Increased AFP as an indicator of ovarian carcinoma and fetal kidney carcinoma - case report

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Summary

We examined a young primipara with increased alpha-fetoprotein (AFP) values and cystic tumefaction of the right ovary. Having in mind a mild decrease in ovarian artery resistance index (RI) and suspected findings of fetal kidney, this situation was delicate due to its double pathology which was later confirmed.

Wilms' tumor is the most common urogenital tumor in childhood, and it is detectable in the prenatal period by ultrasound examination. In *utero* kidney biopsy confirms diagnosis and facilitates decisions concerning the course of pregnancy. Relative risk of intervention limits this diagnostic procedure for indicated cases.

Key words: Borderline carcinoma; Pregnancy; Wilms' fetal tumor; In utero biopsy.

Introduction

Of all gynecologic cancers, ovarian malignancies represent the greatest clinical challenge. Epithelial cancers are the most common ovarian malignancies, and, because their symptoms are nonspecific until they have metastasized, patients present with advanced disease in more than two-thirds of the cases [1]. Ovarian cancer represents a major surgical challenge, requires intensive and often complex therapies, and is extremely demanding of the patient's psychological and physical energy. It has the highest fatality-to-case ratio of all the gynecologic malignancies. There are more than 25,500 new cases annually in the United States, and more than 16,000 women can be expected to succumb to their illness [1]. Ovarian cancer is the fifth most common cancer in women in the United States accounting for 4% of all female cancers and 31% of cancers of the female genital organs. It is the fourth most common cause of death from malignancy in women. A woman's risk at birth of having ovarian cancer sometime in her lifetime is nearly 1.5% and of dying from ovarian cancer almost 1% [1].

Fetal kidneys begin developing within the pelvis approximately the seventh week of gestation from the metanephric mesoderm and the uteric bud. The metanephric tissue develops into the nephrons of kidney, and the uretic bud differentiates into the collecting tubules, calyces, pelvis, and ureter. Between the seventh and 11th week of gestation, as the fetal body grows in length, the kidneys ascend to their permanent position in the flank due to disproportionate growth of more caudal structures [2, 3]. Initially, the kidney is made up of several loosely connected lobes, each with a thin cortex. During the second trimester the lobes fuse, become less distinct, and the cortex thickens, leaving the kidney with a lobular contour that persists for several years after birth [4]. In the second trimester, fetal kidneys become the major contributor to amniotic fluid volume [5]. Adequate amniotic fluid volume is necessary for normal fetal pulmonary and skeletal development, as it provides space for fetal growth and movement. A functioning urinary tract must be present for the lungs and skeleton to develop normally [6]. Using transvaginal ultrasound, normal fetal kidneys can first be seen as early as in the ninth week of gestation and should always be visible by the 13th week. With transabdominal scanning, the kidneys may first be visible at 13 to 14 weeks and are seen in most patients by 16 to 18 weeks. Anomalies of the genitourinary tract result from arrested development early in organogenesis, failure of normal ascent, obstruction of collecting systems, abnormal formation of renal tubules, and they can be genetically determined [7].

Wilms' tumor, the most common genitourinary malignancy of childhood, is a triphasic embrional neoplasm consisting of varying proportions of blastema, stroma and epithelium. It develops from proliferation of metanephric blastema, possibly in the absence of normal stimulation from the metanephric duct to produce differentiated tubules and glomerular filtrate. Although the specific histological appearance was described by Max Wilms in 1899 [6], the eponym is now loosely applied to virtually any malignant tumor arising in the kidney in childhood, some of which are pathologically, clinically, and probably genetically distinct. Recent developments in molecular biology have been applied to Wilms' tumor to isolate the gene whose mutation is responsible for its initiation. The incidence of Wilms' tumor is, according to various publications, about eight per million children under the age of 18 years, or one per 10,000 live births, and the tumor is detected mostly after birth. Lack of specific

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serum markers in maternal and fetal blood challenges prenatal diagnosis of the tumor. Ultrasound, as a proven diagnostic tool, can indicate the presence of tumor but not the nature of the abnormality, and it cannot confirm the diagnosis. Fetal urinalysis obtained by vesicocentesis, although it detects gross abnormalities of renal function, does not contribute to the diagnosis of Wilms' tumor [8]. Biopsy of fetal kidneys is recognized today as a method of choice for establishing the *in utero* diagnosis [9-11]. Advantages are the low risk of intervention, visual control of biopsy by ultrasound, use of Doppler in biopsy site choice and avoiding damage of the vasculature, and controllable fetal kidney function after the intervention. Biopsy of fetal kidneys is the ultimate diagnostic tool, after complete morphological and functional examination of kidneys. Investigations of kidney function and morphology in the neonatal period does not indicate any damage caused by in utero biopsy.

Case Report

We examined a young primipara with increased alpha-fetoprotein (AFP) values and cystic tumefaction of the right ovary. Having in mind a mild decrease in ovarian artery resistance index (RI) and suspected findings of fetal kidneys, this situation was delicate due to the double pathology which was later confirmed. An adnexal mass, established by ultrasound, and increased AFP required CA-125 and CA15-3 markers. As those findings were within normal limits, the only suspected finding, together with increased AFP, was a possible fetal anomaly.

The principal treatment of borderline ovarian tumors is surgical resection of the primary tumor. There are no prospective data to suggest that either adjuvant chemotherapy or radiation therapy improves survival. After a frozen section has determined that the histology is borderline, premenopausal patients who desire preservation of ovarian function may be managed with a 'conservative' operation, i.e., unilateral oophorectomy. In a study of patients who underwent unilateral ovarian cystectomy only for apparent Stage I borderline serous tumors, Lim-Tan *et al.* found that this conservative operation was also safe; only 8% of the patients had recurrences two to 18 years later, all with curable disease confined to the ovaries [10]. Recurrence was associated with 'positive margins' of the removed ovarian cyst. Thus, hormonal function and fertility can be maintained. In patients who have undergone oophorectomy or cystectomy and later a borderline tumor is later documented in the permanent pathology, no additional staging surgery is necessary, but the patient should be monitored with transvaginal ultrasonography [11].

