Journal of Medical Case Reports and Reviews
Received 30 Oct 2021 | Revised 12 Nov 2021 | Accepted 28 Dec 2027 | Published Online 30 Dec 2021

DOI: https://doi.org/10.52845/JMCRR/2021/4-12-2
JMCRR 04 (12), 1037–1047 (2021)

ISSN (O) 2589-8655 | (P) 2589-8647 IF:2.964

CASE REPORT

Small cell carcinoma with paraneoplastic Cushing's syndrome in a 23 -Year-Old. A New Observation And Literature Review

Feki.J [1] | Mnif. A [1*] | Saguem M.H [2] | Khanfir A [1]

[1]Department Of Medical Oncology, Habib Bourguiba University Hospita, Medecine Faculty, University Of Sfax

[2]Tunisia Free Practice Pathology Laboratory

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.

Keywords: Small Cell Lung cancer, Neuroendocrine Tumor, Pediatric, Lung Cancer, cortisol, Paranesoplasic, Cushing syndrome

1 | 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.

hirsutism (Fig 1 to 4).

Supplementary information The online version of this article (https://doi.org/xx.xxx/xxx.xx) contains supplementary material, which is available to authorized users.

Corresponding Author: *Mnif. A*
Department Of Medical Oncology, Habib Bourguiba University Hospita, Medecine Faculty, University Of Sfax

