CASE REPORT

Combined neuroendocrine small cell carcinoma of trachea with crescentic glomerulonephritis as a paraneoplastic manifestation

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Summary
A middle aged female presented with history of breathlessness and swelling of legs of 2 weeks duration; the clinical and laboratory picture was suggestive of rapidly progressive renal failure and the kidney biopsy revealed a crescentic glomerulonephritis. Her renal function improved with the steroid therapy; in view of persistent breathlessness despite good diuresis chest radiograph was repeated which showed reduced lung volume on right and compensatory emphysema on the left side; a computerized tomography (CT) scan of the thorax showed a mass lesion partially obliterating the right main bronchial lumen. The mass on histopathology revealed small cell neuroendocrine carcinoma (SCNC) with adenosquamous carcinoma.

To our knowledge only one case of neuroendocrine tumor presenting as a crescentic glomerulonephritis has been reported in the literature.

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Case report
A 64-year-old female, a known case of essential hypertension of 25 years duration and type 2 diabetes mellitus & bronchial asthma of 2 years duration, presented with breathlessness, swelling of legs and hematuria, progressively worsening over a period of 2 weeks. She was found to
have pedal edema, her blood pressure was 140/90 mmHg and the respiratory system examination on auscultation revealed ronchi. Other systems were normal on examination.

Her hemoglobin was 10 gm/dL, total leukocyte count 10,400/mm³ (66% neutrophils & 34% lymphocytes), platelets 249,000/mm³ and erythrocyte sedimentation rate of 106 per hour. The blood urea was 100 mg/dL, serum creatinine 3.8 mg/dL, sodium 139 meq/L, potassium 4 meq/L, calcium 8.7 mg/dL and phosphorus of 6.5 mg/dL. Her blood sugar levels were within the normal range. Urinalysis revealed proteinuria, numerous red blood cells and 8–10 leukocytes per high power field; granular casts were seen. Twenty-four hours urinary protein estimation revealed 164 mg protein and the urine culture was sterile. Complement levels were normal (C3 136 mg/dL and C4 48 mg/dL), both C and P antineutrophil cytoplasmic antibodies (ANCA) were negative. An abdominal ultrasound showed normal sized kidney.

The initial chest radiograph was suggestive of early pulmonary edema. Electrocardiograph was normal and the echocardiography showed concentric hypertrophy of the left ventricle; ejection fraction was 69%.

The repeat renal function tests in the hospital revealed rising serum creatinine over a week’s time, a clinical diagnosis of rapidly progressive renal failure was considered and kidney biopsy was done which on histopathology showed crescentic glomerulonephritis (Fig. 1). She was given pulse of intravenous methyl Prednisolone (500 mg/day) over a period of 3 days, following which oral steroids were started at 1 mg/kg body weight per day. Her renal function started improving and the serum creatinine came down to 1.5 mg/dL over a period of 10 days. However, she continued to have breathlessness; a repeat chest radiograph was taken which showed reduced lung volume on right side with compensatory emphysema on the left side (Fig. 2). CT thorax revealed a mass partially obliterating the right main bronchial lumen (Fig. 3). There were no lesions in the lungs. The lesion on flexible bronchoscopy was found to be a pedunculated mass arising from the carina and partially obliterating the right main bronchus. Excision biopsy of the mass was done via rigid bronchoscopy and the histopathology demonstrated the combined small cell neuroendocrine carcinoma with adenosquamous carcinoma (Fig. 4).

One month after the admission she received the first cycle of chemotherapy (carboplatin and etoposide). On the second day of chemotherapy her BP started dropping, breathlessness increased and her chest radiograph showed bilateral non-homogenous opacities; renal parameters started worsening again and there was neutrophilic...
leukocytosis. Overall picture was of sepsis with multi-organ dysfunction. Her BP continued to drop despite the inotropic support and the empirical intravenous antibiotics (teicoplanin and aztreonam). She died of septic shock after 1 week.

Discussion

The commonest site of presentation of SCNC is the lung; other extra pulmonary sites being the esophagus, the larynx and the head and neck. Primary laryngeal SCNC is a rare entity accounting for less than 0.5% of the laryngeal carcinomas. It is more common in men especially in smokers. These tumors are well known for their paraneoplastic manifestations like Eaton–Lambert myasthenic syndrome, syndrome of inappropriate secretion of antidiuretic hormone and ectopic adrenocorticotropic hormone syndrome.1

The paraneoplastic manifestation may be the first sign of malignancy or the tumor may initially manifest with the local symptoms like hoarseness of voice and a cervical mass; about 50% of all patients with laryngeal SCNC have cervical lymph node metastases at presentation and the distant metastasis develops eventually in most. The diagnosis of these tumors is entirely based on the histopathological appearance and the confirmation is done by immunocytochemical analysis. Concurrent chemoradiotherapy regimens offer potential for long-term survival, however, this tumor is biologically aggressive, and the stage of the disease is one of the most important independent factors determining long-term survival.1,2

Paraneoplastic syndromes are classified into six types: cutaneous, endocrine, hematological, neurological, rheumatologic, and ocular.2

Renal manifestations of neuroendocrine small cell tumors are rare. There are several case reports describing the association of SCNC with nephrotic syndrome. The commonest lesion described is the membranous glomerulonephritis (MGN).3–5 Our case is unique because the primary neuroendocrine tumors of the trachea are rare and the renal involvement as a paraneoplastic manifestation is unusual and in most of the cases described the histopathology showed MGN; only one case of crescentic glomerulonephritis associated with NCSC has been reported in the literature.6

Another interesting feature is the presence of combined histopathological picture (i.e. component of SCNC with squamous cell carcinoma and/or adenocarcinoma).7 The paraneoplastic syndromes have not been described in association with combined SCNC.1

Apart from the paraneoplastic effect these tumors can also cause renal involvement by various other mechanisms like direct infiltration or distant metastasis from the tumor or secretory diarrhea (hormone induced) causing pre renal type of acute renal failure.8,9

Chemoradiotherapy is the treatment of choice for SCNC. Commonly used agents include cyclophosphamide, doxorubicin hydrochloride and vincristine sulfate; cisplatin and etoposide have been used with success.10

Conflict of interest statement

The authors have no conflict of interest.

References