Case Report

Small Cell Carcinoma with Paraneoplastic Cushing’s Syndrome in A 23-Year-Old A New Observation and Literature Review

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Small Cell Lung Cancer; Neuroendocrine Tumor; Pediatric; Lung Cancer; Cortisol; Paranesoplasic; Cushing Syndrome

1. Abstract
A 23 years old girl, without history, consulted for a neck tumefaction appeared 20 days ago, which spread then to the abdomen and lower limbs with Asthenia, dysphagia, abdominal pain, effort dyspnea. Clinical examination revealed an altered general state, obesity with centripetal fat deposition face, supraclavicular and dorsal and cervical fat pads, facial plethora, rounded face, buffalo-hump, face acne, melanodermia, capillary fragility, face, arms and legs hirsutism.

Imaging revealed a voluminous left para mediastinal Mass. A guided Scan biopsy confirmed the diagnosis of small cell neuroendocrine carcinoma.

The patient had a first line treatment with Etoposide-Carboplatin. Initially the response to the treatment was good with improvement of symptoms. At day 20 of the treatment, the patient had a clinical progression and died after 15 days.

2. Introduction
Adolescent Small Cell Carcinoma is a rare entity. The first case was reported with a 14-year-old boy. It presented 0.2% of children tumors. These neuroendocrine tumors are associated in 1 to 5% of cases to a paraneoplastic Cushing’s syndrome. The second paraneoplastic syndrome in order of frequency is the syndrome of inappropriate secretion of ADH.

Observation
A 23 years old girl, without history, consulted for a neck tumefaction appeared 20 days ago, which spread then to the abdomen and lower limbs with Asthenia, dysphagia, abdominal pain, effort dys-
She had not palpable adenopathy. The abdomen was bloated. She had hepatomegaly with hepatic arrow of 20 centimeter, 2 lower limbs pitting edema. Her blood pressure was 11/9 with oliguria. Chest radiograph (Figure 5), Cerebral, Thoracic, abdominal and pelvic CT (Figure 6-8) imaging revealed a voluminous left para-mediastinal tumor process, multiple mediastinal lymphadenopathies, many bilateral pulmonary nodules, and hepatomegaly with metastasis.

A guided Scan biopsy of the mediastinal mass confirmed the diagnosis of a mediastinal localization of small cell neuroendocrine carcinoma confirmed by immunohistochemistry: it shows ovoid small cells undifferentiated carcinoma, with basophilic cytoplasm and dense hyperchromatic nucleus, sometimes downhill with atypia and mitosis (Figure 9). Immunohistochemistry express intense and diffuse manner of chromogranin, synapophysin and TTF1 (Figure 10).

Laboratory data indicated a disrupted liver status with cytolysis and cholestasis. Plasma protein electrophoresis was normal with negative 24 hours proteinuria. She had hyperglycemia, high cortisol (3 x Normal) and ACTH (6 x Normal). The patient had a first line treatment with Etoposide-Carboplatin. Initially the response to the treatment was good with a slight improvement of the dyspnea, abdominal bloating with a decrease of the edema of the lower limbs. At day 20 of the treatment, the patient had a clinical progression with worsening of the dyspnea, the edema, the abdominal distension and died after 15 days.
3. Discussion

Primary lung cancers are rare in children [1]. It presents 0.16% of all lung cancers occurring in the first decade of life and 0.7% in the second decade [2].

Reported cases of pediatric lung carcinoma in literature are most commonly undifferentiated carcinoma, followed by adenocarcinoma and squamous cell carcinoma.

There was some historical cases of undifferentiated carcinoma truly represent small cell carcinoma or perhaps atypical carcinoid tumors in literature.

In pediatric population, most common benign lung tumor is inflammatory myofibroblastic tumor (52%), and the most common cancer are carcinoblast and pleuropulmonaryblasta [3]. Trachea, bronchus, and lungs cancers represent 0.2% of all children cancers [4]. Eighteen to thirty years old patients with lung cancer have a high incidence of female sex, there is no association with smoking, and favorable prognosis [5].

In 2000, Kim et al published the first case of a 14-year-old boy with Small cell lung cancer. Surveillance Epidemiology and End Results review during twenty one years reported 7 cases of pediatric small cell lung cancer, when Children’s Hospital Boston found 1 case whereas a 90-year review [6-12]. They had the worst prognosis in pediatric lung cancer with median survival less than 5 months. The overall survival was generally poor, and the majority dies with disease recurrence. Two-year survival in patients with extensive stage was 4.6%, and five-year survival of patients with limited stage was 10%. First-line chemotherapy was four to six cycles of Etoposide-Cisplatin. Eighty per cent of limited stage patients and all extensive patients relapse within the first year after initial treatment. In recurrent disease, median survival was 2 to 3 months.

A literature review by PubMed was done by using search terms “small cell lung cancer” and “neuroendocrine carcinoma lung,” and “neuroendocrine tumor lung.” The search was limited to articles describing patients 14 to 18 years old. Six cases were reported (Table 1).

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<tr>
<th>Table 1. Characteristics, Treatment, and Outcome of Small Cell Lung Carcinoma</th>
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<td>Kim et al (11)</td>
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<td>Barbour M et Al (23)</td>
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CARBO: carboplatin; CDDP: cisplatin; CPM: cyclophosphamide; DOXO: Doxorubicin; ; GMZ: Gemcitabine; IFOS: ifosfamide; TOPO: topotecan; VCR: vincristine.

Median age was 15 years old (range, 14 to 18) and only two patient had a metastatic disease [13]. Five patients had no smoke exposure. Five patients received systemic chemotherapy with platinum-based regimen.

One case of small cell cancer treated with gemcitabine. Only patients with limited stage cancer received radiation therapy [16]. Death is reported in four cases. Outcome is not known for 2 of the patients with limited stage disease.

Ectopic corticotropin syndrome or Cushing’s syndrome is present in 2–5% of patients with small-cell lung cancer at the time of presentation [17]. In this literature review, no patients had Cushing paraneoplastic syndrome as our case.

Treatment of ectopic corticotropin production need a reduction of cortisol synthesis by an adrenal enzyme inhibitor such as ke-
toconazole [18] as well as treatment of primary tumor. Jeong et al. suggested achieving longer survival may be attended with controlling the high cortisol level by administering systemic chemotherapy [19]. Associated with systemic chemotherapy, ketoconazole (strong inhibitor of cytochrome P450), metyrapone, etomidate, mitotane, and mifepristone can be used to reduce circulating glucocorticoids [15].

4. Conclusion
Small cell cancer, high grade neuroendocrine lung cancer is extremely rare in adolescent population. Few cases were reported in literature, rarer those associated to paraneoplastic syndrome. Patients with an extensive stage tumor have a bad prognosis with 2 year survival less the 5%.

References