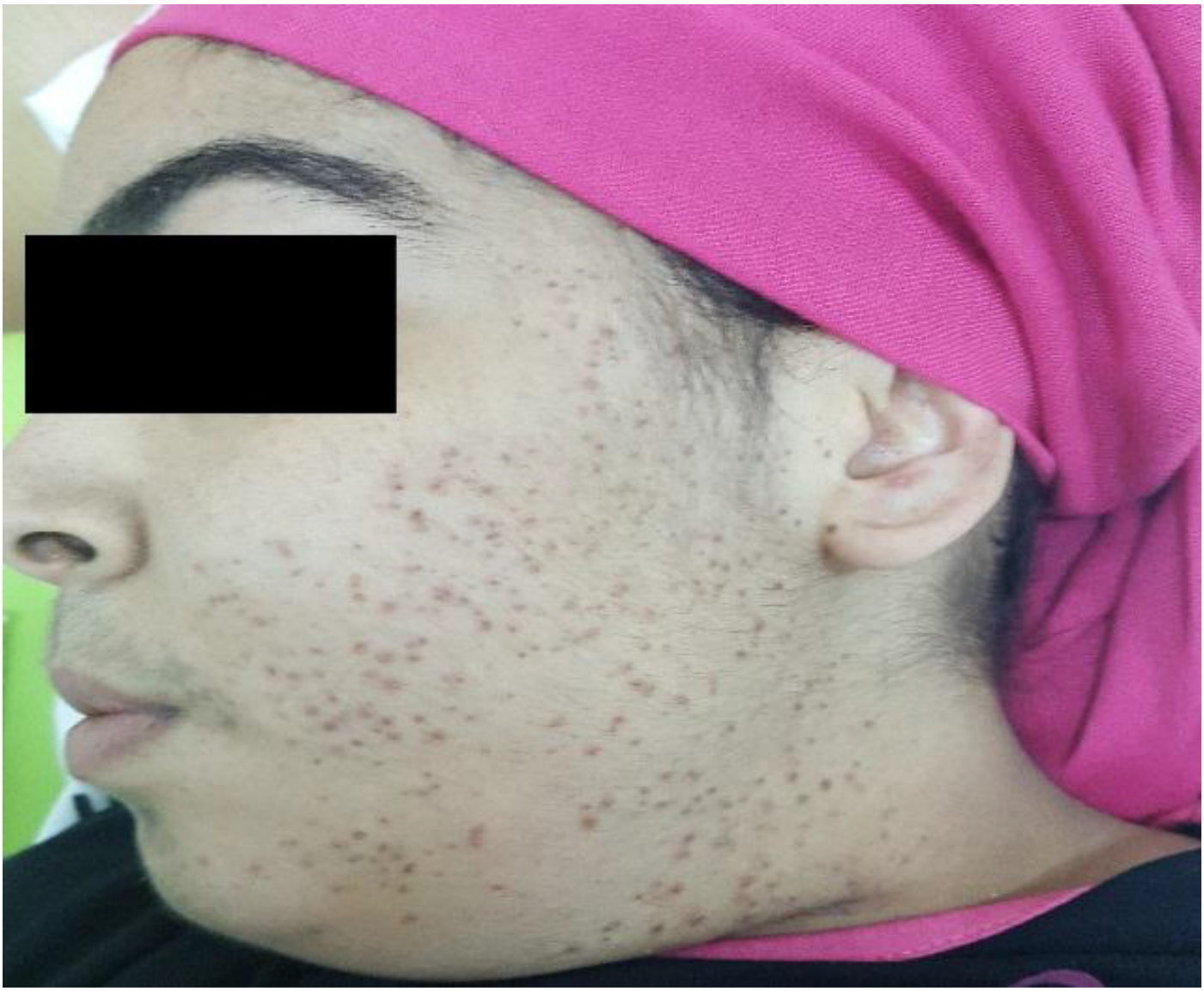

FIGURE 1: Centripetal fat deposition face, facial plethora, rounded face, facial plethora, rounded face, buffalo-hump, face acne,
melanodermia

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 radiographf (Fig 5), Cerebral, Thoracic, abdominal and pelvic CT (Fig 6 to 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 (Fig 9). Immunohistochemistry express intense and diffuse manner of chromogranin, synapotphysin and TTF1 (Fig 10) Figure

