European Journal of Obstetrics & Gynecology and Reproductive Biology 222 (2018) 80–83

Contents lists available at ScienceDirect

European Journal of Obstetrics & Gynecology and Reproductive Biology

journal homepage: www.elsevier.com/locate/ejogrb

Full length article

Isolated fetal horseshoe kidney does not seem to increase the risk for abnormal chromosomal microarray results

Lena Sagi-Dain[a,*], Idit Maya[b], Tzipora Falik-Zaccai[c], Michal Feingold-Zadok[d], Dorit Lev[e], Hagit Yonath[f], Ehud Kaliner[g], Ayala Frumkin[h], Shay Ben Shachar[i], Amihood Singer[j]

[a] Genetics Institute, Carmel Medical Center, Haifa, Israel
[b] Recanati Genetics Institute, Beilinson Hospital, Rabin Medical Center, Petach Tikva, Israel
[c] Institute of Human Genetics, Galilee Medical Center, Nahariya, The Galilee Faculty of Medicine, Bar Ilan, Israel
[d] Genetics Institute, Assaf Harofeh Medical Center, Zerifin, Israel
[e] The Rina Mor Institute of Medical Genetics, Wolfson Medical Center, Holon, Israel
[f] Genetics Institute, Sheba Medical Center, Tel Hashomer, 52621 Ramat Gan, Israel
[g] Israel Ministry of Health, Public Health Services, Jerusalem, Israel
[h] Department of Genetics and Metabolic Diseases, Hadassah, Hebrew University Medical Center, Jerusalem, Israel
[i] Genetics Institute, Sorasky Medical Center, Tel Aviv, Israel
[j] Community Genetics, Public Health Services, Ministry of Health, Jerusalem, Israel

ARTICLE INFO

Article history:
Received 23 September 2017
Received in revised form 11 January 2018
Accepted 15 January 2018
Available online xxx

Keywords:
Chromosomal aberrations
Chromosomal microarray
Horseshoe kidney

ABSTRACT

Objective: To examine the risk for clinically significant chromosomal microarray analysis (CMA) among fetuses with apparently isolated horseshoe kidney.
Methods: Data from all CMA analyses performed due to isolated horseshoe kidney reported to the Israeli Ministry of Health between January 2013 and September 2016 were retrospectively obtained from a computerized database. Risk estimation was performed comparing the rate of abnormal CMA findings to the general population, based on a systematic review encompassing 9272 pregnancies with normal ultrasound, and local data cohort of 5541 pregnancies undergoing CMA due to maternal request.
Results: Of 82 pregnancies with isolated horseshoe kidney, one loss-of-copy-number variant compatible with 16p13.11 microdeletion syndrome was demonstrated (1.2%). In addition, two variants of unknown significance (VOUS) were detected (2.4%). The relative risk for pathogenic CMA findings among pregnancies with isolated single horseshoe kidney was not significantly different from the control population (1.03–1.39%).
Discussion: To our best knowledge, our study is the first report describing the rate of clinically significant CMA findings in fetuses with isolated horseshoe kidney. The detection of one pathogenic CMA findings in our cohort implies that the value of CMA analysis in such pregnancies is similar to the general population.

Introduction

Horseshoe kidney is the most common fusion anomaly of the urinary tract, occurring in about one in every 400–600 individuals [1]. In most cases the kidneys are fused at the lower pole and positioned lower than normal (Fig. 1). This finding is frequently asymptomatic and detected incidentally during renal imaging [2]. However, it can be associated with increased risk for infections, nephrolithiasis with consequent hydronephrosis, ureteropelvic junction obstruction and vesicoureteral reflux [3]. In addition, an increased risk for extrarenal disorders has been associated with this disorder, most prominent of which are gastrointestinal tract and vertebral malformations, CNS disorders and cardiovascular disease [4].

Horseshoe kidney has been associated with numerous genetic disorders. For instance, BK Je et al. reviewed clinical data of 380 patients with horseshoe kidney and reported various syndromes in 49 cases (12.9%), the most common of which was Turner syndrome (45,X karyotype – 16 patients, 4.2% of the overall cohort) [4]. Indeed, horseshoe kidney is demonstrated in about 15–35% of patients with Turner syndrome [5]. In addition, horseshoe kidney has been described in association with 11p13 deletions at WAGR (Wilms tumor, aniridia, genitourinary abnormalities, and mental retardation) locus [6]. Also, it has been reported in diverse single gene disorders, such as Fanconi anemia, Tuberous Sclerosis complex, Townes-Brocks syndrome, Aicardi-Goutières syndrome,

* Corresponding author.
E-mail address: lenada@clalit.org.il (L. Sagi-Dain).

