LETTER TO THE EDITOR
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Unusual Comorbid Condition in a Child with Severe Factor XI Deficiency: Spina Bifida

Ağır Faktör 11 Eksikliği Olan Bir Çocukta Olağandışı Komorbid Durum: Spina Bifida

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To the editor,

Factor (F) XI deficiency is a rare autosomal recessive inherited bleeding disorder. FXI deficiency 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 and coexisting with spina bifida.

A 7-year-old girl with a history of spina bifida, lipomyelomeningoceles, and neurogenic bladder since birth, and 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. (Figure-1a-c). There was no consanguinity between parents. Familial history was negative for spina bifida and bleeding tendency. The preoperative activated partial thromboplastin time (aPTT) test was prolonged to 92.9 seconds (normal: 24-36 seconds). Her FXI level was 0.09% (normal: 50-150%), suggesting severe FXI deficiency. Her inhibitor status was negative. The patient 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 more FFP, although tranexamic acid was administered for 5 days. The patient was currently using oxybutynin hydrochloride as prescribed by the urologist for enuresis and emptying her bladder every 6 hours utilizing clean intermittent catheterization without any intervention. Her mother had no medical problems and didn't remember receiving folate during her pregnancy. The genetic test revealed that the present case was homozygous for the MTHFR A1298C mutation, whereas the parents were heterozygous mutants (carriers). The index case and her brother have a homozygous nonsense mutation in the FXI gene (c.1566G>A; p.Trp519Ter). Their parents have a heterozygous FXI mutation.

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 research in Turkey reported that the frequency of NTD patients at birth was 27.5 per 10,000 individuals. Spina bifida (82.6%) was the most common NTD, characterized by a lack of folate consumption during pregnancy [4]. MTHFR gene polymorphisms associated with NTDs were reported as MTHFR C677T, MTHFR A1298C, and MTRR A66G [5]. Nasri et al. showed that the only MTHFR A1298C polymorphism in the Tunisian population was not associated with a significant risk for NTDs [5]. However, having all three MTHFR gene polymorphisms was reported to increase the risk of NTDs by 3.96-fold [5]. 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 patient's mother was unsure whether she received folate during her pregnancy. Our case had only a homozygous MTHFR A1298C mutation, however, we did not investigate MTRR A66G.

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

Compliance with Ethical Standards
Conflicts of interest: The authors have no conflict of interest.
Informed consent: Informed consent was obtained from parents
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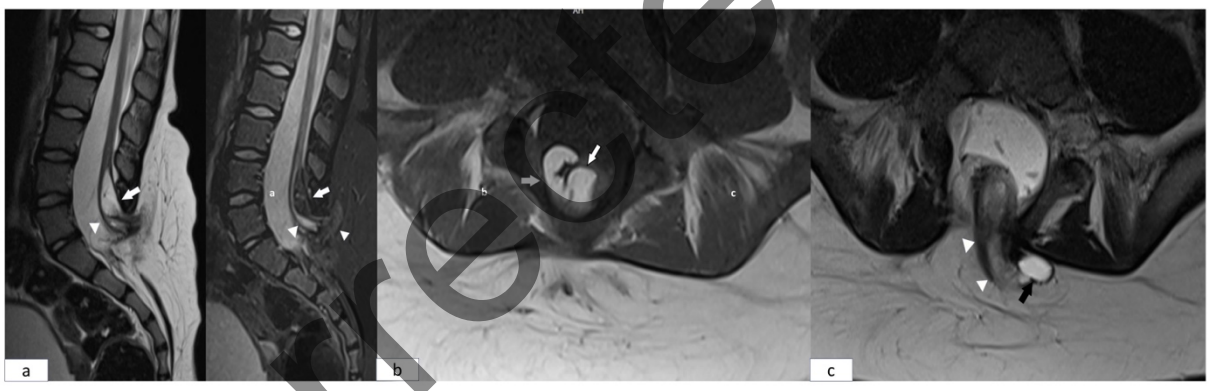

Figure 1. (a) Sagittal T2-weighted MR image demonstrates a posterior arch fusion defect of the L5 vertebra and inferior levels. (b) Sagittal T2 fat-suppressed MR image reveals subcutaneous fat tissue thickening consisting of lipomyelomeningocele at the L4-S3 vertebral levels posteriorly (white arrow).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