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

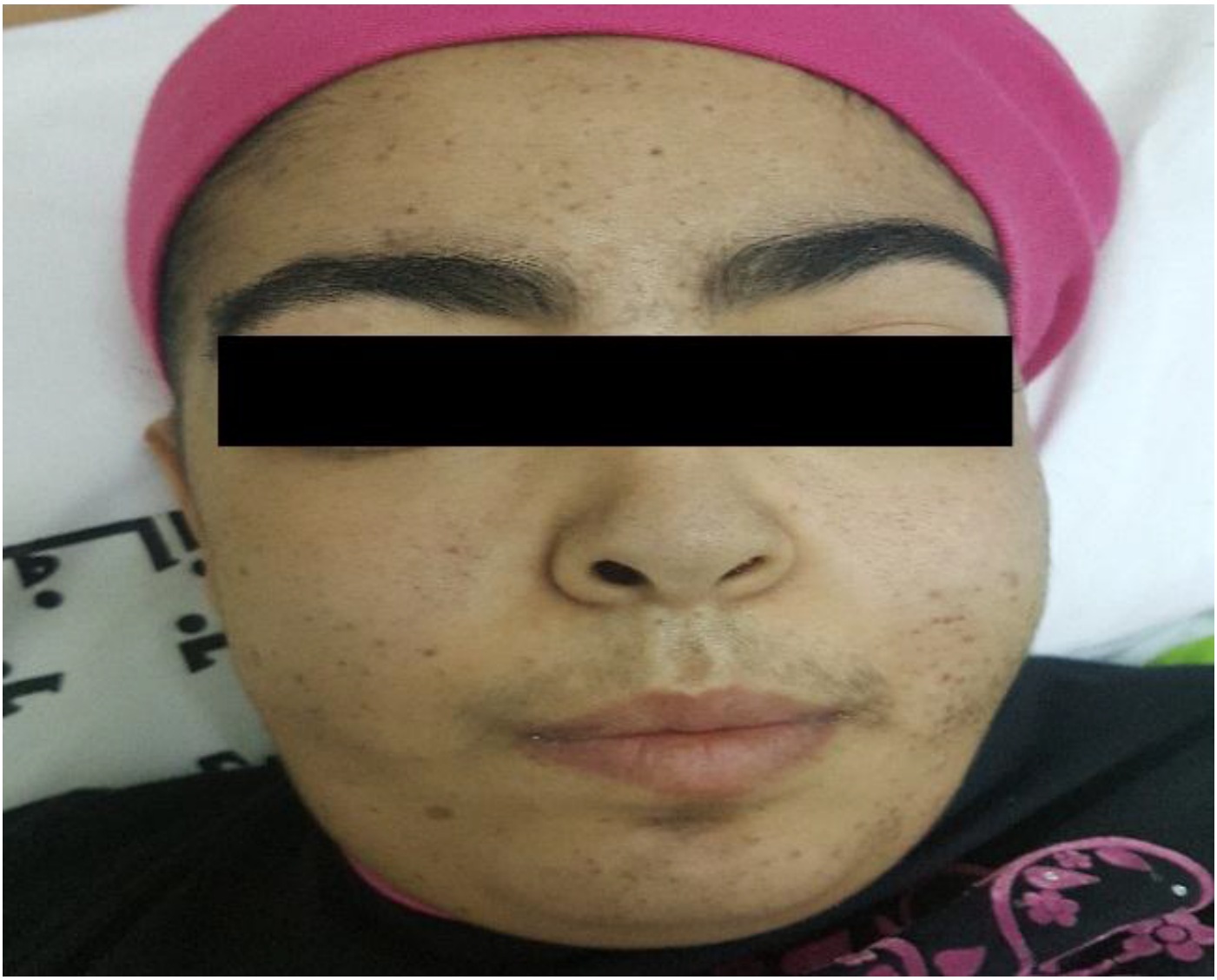

FIGURE 2: Centripetal fat deposition face, facial plethora, rounded face, facial plethora, rounded face, buffalo-hump, face acne,
melanodermia

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.

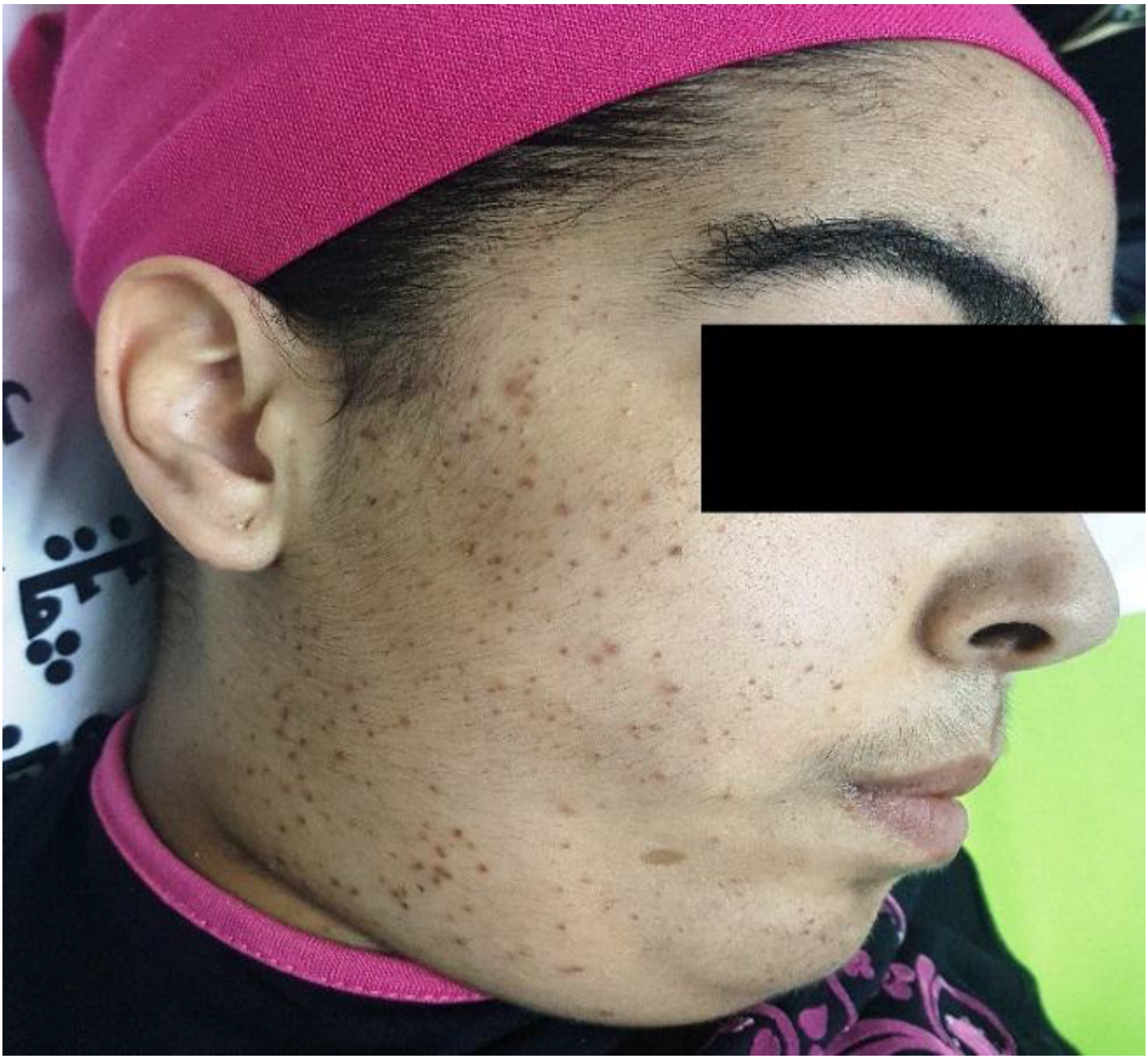

FIGURE 3: Centripetal fat deposition face, acial plethora, rounded face, buffalo-hump, face acne, melanodermia