A 26-year-old primipara was admitted to the department of high-risk pregnancies for further investigation of a possible tumor of the right fetal kidney. There was no history of previous renal disease. Biochemical parameters were all within normal range, except for AFP, which was 17.3 MoM. Examination by ultrasound showed a normal left kidney, 2.9 cm in length, with normal morphology and echogenocity. The right kidney was 4.1 cm in length, hyperechogenic and without any kidney tissue pattern. The amniotic fluid index was 125 with no other fetal abnormalities. Doppler examination of the renal arteries showed a high resistance index in the right kidney, and power Doppler showed an emphasized vascular network. After analysis of the obtained data, cordocentesis and vesicocentesis were indicated. Normal female karyotype 46 XX was obtained, with sodium values of 84 mmol/l, potassium 2 mmol/l, chloride 85 mmol/l, osmolality 148 mOsm/l, and beta 2 microglobulin 1.34 mg/l. After obtaining this data we decided to perform a fetal kidney biopsy. After premedication with 10 mg of diazepam a free-hand ultrasound-guided biopsy of the right fetal kidney was performed with a biopsy needle WESTCOTT 18 gauge for three-point aspirational biopsy. As RI values pointed to possible borderline carcinoma and keeping in mind the incidence of the disease in our country and worldwide, we treated the patient from both aspects.

Prior to the procedure it is very important to map out the entire vascular supply to the kidney with color Doppler. Through careful mapping, a pathway for the needle can be mapped out, avoiding damage to the vasculature when obtaining the specimen. The biopsy needle was carefully guided into the tumor tissue and three obtained specimens were sent for pathohistological examination. Both the mother and the fetus tolerated the procedure well. No sonographic evidence of hemorrhage in the kidney tissue was present after the procedure. The pathohistological result was classical triphasic tumor with presence of epithelial, blastema and stromal elements, which indicated Wilms' tumor. Concerning unpredictable prognosis, with the parents' consent, feticide and abortion were performed. Postpartum evaluation of the fetal kidneys was performed and biopsy results were confirmed.

After the procedure, the described tumefaction persisted with still increased AFP values. Forty days after feticide, the patient was subjected to ovariectomy. *Ex tempore* pathohistology showed borderline carcinoma and confirmed that the treatment ended by surgery. Considering the fact that our patient was a primipara, all markers and parameters were followed for a period of six months and a stable physiologic condition was confirmed.

Diagnosis of kidney tumors is facilitated today by widely used ultrasound examinations. Prenatal diagnosis of not so rare Wilms' tumor due to its high malignant potency requires all invasive diagnostic procedures in the early detection of kidney tissue damage and staging. The final decision of terminating the pregnancy is based on medical knowledge and parents' consent.

Conclusion

Regardless of the established pathology - fetal kidney tumor, the possibility of comparative pathology should not be neglected. Borderline carcinoma is very common in the young female population in our country. Malignancies in the prenatal period are extremely rare, but with invasive ultrasound-guided procedures they are detectable today even before birth. In spite of the high risk for mother and fetus, benefits of early established diagnosis justify invasive diagnostic procedures such as fetal kidney biopsy.

References

[1] Nicolini U., Spalzini F.: "Invasive assessment of fetal abnormalities: urinanalysis, fetal blood sampling and biopsy". *Prenat. Diagn.,* 2001, *21,* 964.

[2] Moore K.J., Persaund T.V.N.: "The Developing Human". 6th edition, Philadelphia, Saunders 1998.

[3] Paten R.M., Marc L.A., Wang K.Y. *et al.*: "Fetal genitourinary tract". *Radiol. Clin. North Am.,* 1990, *28,* 115.

[4] Partiqin H., Lefortune M. *et al.*: "Fetal lobation: An anatomo-ultrasonographic correlation". *J. Ultrasound Med.,* 1990, *9,* 191.

[5] Brace R.A., Wolf E.J., Brandes J.M. *et al.*: "Normal amniotic fluid throughout pregnancy". *Am. J. Obstet. Gynecol.,* 1998, *161,* 382.

[6] Smith D., Eggington J.A., Brookfild D.S.K.: "Detection of abnormality of fetal urinary tract as a predictor of renal tract disease". *Br. Med. J.*, 1987, *294,* 27.
[7] Rosendahl H.: "Ultrasound screening for fetal urinary tract malformations: a prospective study in general population". *Eur. J. Obstet. Gynecol. Reprod. Biol.,* 1990, *36,* 27.
[8] Jonson M.P., Corsi P., Bradfild W., Hume R.F. *et al.*: "Sequential urinalysis improves evaluation of fetal renal function in obstructive uropathy". *Am. J. Obstet. Gynecol.,* 1995, *91,* 144.
[9] Greco P., Lovero G., Caroso G., Clemente R., Selvaggi L.: "The diagnostic potential of fetal renal biopsy". *Prenat. Diagn.,* 1993, *13*, 551.
[10] Bunduki V., Saldanha A., Sadek J., Miguelez S. *et al.*: "Fetal renal biopsies in obstructive uropathy: feasibility and clinical correlations: preliminary results". *Prenat. Diagn.,* 1998, *18,* 101.
[11] Berek J.S., Hacker N.F.: Practical Gynecologic Oncology, 4th edition, Philadelphia, Lippincott Williams & Wilkins, 2005.

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