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Case Report

Presacral teratoma in a Curarrino syndrome woman with an unreported insertion in *MNX1* gene

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Abstract

Objective: Currarino syndrome (CS) comprises a presacral mass, anorectal malformation, and a sacral bony defect. It is rarely reported in the gynecological field.

Case Report: We describe here the case of a 26-year-old married woman with Currarino syndrome who presented with a presacral teratoma and a previously unreported insertion in MNX1 gene. She had had a pelvic teratoma diagnosed by laparoscopy 8 years previously. She was referred to our clinic because of the increasing size of the teratoma and associated compression symptoms. Computed tomography demonstrated a heterogeneous 12 cm mass in the presacral region. Spina bifida at S2eS5 was also noted. Laparotomy confirmed the diagnosis of presacral teratoma. Genetic analysis disclosed a triple CGC repeat insertion in exon 1 of MNX1, resulting in three in-frame shifts encoding for the amino acid alanine. No siblings had known similar symptoms.

Conclusion: Currarino syndrome is known to be an autosomal dominant disorder. The presence of constipation can lead to a diagnosis of the syndrome early in childhood. In sporadic cases diagnosis is late because of atypical symptoms. Delayed treatment of a presacral tumor may cause serious complications such as central nervous system infection or subsequent neurological dysfunction. In clinical practice, a presacral tumor with a sacral bony defect may indicate Currarino syndrome. Genetic analysis of the family may provide information on the hereditary traits of specific MNX1 mutation.

Keywords: Presacral teratoma; Sporadic Currarino

Introduction

Currarino syndrome [CS; Online Mendelian Inheritance in Man (OMIM) no. 176450] is an autosomal dominant disorder that was first described in 1981 [1]. It is characterized by three main clinical features: sacral dysgenesis, anorectal malformation and presacral tumors, resulting from incomplete separation of the endodermal and ectodermal layers in the developing embryo. Mutations have been found in *MNX1* (motor neuron and pancreas homeobox 1) located at 7q36 in patients with CS. Here, we describe a previously unreported insertion in a sporadic case of CS.

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Case report

A 26-year-old married woman, gravida 1, presented at our clinic with a retroperitoneal tumor about 8 cm in diameter. The tumor had been known about since a diagnostic laparoscopy 8 years previously had revealed a presacral teratoma. Her menstrual cycles were regular without dysmenorrhea or menorrhagia. Computed tomography revealed a heterogeneous low-attenuation mass about 11.03 × 8.15 cm in size in the presacral region with two components and fatty content. Spina bifida at S2–S5 was also noted (Fig. 1A). Laparotomy showed a well capsulated cystic mass in the presacral region, consisting of hair and sebaceous tissue and compatible with the pathology of a mature cystic teratoma. We removed most tumor parts except for those deeply implanted in the sacral promontory. Given the clinical features of a presacral tumor

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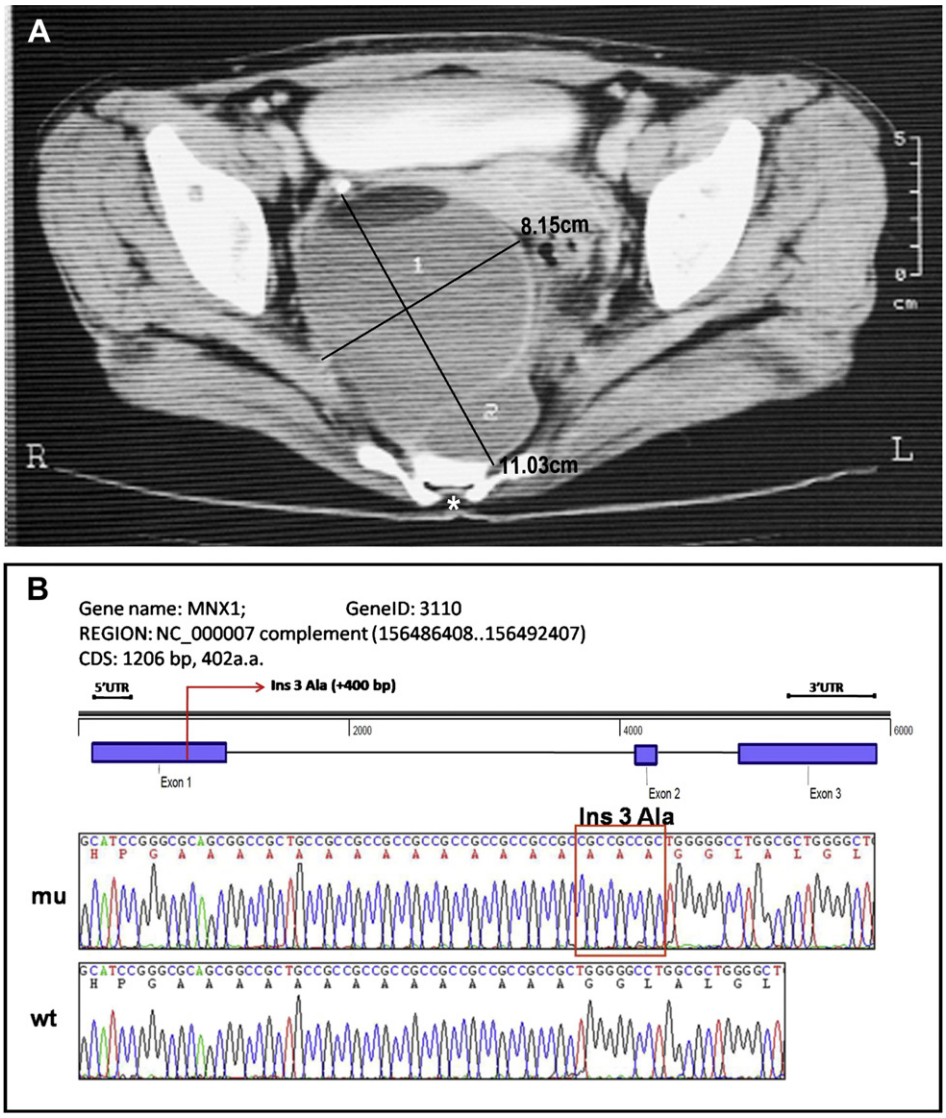