In pediatric population, most common benign lung tumor is inflammatory myofibroblastic tumor (52%), and the most common cancer are carcinoid tumor and pleuropulmonary blastoma (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 pa-

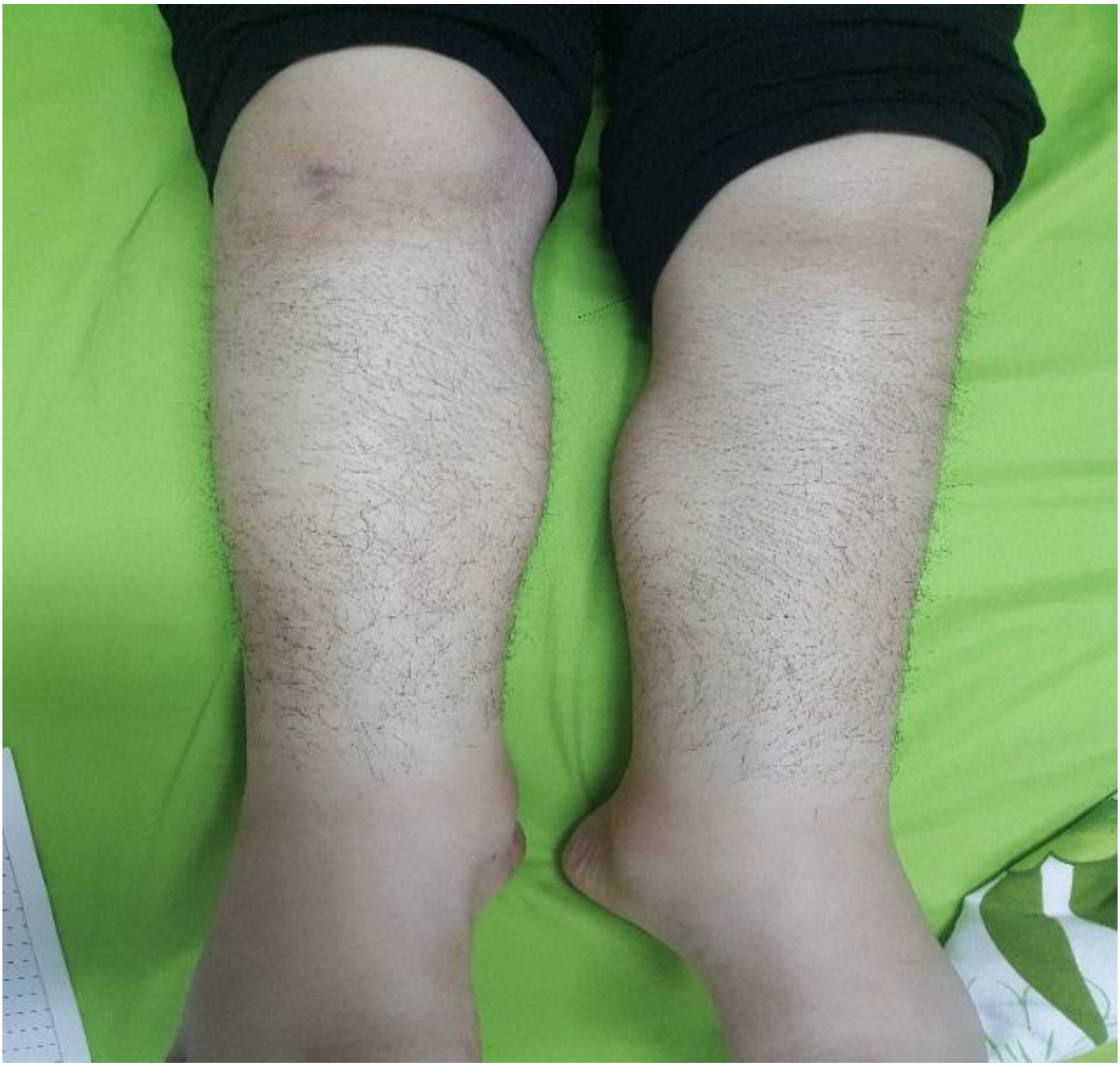

FIGURE 4: Legs Hirsutism

tients 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 Etposide-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) .

