CASE REPORT

Two siblings with unbalanced t(10;21) translocations and non-neuropathic neuropathic bladder

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SUMMARY

We describe an unusual case of two siblings, aged 5 years and 5 months, with an unbalanced t(10;21) translocation and concomitant non-neuropathic neuropathic bladder abnormalities, whose father was a known balanced carrier of the translocation, t(10;21). Postnatally both siblings had normal spine and neurological examination. However, ultrasound scans and micturition cystourethrograms revealed grossly distended non-neuropathic neuropathic bladder. In both siblings, the bladder abnormalities responded to clean intermittent catheterisation. On follow-up, dimercaptosuccinic acid scans for both siblings showed equal split function with no scarring.

BACKGROUND

First description of non-neuropathic neuropathic bladder (NNNB) abnormalities in siblings with similar unbalanced translocation, which may provide an opportunity for our understanding of particular genes that may be responsible for this urological phenotype.

CASE PRESENTATION

Two siblings, aged 5 years and 5 months, born to non-consanguineous Caucasian parents, with unbalanced t(10;21) translocations inherited from a t(10;21) translocation carrier father are presented.

Sibling 1 (5-year-old female child) was born at 39+2 weeks gestation. Antenatal course was uneventful except for a slightly large bladder and mild left-sided hydronephrosis (34 and 38 weeks). Postnatal ultrasound (US) scan showed large volume urinary bladder and mild bilateral hydronephrosis (figure 1A,B). She had a normal dimercaptosuccinic acid (DMSA) and MRI of her spine. Micturating cystourethrogram (MCUG) revealed a large volume bladder, no vesicoureteric reflux and a large postvoid residue (figure 2). Cystoscopy revealed a good capacity, non-trabeculated bladder. She was started on clean intermittent catheterisation (CIC) at the age of 2 months and continued till the age of 3 years. She underwent an excision of a patent urachus, aged 5 months.

Phenotypically, apart from her bladder abnormalities, she had subtle facial features, including a prominent forehead, thin upper lip and small irregular teeth, widely spaced nipples, in keeping with her chromosomal abnormalities. She had a structurally and functionally normal heart on

echocardiography. She now voids spontaneously and has had no urinary problems and remains under surveillance in our paediatric urology clinic.

Sibling 2 (5-month-old male child) was born prematurely at 36+4 weeks gestation, birth weight 1.79 kg following a pregnancy complicated by maternal hypertension. He was referred to our unit for assessment of a large bladder and mild pelvicalyceal system dilation with suspected posterior urethral valves. He had normal urea and electrolytes and normal urine cultures however the bladder was distended on postnatal US. MCUG showed large volume urinary bladder with urine retention in keeping with neuropathic bladder and a normal urethra. He was instituted on CIC on day 3 of life. US of the spine excluded spinal abnormality. Phenotypically he had similar features as his older sibling. On follow-up, he had normal kidneys and urinary bladder on renal US and his DMSA scan was also normal.

INVESTIGATIONS

Genetic analysis

Siblings' father has a balanced form of the translocation (46,XY,t(10;21)(q25.2;q22.1) male karyotype. Sibling 1's chromosome analysis showed an abnormal karyotype with a paternally inherited unbalanced translocation between the long arm of chromosome 10 and the long arm of chromosome 21. Her G-banding karyotype was 46,XX,der(10)t(10;21)(q26.13;q22.3)pat. Array comparative genomic hybridisation with patient's DNA identified two copy number changes: copy number loss on chromosome 10 between q26.13 and q26.3, which is approximately 9.8 Mb in size and copy number gain of 21q22.3, which is approximately 4.7 Mb in size. Both of these copy number changes were telomeric. Her G-banding karyotype can be written as 46, XX, der(10)t(10;21)(q26.13;q22.3)pat. The copy number loss of 10q26.13 to 10q26.3 involves 57 genes, 34 of which are known OMIM genes and the copy number gain of 21q22.3 involves 73 genes, 52 of which are known OMIM genes. Similarly, sibling 2 had similar abnormal karyotype and inherited translocation and his G-banding karyotype was 46,XY,der(10)t(10;21)(q26.13;q22.3)pat.

Other investigations

Postnatal renal and spine US scans, MCUG and DMSA.

