THSD7A Associated Membranous Nephropathy Leading to Metastatic Neuroendocrine Carcinoma

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Objective

The objective of this case report is to highlight the importance of cancer screening in individuals with THSD7A positive PMN.

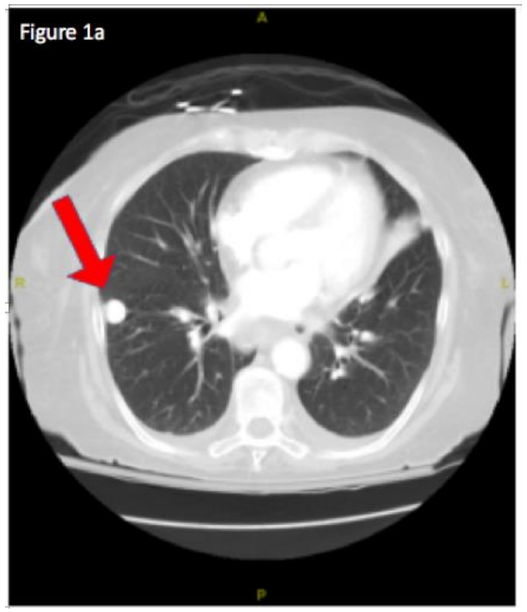
Introduction

Idiopathic membranous nephropathy (IMN) is the most common cause of primary nephrotic syndrome in adults. The classic presentation of membranous nephropathy is a patient with fatigue, malaise, and edema. Presentation is usually insidious in nature with one-third of patients with risk of progression to end-stage renal disease. The diagnosis of membranous nephropathy is based on renal biopsy. Anti-PLA2R was the first antigenic target to be recognized in IMN, discovered in 2009 [3]. THSD7A was described as a second autoantigen involved in Idiopathic membranous nephropathy. The prevalence of THSD7A has a reported range of 3-5%. Among individuals with THSD7A-associated membranous nephropathy, studies have shown a development of a malignancy within a median follow-up of 3 months from the time of initial diagnosis [3]. Due to this, physicians should be aware of the possible development of malignancy and emphasize age-appropriate cancer screening during routine outpatient visits.

Hospital Course

- 72 year old female with history of hypothyroidism, tobacco use, and endometrial cancer status post hysterectomy presenting with worsening lower extremity edema.
- UA with proteinuria 1 year prior.
- Physical exam: minimal wheezing, 3+ pitting edema, and minimal periorbital edema.
- Basic labs: Hemoglobin 11.2 gm/dl, anion gap -2 mEq/L (normal values 3.0-11.0), Albumin 2.2 gm/dl (normal 3.5-5.0), Urine random total protein 700 mg/dl, Urine creatinine 12 mg/dl, Urine protein-to-creatinine ratio 58.3 g/day
- One year prior: CT chest which showed extensive mediastinal adenopathy which was not evaluated due to patient hesitancy to follow-up.
- Repeat CT Chest with contrast showed mediastinal and left hilar adenopathy significantly increased, with a slight increase in size of spiculation in the right upper lobe measuring 1.5 cm as compared to 1.0 cm from the prior study (Figure 1a and 1b).
- Bronchoscopy with fine needle aspiration of right paratracheal lymph node: positive for synaptophysin and chromogranin indicating metastatic neuroendocrine carcinoma, small cell type.
- CT guided left renal biopsy was obtained resulting in Anti-PLA2R negative, THSD7A positive membranous glomerulopathy and acute tubular injury.

Images



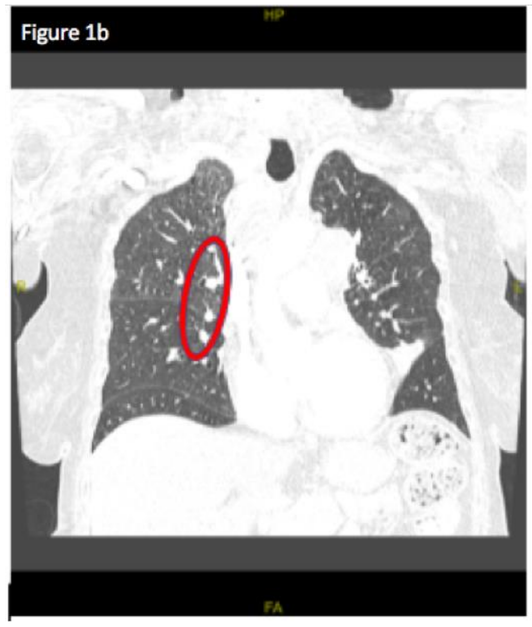


Figure 1: CT Chest with contrast. Figure 1a shows a right sided coin lesion shown by the red arrow. Figure 1b shows mediastinal and left and right hilar adenopathy. Right sided adenopathy is shown in the red circle.

Discussion

- Membranous nephropathy (MN) is a unique glomerular lesion that can be further classified as primary or secondary MN. In primary MN, circulating IgG4 autoantibodies to the podocyte membrane antigen PLA2R (anti-PLA2R) have been seen in 70-80% of individuals with idiopathic MN. However, as in our case, a small percentage of individuals, around 3-5%, demonstrate THSD7A positivity with or without a concomitant positive anti-PLA2R. Among individuals with THSD7A-associated membranous nephropathy, studies have shown development of malignancy within a median follow-up of 3 months from the time of initial diagnosis [3]. In our case, the patient had a recorded history of mild lower extremity edema 2 years prior to hospitalization which, along with decreased adherence to medical follow-up, enabled the progression of the nephrotic syndrome. As membranous nephropathy is insidious in nature, it is likely that this was a prelude to the development of malignancy, which was first noted a year after onset of lower extremity edema. As mentioned in the case presentation, it was discovered that the patient developed metastatic neuroendocrine carcinoma, small cell type. The development of a malignancy in individuals with THSD7A carry a varying incidence of 6-25% [3].

Conclusion

- This case raises the question of whether the patient developed membranous nephropathy as a complication of the small cell metastatic neuroendocrine carcinoma or whether a chronic and insidious THSD7A associated membranous nephropathy is a risk factor for development of malignancy. However, due to symptom onset of lower extremity edema, the latter appears to be the most likely.
- We shed light on the importance of screening for malignancy in this subtype of membranous nephropathy.

References

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This research was supported (in whole or in part) by HCA Healthcare and/or an HCA Healthcare affiliated entity. The views expressed in this publication represent those of the author(s) and do not necessarily represent the official views of HCA Healthcare or any of its affiliated entities.