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

One case of small cell cancer treated with gem-

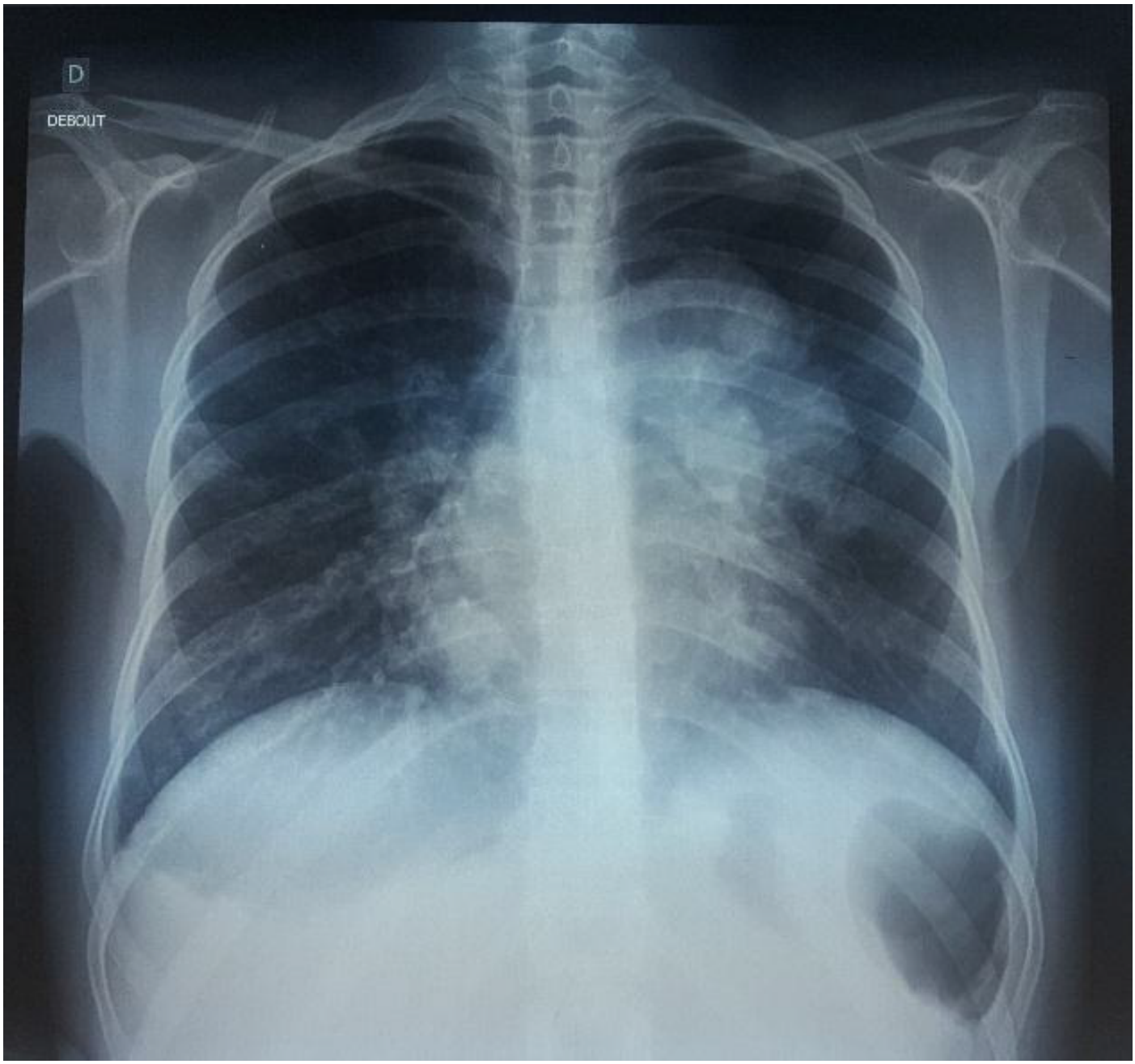

FIGURE 5: Chest radiographf: left para-mediastina mass

citabine. 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 a cushing paraneoplasic syndrome as our case.

