LETTER TO THE EDITOR

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Unusual Comorbid Condition in a Child with Severe Factor XI Deficiency: Spina Bifida

Ağır Faktör XI Eksikliği Olan Bir Çocukta Olağandışı Komorbid Durum: Spina Bifida

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To the Editor,

Factor XI (FXI) deficiency is a rare autosomal recessive inherited bleeding disorder. It has the weakest correlation between factor levels and bleeding symptoms [1]. A few cases have been described with concurrent diseases such as Prader-Willi syndrome and supernumerary nipples [2,3]. However, spina bifida has not previously been reported in patients with FXI deficiency. We present a child with severe FXI deficiency coexisting with spina bifida.

A 7-year-old girl with a history of spina bifida, lipomyelomeningoceles, and neurogenic bladder since birth with no prior history of pathological bleeding was diagnosed with severe FXI deficiency coincidentally when she was scheduled for a urological surgical operation at age 3 (Figures 1a-1c). There was no consanguinity between her parents. Familial history was negative for spina bifida and bleeding tendency. The preoperative activated partial thromboplastin time was prolonged to 92.9 s (normal range: 24-36 s). Her FXI level was 0.09% (normal range: 50%-150%), suggesting severe FXI deficiency. Her inhibitor status was negative. She was given 10 mL/kg of fresh frozen plasma (FFP) twice a day and 10 mg/kg of tranexamic acid three times a day before and after urological surgery. There was no further FFP administration, although tranexamic acid was administered for 5 more days. The patient was currently using oxybutynin hydrochloride as prescribed by the urologist for enuresis and emptying her bladder every 6 h utilizing clean intermittent catheterization without any intervention. Her mother had no medical problems but did not remember receiving folate during her pregnancy. Genetic testing revealed that the patient was homozygous for the *MTHFR* A1298C mutation, whereas her parents were heterozygous mutants (i.e., carriers). The patient and her brother both had a homozygous nonsense mutation in the *FXI* gene (c.1566G>A; p.Trp519Ter). Their parents had a heterozygous FXI mutation.

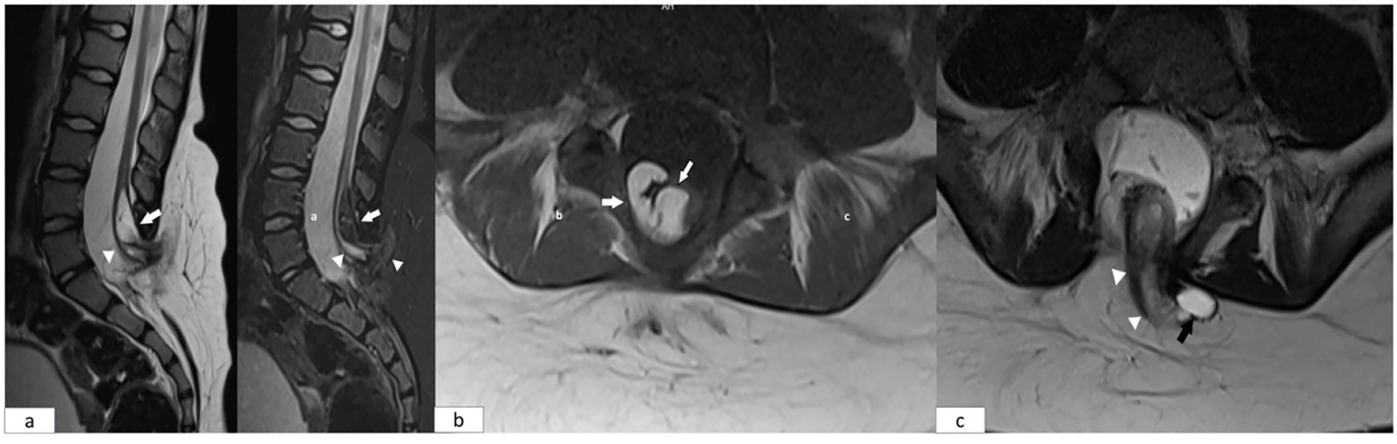

Figure 1. (a) Sagittal T2-weighted magnetic resonance image demonstrates a posterior arch fusion defect of the L5 vertebra and inferior levels. (b) Sagittal T2 fat-suppressed magnetic resonance image reveals subcutaneous fat tissue thickening consisting of lipomyelomeningoceles at the L4-S3 vertebral levels posteriorly (white arrows). (c) Axial T1-weighted magnetic resonance image shows the fat component extending into the right neural foramen at the S1 level (white arrows) and the cystic lesion in the posterior elements of the L5 vertebra (black arrow).

We report for the first time that spina bifida has been identified in a child with severe FXI deficiency. Spina bifida is a type of neural tube defect (NTD). A study in Türkiye reported that the frequency of NTD at birth was 27.5 per 10,000 individuals, and spina bifida (82.6%) was the most common NTD, characterized by a lack of folate consumption during pregnancy [4]. Gene polymorphisms associated with NTDs were reported as including *MTHFR* C677T, *MTHFR* A1298C, and *MTRR* A66G [5]. Nasri et al. [5] showed that the *MTHFR* A1298C polymorphism was not associated with a significant risk of NTDs in the Tunisian population. However, having all three *MTHFR* gene polymorphisms was reported to increase the risk of NTDs by 3.96-fold [5]. The *MTHFR* C677T and *MTHFR* A1298C genetic defects account for approximately 35%-50% of NTD cases and folic acid supplementation is crucial in preventing NTDs during pregnancy [6]. The mother of our patient was unsure whether she had received folate during her pregnancy. Our patient had only a homozygous *MTHFR* A1298C mutation; however, we did not test for *MTRR* A66G.

Our experience with this case of severe FXI deficiency suggests that the *MTHFR* A1298C homozygous gene mutation and the uncertainty of folic acid consumption by the patient's mother during pregnancy may have contributed to the development of spina bifida.

Keywords: Factor XI deficiency, Spina bifida, Child

Anahtar Sözcükler: Faktör XI eksikliği, Spina bifida, Çocuk

Ethics

Informed Consent: Informed consent was obtained from the patient's parents.

Footnotes

Authorship Contributions

Surgical and Medical Practices: A.K., M.Y., G.K., Z.K.; Concept: A.K., M.Y., G.K., Z.K.; Design: A.K., M.Y., G.K., Z.K.; Data Collection or Processing: A.K., M.Y., G.K., Z.K.; Analysis or Interpretation: A.K., M.Y., G.K., Z.K.; Literature Search: A.K., M.Y., G.K., Z.K.; Writing: A.K., M.Y., G.K., Z.K.

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