Dear Editors and Reviewers:

Thank you for your letter and for the reviewers' comments concerning our manuscript entitled "**Imaging of mixed epithelial and stromal kidney tumor: A case report**" (ID:47354). Those comments are all valuable and very helpful for revising and improving our paper, as well as the important guiding significance to our researches. We have studied comments carefully and have made correction which we hope meet with approval. Revised portion are marked in red in the paper. The main corrections in the paper and the responds to the reviewer's comments are as flowing:

Responds to the reviewer's comments:

Being more common in postmenopausal women, and as you describe a quiet rare case in adolescent male, do you have any reference about the hormonal factor in the pathogenesis of this tumor ? If any, are there any role for the hormonal therapy as an alternative therapy so long as the tumor is benign ?

Response: At present, the pathogenetic mechanism of MESTK and its relationship to other renal neoplasms is still unclear. Most cases occur in menopausal woman (approximately 1:6 male-to-female ratio) and some cases had long-term history of estrogen therapy[1-5]. Therefore, the hormonal milieu may plays a critical role in the tumorigenesis of MESTK. Adsay N et al. [1] reported that it is plausible that the spindle cells of these lesions arise from a periductal fetal mesenchyme, present around epithelial structures in organs like the kidney, pancreas, and liver. This primitive mesenchyme may have the capacity to interact with the epithelia[6]. One can postulate that a deranged hormonal milieu (perimenopausal changes or therapeutic hormones with unopposed estrogen) induces the proliferation of this mesenchyme, which in turn drives the growth of the epithelial component. It may be relevant that mucinous cystic neoplasms of the liver and pancreas are also mixed tumors that arise almost exclusively in women of perimenopausal age, and characteristically show a condensation of ovarian-like stroma (of smooth muscle phenotype and hormone receptor-positive) around their cystic epithelial components[7,8]. In addition, the stromal component of these tumors resembles the periductal fetal mesenchyme in the developing fetus. Therefore, it is possible that these mixed lesions of the solid organs have a common, hormone-induced pathogenesis. In the case reported here, MESTK occurred in a 19-year-old male and three cases of MESTK in adolescent males has also been described[9-11]. Therefore, we assume that hormone secretion disorder of adolescent man may lead to the growth of neoplastic cells. The rarity of the disease precludes investigation into the matter and the exact pathogenesis of MESTK needs further researches and studies.

Because of hormonal factor was closely related to tumor development, hormone treatment could be a potential therapeutic approach in treatment of MESTK. But preoperative radiologic diagnosis of MESTK is difficult. Although the great majority of MESTK cases are benign and prognosis is good, according to research on the treatment of cystic renal mass, Bosniak Category III lesions have 30-100% chance of malignancy and surgery is recommended, whereas Bosniak Category IV is deemed malignant until proven otherwise. Therefore, surgery is the first selection for most MESTK cases[12,13]. Hormonal therapy in clinic use needs further researches and studies.

References:

1. **Adsay N**, Eble J, Srigley J, Jones E, Grignon D. Mixed epithelial and stromal tumor of the kidney. *Am J Surg Pathol* 2000; **24**: 958-970

2 **Lane BR**, Campbell SC, Remer EM, Fergany AF, Williams SB, Novick AC, Weight CJ, Magi-Galluzzi C, Zhou M. Adult cystic nephroma and mixed epithelial and stromal tumor of the kidney: clinical, radiographic, and pathologic characteristics. *Urology* 2008; **71**: 1142-1148

3. **Michal M**, Hes O, Bisceglia M, Simpson RH, Spagnolo DV, Parma A, Boudova L, Hora M, Zachoval R, Suster S. Mixed epithelial and stromal tumors of the kidney. A report of 22 cases. *Virchows Archiv : an international journal of pathology* 2004; **445**: 359-367

4. **Turbiner J**, Amin M, Humphrey P, Srigley J, De Leval L, Radhakrishnan A, Oliva E. Cystic nephroma and mixed epithelial and stromal tumor of kidney: a detailed clinicopathologic analysis of 34 cases and proposal for renal epithelial and stromal tumor (REST) as a unifying term. *Am J Surg Pathol* 2007; **31**: 489-500

5. **Tsai SH**, Wang JH, Lai YC, Chang YH, Chung HJ, Chang LS. Clinical-radiologic correlation of mixed epithelial and stromal tumor of the kidneys: Cases analysis. *Journal of the Chinese Medical Association : JCMA* 2016; **79**: 554-558

6. **Hay ED**, Zuk A. Transformations between epithelium and mesenchyme: normal, pathological, and experimentally induced. Am J Kidney Dis 1995;26:678 90

7. **Devaney K**, Goodman ZD, Ishak KG. Hepatobiliary cystadenoma and cystadenocarcinoma. A light microscopic and immunohistochemical study of 70 patients. Am J Surg Pathol 1994;18:1078 91.
8. **Thompson LDR**, Becker RC, Pryzgodski RM, Adair CF, Heffess C. Mucinous cystic neoplasm (mucinous cystadenocarcinoma of low malignant potential) of the pancreas: a clinicopathologic study of 130 cases. Am J Surg Pathol 1999;23:1 16
9. **Choy B**, Gordetsky J, Varghese M, Lloyd GL, Wu G, Miyamoto H. Mixed epithelial and stromal tumor of the kidney in a 14-year-old boy. *Urologia internationalis* 2012; **88**: 247-248
10. **Teklali Y**, Piolat C, Durand C, Boillot B, Pasquier D, Jacquier C, Dyon JF. Mixed epithelial and stromal renal tumour in a 12-year-old boy. *Journal of pediatric urology* 2010; **6**: 320-323
11. **Lang N**, Li J, Liu J, Zeng X, Yang Y. Mixed epithelial and stromal tumor of the kidney: an analysis of multidetector computed tomography manifestations and clinicopathologic findings. *J Comput Assist Tomogr* 2010; **34**: 177-181
12. **Cecil GW,** Leroy JS, Harmath CB, Horowitz JM, Feng C, Hammond NA, et al. CT and MR imaging for evaluation of cystic renal lesions and diseases. Radiology 2015;35:125e41.
13. **Ljungberg B**, Bensalah K, Canfield S, Dabestani S, Hofmann F, Hora M, et al. EAU Guidelines on Renal Cell Carcinoma: 2014 Update. Eur Urol 2015;67:913e24