Treatment of ectopic corticotropin production need a reduction of cortisol synthesis by an adrenal enzyme inhibitor such as ketoconazole (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

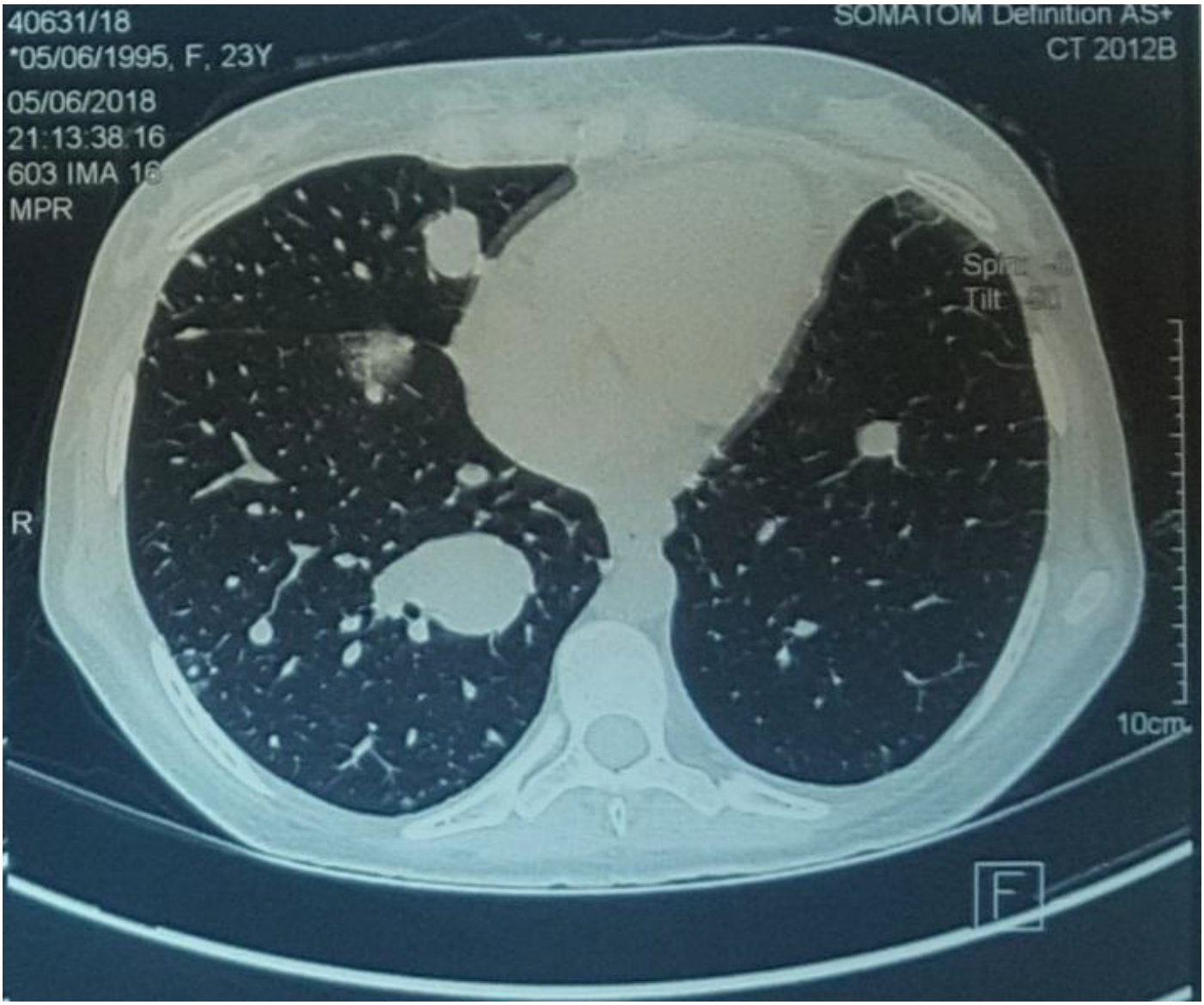

FIGURE 6: Thoracic CT: lef mediastina mass mediastinal lymphadenopathies, bilateral pulmonary nodules

P450) , metyrapone, etomidate, mitotane, and mifepristone can be used to reduce circulating glucocorticoids (15) .

4 | CONCLUSIONS

Small cell cancer, high grade neuroendocrine lung cancer is extremely rarein 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 %. (20) (21) (22) (23)

REFERENCES

1. Primary and Metastatic Lung Tumors in the Pediatric Population: A Review and 25-Year Experience at a Large Children's Hospital. Arch Pathol Lab Med. 2008;132:25.;.
2. Fontenelle LJ. Primary adenocarcinoma of lung in a child: review of the literature. Am Surg. avr 1976;42(4):296-9.;.