Fig. 1. **(A)** Computed tomography scan in a 26-year-old woman showed a presacral tumor measuring about 11.03 × 8.15 cm with two components and spina bifida (white star). **(B)** Genetic analysis of *MNX1* in this patient disclosed three CGC (alanine) repeats in exon 1.

combined with spina bifida and the patient's history of constipation during her teenage years, CS was suspected. Mutation analysis of *MNX1* by sequencing the three exons disclosed a triple CGC repeat insertion in exon 1, resulting in three in-frame shifts encoding for the amino acid alanine (Fig. 1B). The patient developed severe anal pain and intractable diarrhea 13 months later, and colorectal surgeons at another hospital performed a complete resection of a recurrent presacral teratoma measuring about 6–7 cm.

Discussion

Clinical data and molecular studies have shown overall mutation detection rates in subjects with CS of about 50%, and up to 90% in familial cases [2]. To date, more than 66 different heterozygous mutations have been reported in patients fulfilling the CS diagnostic criteria, including 10 cytogenetic anomalies, 29 frameshift mutations, seven nonsense mutations, three splice-site mutations and a total of 17 missense mutations [2]. Most insertions occur at the mutational 'hot spot' in exon 1 with a CCCCCC or a GGGGGG repeat, resulting in a premature truncation of the protein and loss of the homeodomain, affecting DNA binding. The pesence of constipation can lead to a diagnosis of CS early in childhood, although about 33% of the patients reported showed no clinical symptoms [3].

We report here an observation not previously published, namely a triple alanine repeat in a patient with CS which may not cause truncation of the protein. This could explain the delayed diagnosis of the phenotype in this patient, arising from a compromised protein function instead of a truncated one. However, the phenotypes vary widely, without apparent correlation between the types of *MNX1* mutations [4]. Autosomal dominant transmission and low clinical penetrance of CS indicate that the possibility of a multigene disorder and numbers of patients affected by *MNX1* mutations remain underestimated. Therefore, this syndrome should be considered for early intervention and genetic testing when patients

with suspicious phenotypes present. Early and appropriate surgical treatment is important to prevent morbidity, particularly when dealing with presacral lesions that can cause tethered cord syndrome, meningitis, chronic neurological dysfunction, or malignant transformation [5]. A surgical team including a neurosurgeon, a colorectal surgeon and a gynecological surgeon might provide better care for patients with CS presenting with presacral tumors. Genetic testing of the family might also provide information on the hereditary traits of specific *MNX1* mutations and help explain symptoms that might develop later in life among patients without truncation of the *MNX1* protein.

References

[1] Currarino G, Coln D, Votteler T. Triad of anorectal, sacral, and presacral anomalies. AJR Am J Roentgenol 1981;137:395–8.
[2] Crétolle C, Pelet A, Sanlaville D, Zérah M, Amiel J, Jaubert F, et al. Spectrum of HLXB9 gene mutations in Currarino syndrome and genotype-phenotype correlation. Hum Mutat 2008;29:903–10.
[3] Lynch SA, Wang Y, Strachan T, Burn J, Lindsay S. Autosomal dominant sacral agenesis: Currarino syndrome. J Med Genet 2000;37:561–6.
[4] Emans PJ, Kootstra G, Marcelis CL, Beuls EA, van Heurn LW. The Currarino triad: the variable expression. J Pediatr Surg 2005;40:1238–42.
[5] Urioste M, Garcia-Andrade Mdel C, Valle L, Robledo M, González-Palacios F, Méndez R, et al. Malignant degeneration of presacral teratoma in the Currarino anomaly. Am J Med Genet A 2004;128A:299–304.