical details or absence of photographic support. Some families have been reported as showing autosomal recessive inheritance and four families have so far been reported as showing autosomal dominant inheritance. Of these dominant cases, however, Cole et al considered case 2 described by Majewski et al as being more typical of benign familial macrocephaly and the information in Ardinger et al and Stoll et al insufficient to confirm or refute the suggestion that the two mothers showed a mild expression of WSS.

The most recent report of autosomal dominant inheritance by Dumic et al describes non-identical twins (brother and sister) with features suggestive of Weaver syndrome, but no early photographs were included. The mother of the twins was said to have been a big baby and to have had some of the clinical features of her children, such as macrocephaly, long phallic, large ears, hoarse voice, prominent finger tip pads, deep set nails, hyperextensible fingers, and hyperhidrosis of the palms. However, no photographs were included and therefore the diagnosis in this family remains open to debate.

We present a family in which a child and her father both have features of Weaver syndrome, thereby providing convincing evidence of autosomal dominant inheritance.

Case reports
Case 1, the third child of unrelated parents, is female and was born at 42 weeks' gestation by elective caesarean section, weighing 4100 g (90th centile). During the pregnancy, there was relatively little fetal movement and she main-

Figure 1 Appearance of case 1 at 3 years of age with her father (case 2).

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his parents are said to be approximately 165 cm tall. He has a very large head (OFC 61 cm) and large hands (21 cm total hand length). He went to a normal school and now works as a builder's labourer. His facial appearance is similar to that of his daughter and fig 3 illustrates his appearance on one occasion during childhood. He also has deep set nails (fig 4) but no history of camptodactyly or other digital features of Weaver syndrome.

Discussion

The dramatic pattern of overgrowth shown in case 1, together with the facial features and advanced bone age, allow a diagnosis of Weaver syndrome. The features in her father (case 2) strongly indicate that he too is affected. This family provides convincing evidence of autosomal dominant transmission of Weaver syndrome with case 2 probably representing a new mutation.

All of the previous reports of autosomal dominant inheritance have been open to doubt and, as most cases of WSS are sporadic, other mechanisms such as uniparental disomy (UPD) are possible. There are no published data on studies looking for UPD in Weaver syndrome, though no evidence has so far been forthcoming in Sotos syndrome, an overgrowth syndrome with which WSS may be confused. Most cases of Sotos syndrome are also sporadic and the most likely mode of inheritance in the familial cases is autosomal dominant. In another overgrowth disorder, Beckwith-Weidemann syndrome (BWS), which exhibits autosomal dominant inheritance in approximately 10% of cases, UPD has been identified and parent of origin effects have also been observed. In our case of Weaver syndrome, transmission has been from father to child and if the previous reports are accepted as dominant families with WSS, the transmission has been from mother to child. Therefore, there is no evidence so far of any parent of origin effect in the transmission of the WSS phenotype.

Weaver syndrome may thus be inherited as an autosomal dominant trait and the discovery and publication of other families may allow further clarification of its genetic basis.

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