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LETTER

MEHMO, a novel syndrome: assignment of disease locus to Xp21.1–p22.13

We read with interest the article by Steinmüller *et al*[1] entitled MEHMO (mental retardation, epileptic seizures, hypogonadism and genitalism, microcephaly, obesity), a novel syndrome: assignment of disease locus to Xp21.1–p22.13.[1] We believe, however, that this is not a novel disorder, but the same syndrome we described in a French-language publication in 1989.[2]

The clinical similarities between the patients of Steinmüller *et al* and our own – particularly the facies, obesity, severe developmental delay and peculiar neurological status – are so striking that one can hardly doubt that these boys all suffer from the same syndrome (Figure 1).

Their patients appear, however, to be more severely affected than were ours, attested to by shorter life spans and epilepsy. The patients described by Steinmüller *et al* died between 2 months and 2 years of age; one of our brothers died at age $4\frac{1}{2}$ years, but the second is alive, at age 14. According to his parents there has been absolutely no developmental progress since we last saw him at age $3\frac{1}{2}$, as he does not even sit or vocalise more than sounds, remains extremely hypertonic and irritable and has gained in weight but not in length (30 kilos for 96 cm at age 14). The patients we described did not have overt epilepsy, although EEGs were highly abnormal (VD's were described as nearly flat); their neurological status was characterised by hypertonia (the typical posture being the same as that seen in Steinmüller's patient IV/2, Figure 1a) and hyperreflexia, nystagmus and an extremely agitated and irritable behavioral pattern. Such variability in clinical presentation between two families (with allelic mutations?) is not surprising, given the small number of patients described to date.

The differential diagnosis which we considered at that time was similar to that discussed by Steinmüller *et al*. The disorder which seemed the most similar among those described then was the Borjeson-Forssman-Lehmann syndrome, which does not have the severe growth retardation nor the short life span described by Steinmüller *et al* and by ourselves. Clinical characteristics of the three patients they described in detail are compared with those of our two patients (Table 1). We would point out that if one searches the London Dysmorphology Database[3] using, for example, the search terms 'mental retardation, seizures/abnormal EEG, microcephaly, generalized obesity and hypogonadism', only two syndrome are suggested, one being the disorder we described 10 years ago.

The brothers we reported on lived in a small town in the south of Italy; as there was no autopsy after the death of the first and we have no DNA sample from him, it is impossible to investigate a potential Xp localisation. The mother does not have a brother and

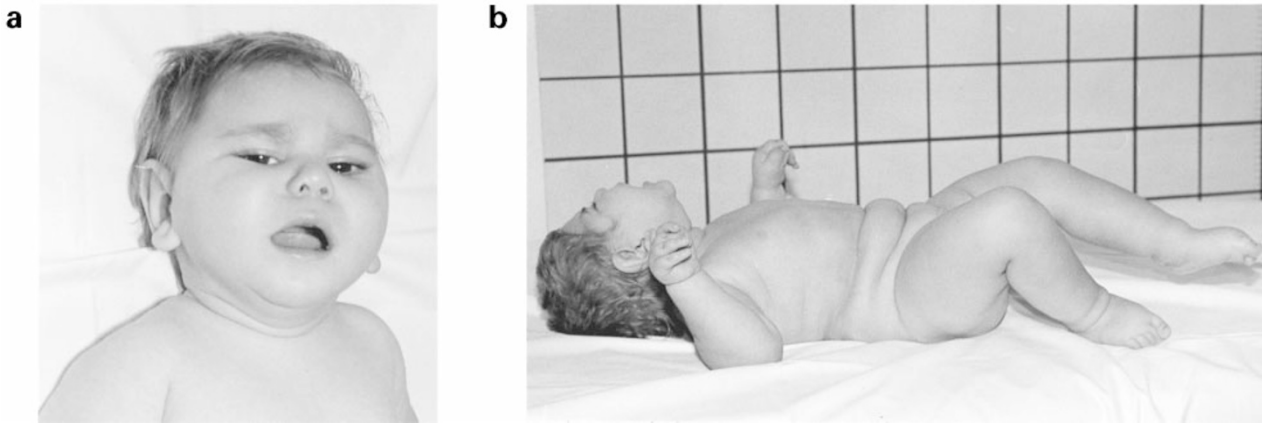

Figure 1 **a**: *VD at age 15 months, showing characteristic facies;* **b**: *SD at age 3 years 3 months, showing typical posture (modified from J Génét Hum,*[2] *with permission)*

Table 1 Clinical comparison of patients with MEHMO syndrome

	Steinmüller, pat. IV-1	*Steinmüller, pat. III/7*	*Steinmüller, pat. IV/7*	*DeLozier-Blanchet, SD*	*DeLozier-Blanchet, VD*
Normal birth length	+	?	?	+	+
Severe postnatal growth retardation	+	+	+	+	+
Microcephaly	+	+	+	+	+
Infancy-onset obesity	+	+	+	+	+
Characteristic facies	+	?	?	+	+
Dramatic developmental delay	+	+	+	+	+
Seizures/abnormal EEG	+	+	+	+	+
Hypertonia, typical posture	+	?	?	+	+
Hypogenitalism	+	+	+	+	+
Diabetes	+	?	?	– neonatal hyperglycaemia	– episodes hyperglycaemia
Age at death	2 years	7 months	10 months	4½ years	alive at age 14 years

Included are the three children from Steinmüller *et al*[1] for whom the most information was available, and the two patients from DeLozier-Blanchet *et al*[2].

the parents have no other biological children, having adopted a boy instead of taking the high risk of having a third affected child.

In conclusion, the family described by Steinmüller is (at least) the second with this disorder. The eponym 'MEHMO' which the authors suggest, seems appropriate, although epilepsy is apparently a variable feature. A metabolic deficit may well be at the origin of this syndrome, as suggested by the finding of obesity and hypogenitalism in all patients, altered glycaemia in at least two, and fatty liver and small thymus in the one patient in Steinmüller's report who underwent autopsy. This will hopefully be resolved by the cloning of the responsible gene, towards which the linkage proposed by Steinmüller *et al* represents a first major step.

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