https://doi.org/10.1016/j.ejogrb.2018.01.015
0301-2115/

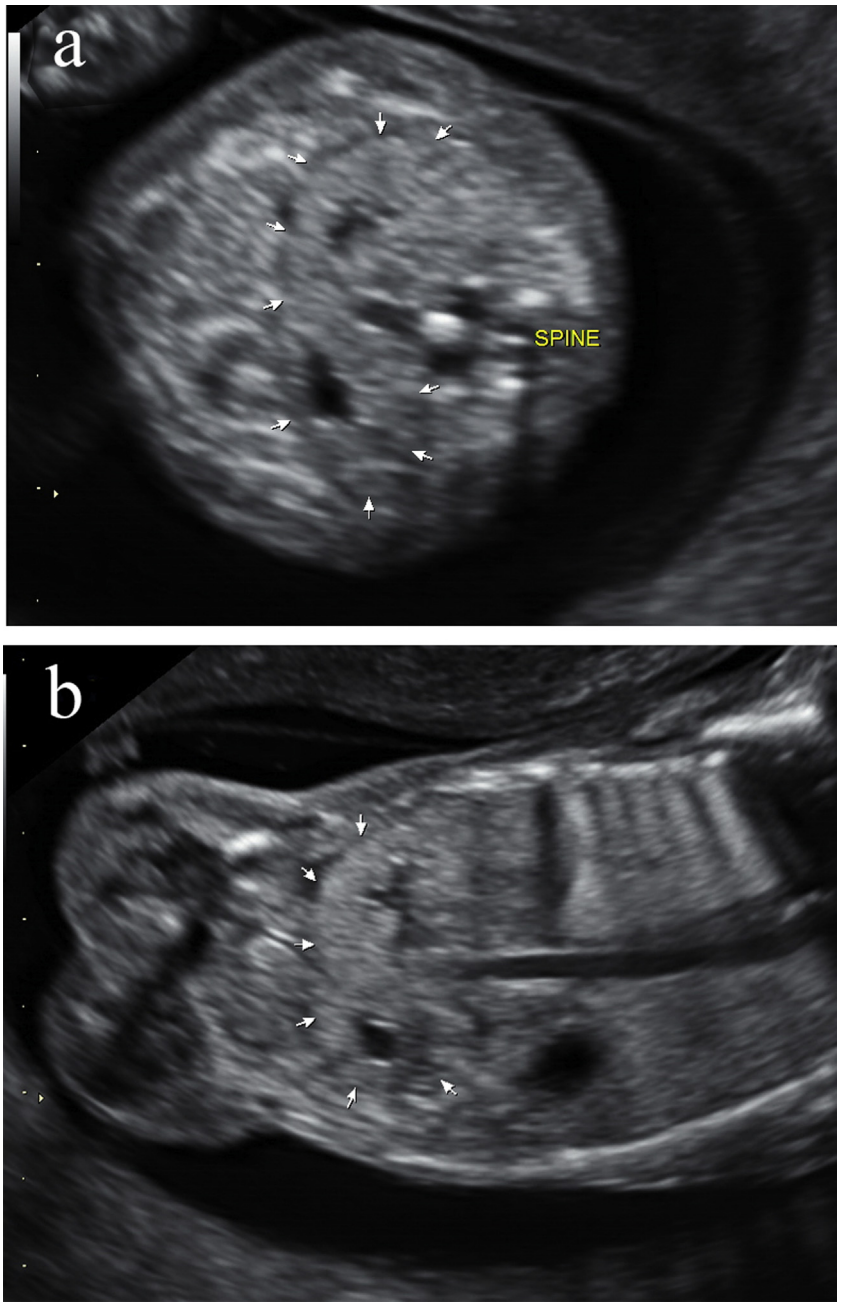

Fig. 1. Sonographic demonstration of horseshoe kidney (marked by arrows), in (a) axial and (b) coronal views. On the courtesy of Dr. Israel Shapiro, Ultrasound Unit, Department of Obstetrics and Gynecology, Bnai-Zion Medical Center, Haifa, Israel.

SOX2 gene related anophthalmia syndrome, Alagille Syndrome and many other monogenic disorders [7–12]. Furthermore, horseshoe kidney was reported to be associated with several copy number variants detectable by chromosomal microarray analysis (CMA). For instance, it has been reported in patients with a rare 3q29 microdeletion syndrome, characterized by mild-to-moderate mental retardation, slightly dysmorphic facial features and non-specific malformations [13]. Of note, in most of these conditions renal fusion is usually associated with additional anatomic abnormalities.

The accepted evaluation of prenatally detected horseshoe kidney frequently includes genetic counseling and recommendation for invasive prenatal testing by CMA. However, the exact frequency of clinically significant CMA findings in this isolated anomaly has not been reported yet. Thus, the objective of our study was to shed light on this issue.

Methods

In Israel, every pregnant woman is advised to undergo a fetal anatomic survey, as well as routine screening testing for Down syndrome. In cases of abnormal sonographic findings the woman is usually referred to genetic counseling, which includes explanation regarding the nature of the finding, discussion of potential diagnoses and recommended investigation, usually by CMA analysis. Each CMA analysis is financially covered as part of the national medical health services, and thus routinely reported to the Ministry of Health.