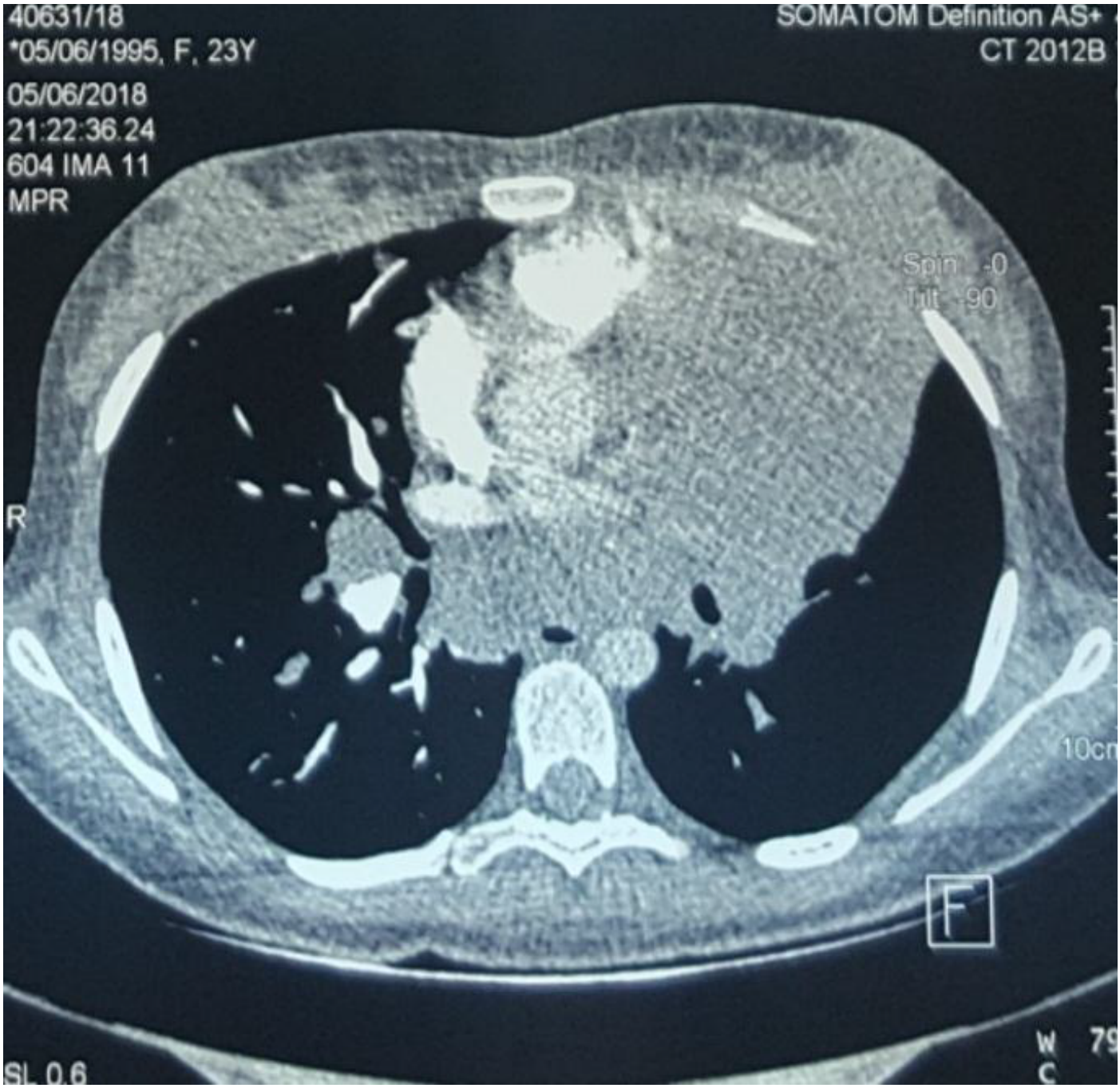

FIGURE 7: Thoracic CT: left para-mediastinal mass

3. Hancock BJ, Di Lorenzo M, Youssef S, Yazbeck S, Marcotte JE, Collin PP. Childhood primary pulmonary neoplasms. J Pediatr Surg. sept 1993;28(9):1133-6.;.

4. Experience in surgical treatment of pulmonary and bronchial tumours in childhood. - PubMed - NCBI [Internet]. [cité 17 mai 2020]. Disponible sur: https://www.ncbi.nlm.nih.gov/pubmed/3107068;.

