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NEPHROLOGY - LETTER TO THE EDITOR

THSD7A as a marker for paraneoplastic membranous nephropathy

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Editor,

The phospholipase A2 receptor (PLA2R) and thrombospondin type-1 domain containing 7A (THSD7A) are the two major autoantigens in primary membranous nephropathy (MN) [1, 2]. In particular, the THSD7A-associated MN may have a unique relationship with malignancy [3]. However, no study has examined renal pathology and expression of THSD7A in the same kidney, respectively, without and with malignancy, which may convincingly rule out the action of pre-existing THSD7A as 'background clutter.' Therefore, we have surveyed our patients closely and came up with the following report. The study had acquired proper institutional approval and necessary consent from the participants.

The index case was a 68-year-old female with repeated renal biopsies showing distinct changes of renal pathology, tissue THSD7A expression, and its serum antibody, in parallel with the evolution of malignancy (Fig. 1). At the first biopsy, the patient had acute tubular injury but not discernible glomerular lesion and negative THSD7A staining. She later developed MN with glomerular expression of the THSD7A and existence of its serum antibody, manifested malignant tumor, underwent surgical resection, received chemotherapy, and eventually displayed remission of proteinuria and disappearance of the said antibody. Of note, antibody to the phospholipase A2 receptor was undetected during both hospital stays. Moreover, we have screened new cases of hepatobiliary malignancies operated within the past year and collected serum samples of those with proteinuria but free of known proteinuric kidney diseases. Among 37 (70% male) such patients, one woman of pancreatic cancer with nephrotic syndrome had positive THSD7A antibody and showed similar pattern of changes after operation and chemotherapy.

These findings were in general consistence with the knowledge that THSD7A-associated malignancies were mainly involved in the gastrointestinal and genitourinary systems, with a female predominance [4]. Since the THSD7A may have a role in angiogenesis and cell adhesion [5], its disparate prevalence under different neoplastic conditions may indicate biological heterogeneity in the growth and metastasis of the malignancies per se. Nevertheless, our report conferred explicit evidence supporting THSD7A as a paraneoplastic marker for MN caused by malignancy. Patients manifesting MN with positive antibody to the THSD7A should be scrutinized for malignancy, especially in the susceptible systems.

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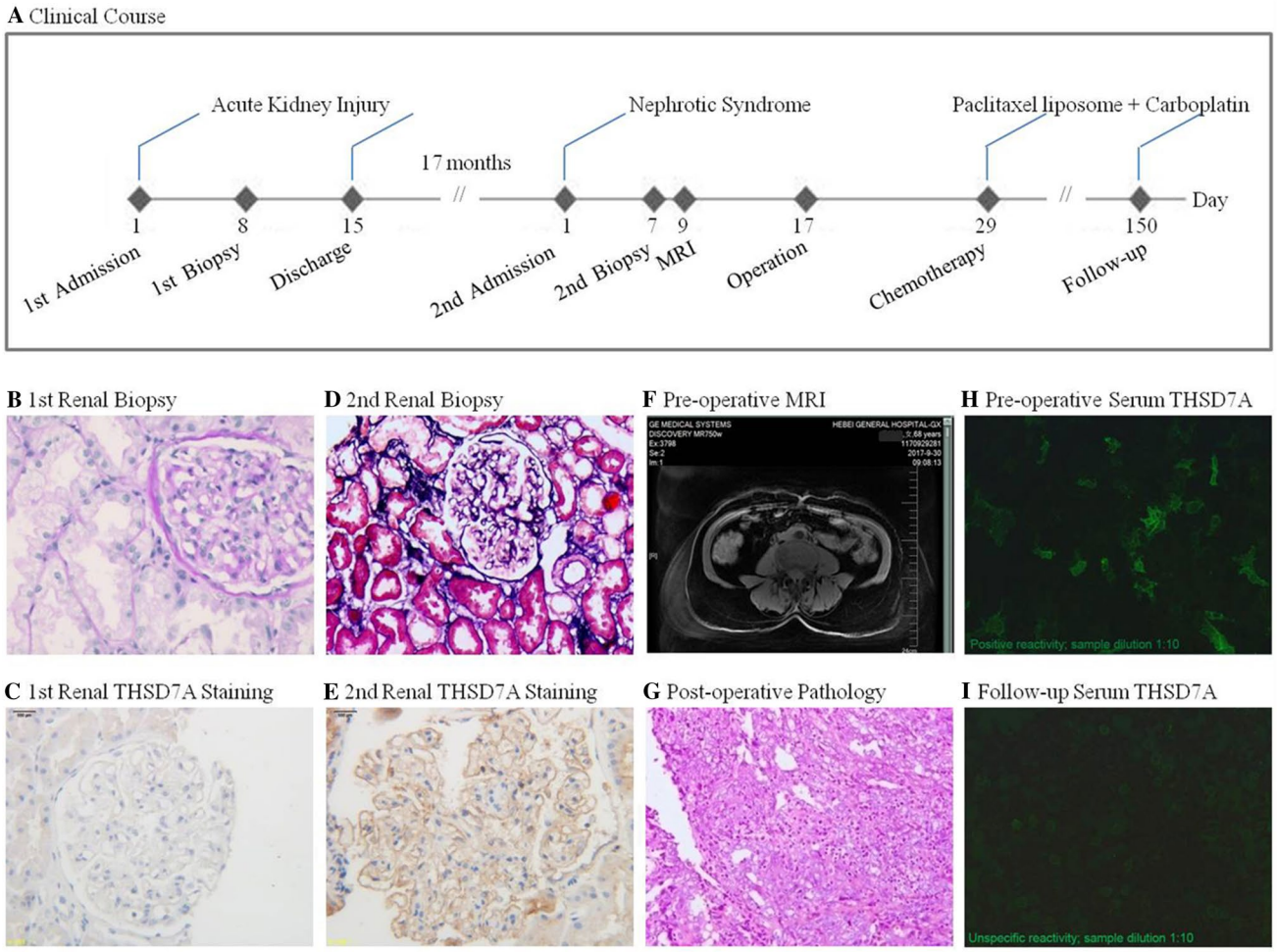

Fig. 1 Clinical and morphologic characterization of the index patient. **a** The clinical course of the patient's two hospital stays, respectively, due to acute kidney injury and nephrotic syndrome. The 24-h urinary protein excretion (reference: 0–0.14 g) was 0.22 g, 4.59 g, and 0.11 g in the first, second admission and prior to the marked follow-up, respectively. **b, c** The results of the first renal biopsy showing acute tubular injury and negative glomerular immunohistologic stains for THSD7A. **d** and **e** The results of the 2nd renal biopsy showing membranous nephropathy and positive glomerular immunohistologic stains for THSD7A. **f** The MRI image showing the mass indistinguishably adjacent to the right ovary. **g** The pathology-confirmed serous adenocarcinoma of the fallopian tube. **h** Positive serum THSD7A antibody on arrival as expressed in a semi-quantitative measurement. **i** Negative serum THSD7A antibody at approximately 120 days after the initiation of chemotherapy

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Compliance with ethical standards

Conflict of interest No potential conflict of interest relevant to this letter was declared.

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