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To cite: Thyoka M, Henderson A, Starzyk B, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-201757

Figure 1 (A) Ultrasound appearances of a large volume urinary bladder of the older sibling. (B) Ultrasound appearances of mild hydronephrosis and hydroureter in the older sibling.

Figure 2 Micturating cystourethrogram (MCUG) of the older sibling—delayed 1 h 30 min film post-MCUG—showing contrast retention in the urinary bladder.

TREATMENT

CIC for bladder emptying.

OUTCOME AND FOLLOW-UP

Well at last follow-up (5 years and 5 months).

DISCUSSION

NNNB is a spectrum of bladder dysfunction with an unidentifiable neurological disease/cause.¹ The diagnosis is dependent on the absence of underlying neurological abnormality despite the bladder exhibiting dysfunctional voiding akin to neurogenic bladder. CIC achieves bladder emptying and helps to decompensate for dysfunctional voiding seen in NNNB.

Chromosomal translocations are produced when a two-way exchange occurs between non-homologous chromosomes resulting in either balanced translocation (no loss or increase in genetic materials) or unbalanced translocation (loss or increase in genetic materials). Balanced chromosomal translocations are common with an incidence of approximately 1 in 500 whereas unbalanced translocations are relatively frequently detected antenatally following the identification of fetal abnormalities on

US.² Unbalanced translocations can either be inherited or occur do novo, with neither parent having balanced rearrangement. However, many individuals may not be aware of their actual or potential carrier status as the decision to inform relatives is left to the known carrier individual.³ In a large retrospective review of 16 749 pregnant women undergoing midtrimester amniocentesis Chang *et al*⁴ reported reciprocal translocation in 0.44%, the commonest type being balanced translocation (76%). Prenatal karyotype analysis in cases of parental balanced chromosome translocation can guide parents in assessing abnormalities in the unborn fetus.⁵ In seven cases of parental balanced chromosome translocation that underwent prenatal karyotype analyses, one fetus showed unbalanced translocation karyotype, four had a balanced translocation identical to that of the parents and two had normal karyotypes.

These cases, to our knowledge, are the first description of NNNB abnormalities in siblings with similar unbalanced chromosome translocation. Both siblings demonstrated an inability to spontaneously void and underwent investigations to rule out underlying neurological abnormalities. The first sibling aged 5 years had a lot of investigations including cystoscopy and was ultimately instituted on CIC at 2 months of age. However with the benefit of hindsight the second sibling was started on CIC on day 3 of life. The fact that the first sibling responded so

well to CIC gave us, as well as the parents, hope that CIC is temporary and not a life-long intervention. Also the fact that no bladder surgery apart from excision of the urachus was required to cure the first sibling gives us an indication that the bladder recovers with time. It would be really interesting to see if the younger sibling would also require an excision of the urachus. These cases highlight the importance of expectant management with CIC without early recourse to anticholinergics or operative intervention.

Our presumption, regarding the aetiology is a transient fetal bladder outlet obstruction leading to a lazy bladder. However, it remains unclear which genes are particularly responsible for this urological phenotype seen in these two siblings. Elucidation of the function of all the involved genes would require further directed research. To the best of our knowledge our report, is the first description of NNNB abnormalities in siblings with similar unbalanced translocation.

Acknowledgements The authors would like to thank the family for participating in this study; the clinical genetic team at Newcastle for carrying out the array comparative genomic hybridisation analysis and family tree.

Contributors MT and AL presented the case history, reviewed the literature and wrote the first draft of the manuscript. AL was the supervising consultant who had the sole responsibility of the care of the patients and performed the surgery, obtained consent for publication and edited the manuscript. AH reviewed the genetic content and provided the family pedigree. BS provided all the radiological images and their interpretation. All four authors (MT, AH, BS and AL) participated in the review of the literature and have seen and authorised the final manuscript for publication.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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Learning points

- ▶ This report highlights the association of non-neuropathic neuropathic bladder in two siblings with an unbalanced t (10;21) translocation. Although possible that it may have occurred by chance; however, occurrence in both siblings points toward a possible association.
- ▶ It appears to be transient and effective CIC is the only intervention required as with time it appears that the bladder responds and the child can void spontaneously and become continent. This is really important to achieve before school going age.
- ▶ Further such reports may help in directing genetic research into the recognition of the genes involved in this particular urological phenotype.

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