FIG 2 Southern blot of genomic DNA of members of the family digested with *TaqI* and probed with cDNA subclone 44.1. This probe detects two allelic bands: 6.8 kb (A_1) and 5.7 kb (A_2) as well as four constant bands (4.8, 3.9, 3.5, and 2.5 kb).

with DMD, and that subject I.2 had transmitted three types of gametes: (1) one bearing the deletion (II.3); (2) one non-deleted and non-recombined (II.2, II.5, II.6); (3) one recombined but non-deleted (II.4). These results show that II.4 (in spite of the intragenic recombination), II.2, II.5, and II.6 are in fact not carriers and therefore the prenatal diagnosis performed in 1987 for II.6 misdiagnosed a normal male fetus (III.3).

This is the first case report of erroneous prenatal diagnosis owing to germinal mosaicism overlooked by genomic probes: carrier status had been evaluated with 5' informative markers, whereas the DMD mutation was located towards the 3' end of the gene. This stresses the importance of systematically searching for a DMD associated deletion. In these families all potential carriers should be re-evaluated regardless of previous results, using informative markers or densitometric scanning to investigate the deleted region. Our results also stress that germinal mosaicism must be looked for not only in families with an ascertained *de novo* mutation but also in those presenting as straightforward familial cases.

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Three different, non-mosaic sex chromosome abnormalities (direct cytotrophoblasts, mesenchymal core cultures, and abortus skin fibroblasts): implications for elucidating chorionic villi mosaicism

A 39 year old Caucasian woman (G2P1001) desired chorionic villus sampling (CVS) because of her age. Her only previous pregnancy resulted in the delivery of a healthy boy (2780 g) after a 39 week gestation. Her past medical history was unremarkable; no family members had had congenital malformations or spontaneous abortions. During this pregnancy she reported no exposure to toxins or radiation. The father of the fetus was 41 years old, in good health, and had no family members with anomalies.

Ultrasound examination showed a single intrauterine conception consistent with menstrual dates (crown-rump length 44 mm, corresponding to 50th centile for 11.4 weeks' gestation). No anomalies were seen. Transabdominal CVS was performed without difficulty, yielding 20 mg of chorionic villi. In accordance with our routine,¹ cleansed villi were incubated overnight in alpha-MEM supplemented with 15% Chang medium, 15% fetal bovine serum, and final concentrations of 0.8% L-glutamine, 100 IU/ml penicillin, and 100 µg/ml streptomycin. Each of 25 metaphases analysed from cytotrophoblasts contained 44 autosomes, one normal X chromosome, and one abnormal, nearly acrocentric, chromosome (figure a), which appeared to be an inverted X chromosome. Each of

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20 metaphases derived from the cultured mesenchymal core cells showed a 45,X complement (figure b). Chromosome analyses of both parents were normal.

The proband was counselled that results indicated a 'high' likelihood of the fetus manifesting the Turner's syndrome phenotype. Ultrasonography and amniocentesis were thus recommended to evaluate interval fetal growth and to determine the chromosome complement of amniotic fluid cells. However, neither ultrasonography nor amniocentesis was chosen, but rather pregnancy termination. Surprisingly, chromosome analysis of 30 metaphases from cultured abortus skin fibroblasts showed yet a third non-mosaic complement: ostensibly 46,X,del(X)(p11.2) (figure c).

This is the first report, to our knowledge, in which each of three tissues analysed (direct cytotrophoblasts, cultured mesenchymal core cells, and abortus skin fibroblasts) showed a different, non-mosaic complement. Cytogenetic

discrepancies between different chorionic villi preparations and between villi and embryonic tissue are well documented.² However, most reports involve analysis of only cytotrophoblast or mesenchymal core cells; rarely have both villous preparations as well as embryonic preparations been available.

How are our findings best explained? An interpretation based upon the model proposed by Crane and Cheung³ can be envisaged. Possibly the zygote was 46,X,inv(X)(p11.2q28). During early cell division, there arose a terminal deletion in the inverted X at band q26, resulting in an acrocentric chromosome that appears similar to a simple X chromosome deletion [del(X)(p11.2)] (figure d). (Actually, the very telomeric region of Xq (q28) would be presumed to exist on Xp.) This cell line might be restricted to the epiblast, whereas the inv(X) line might be restricted to the cytotrophoblast. The mesenchymal core, which also originates from the epiblast,³ may then have lost the ostensible del(X)(p11.2) chromosome during differentiation and persisted as a 45,X cell line. Loss of the deleted X chromosome could also have arisen during in vitro cultivation of mesenchymal core cells. A second possible interpretation is independent origin for the inverted X chromosome in cytotrophoblasts and the deleted X chromosome in fetal skin fibroblasts. Again, the monosomy X line could have arisen secondarily.

Our detection of three different, non-mosaic complements illustrates the potential hazard if the origin of mosaicism is deduced on the basis of fewer than the three analysed tissues. Thorough investigations of cytotrophoblasts, mesenchymal core cells, and embryonic cells are desirable when attempting to clarify the incidence and type of mosaicism encountered at chorionic villus sampling.

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FIGURE Sex chromosome complements from two different metaphases derived from each of the three cell lines: (a) 46,X,inv(X)(p11.2q28) in cytotrophoblasts; (b) 45,X in mesenchymal core cells; (c) ostensible 46,X,del(X)(p11.2) in abortus skin fibroblasts. (d) Arrow indicates probable breakpoint (q26) on inverted X chromosome that could have then resulted in a chromosome appearing similar to the ostensible del(X)(p11.2) in abortus skin fibroblasts.