5. Lung carcinoma in patients age younger than 30 years - Mizushima - 1999 - Cancer - Wiley Online Library [Internet]. [cité 17 mai 2020]. Disponible sur: https://acsjournals.onlinelibrary.wiley.com/doi/full/10.1002/(SICI)1097-0142(19990415)85:8%3C1730::AID-CNCR12%3E3

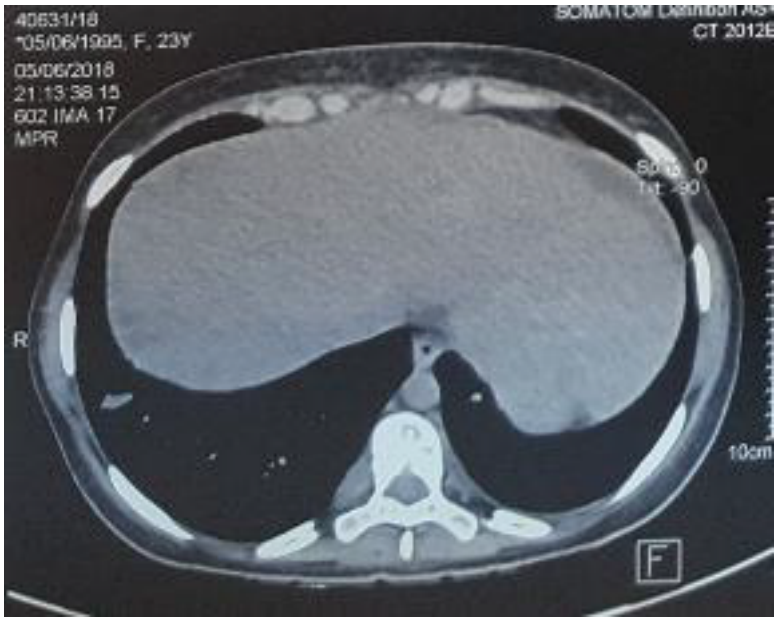

FIGURE 8: Abdominal CT: hepatomegaly

.0.CO;2-G;.

6. Neville HL, Hogan AR, Zhuge Y, et al. Incidence and outcomes of malignant pediatric lung neoplasms. J Surg Res. 2009;156:224–230.;.

7. Dishop MK, Kuruvilla S. Primary and metastatic lung tumors in the pediatric population: a review and 25-year experience at a large children's hospital. Arch Pathol Lab Med. 2008;132: 1079–1103.;.

8. Altekruse SF. SEER Stat Fact Sheets: Lung and Bronchus [Surveillance Epidemiology and End Results Web site]. 2010. Available at: http://seer.cancer.gov/statfacts/html/lungb.html. Accessed January 19, 2011;.

9. Jackman DM, Johnson BE. Small-cell lung cancer. Lancet. 2005;366:1385–1396.;.

10. Govindan R, Page N, Morgensztern D, et al. Changing epidemiology of small-cell lung cancer in the United States over the last 30 years: analysis of the surveillance, epidemiologic, and end results database. J Clin Oncol. 2006;24: 4539–4544. 6. Kim CK, C;.

11. Kim CK, Chung CY, Koh YY. Primary small cell bronchogenic carcinoma in a 14-year-old boy. Pediatr Pulmonol. 2000;29: 317–320.;.

12. Yu DC, Grabowski MJ, Kozakewich HP, et al. Primary lung tumors in children and adolescents: a 90-year experience. J Pediatr Surg. 2010;45:1090–1095;.

13. Kim CK, Chung CYPost GR, Lewis JA, Hudspeth MP, et al. Disseminated neuroendocrine carcinoma in a pediatric patient: a rare case and diagnostic challenge. J Pediatr Hematol Oncol. 2012;34: 200–203., Koh YY. Primary small cell bronchogenic carcinoma in a 14-year-old boy. Pediatr Pulmonol. 2000;29: 317–320.;.

14. Tronnes H, Haugland HK, Bekassy AN, et al. Small cell lung cancer in a 14-year-old girl. J Pediatr Hematol Oncol. 2012;34: e86–e88. 11. Yonemori;.

15. Yonemori K, Kunitoh H, Sekine I. Small-cell lung cancer with lymphadenopathy in an 18-year-old female nonsmoker. Nat Clin Pract Oncol. 2006;3:399–403. quiz following 403.;.

16. Jett JR, Schild SE, Kesler KA, et al. Treatment of small cell lung cancer: diagnosis and management of lung cancer, 3rd ed: American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2013;143 (suppl):e400S–e419S.;.

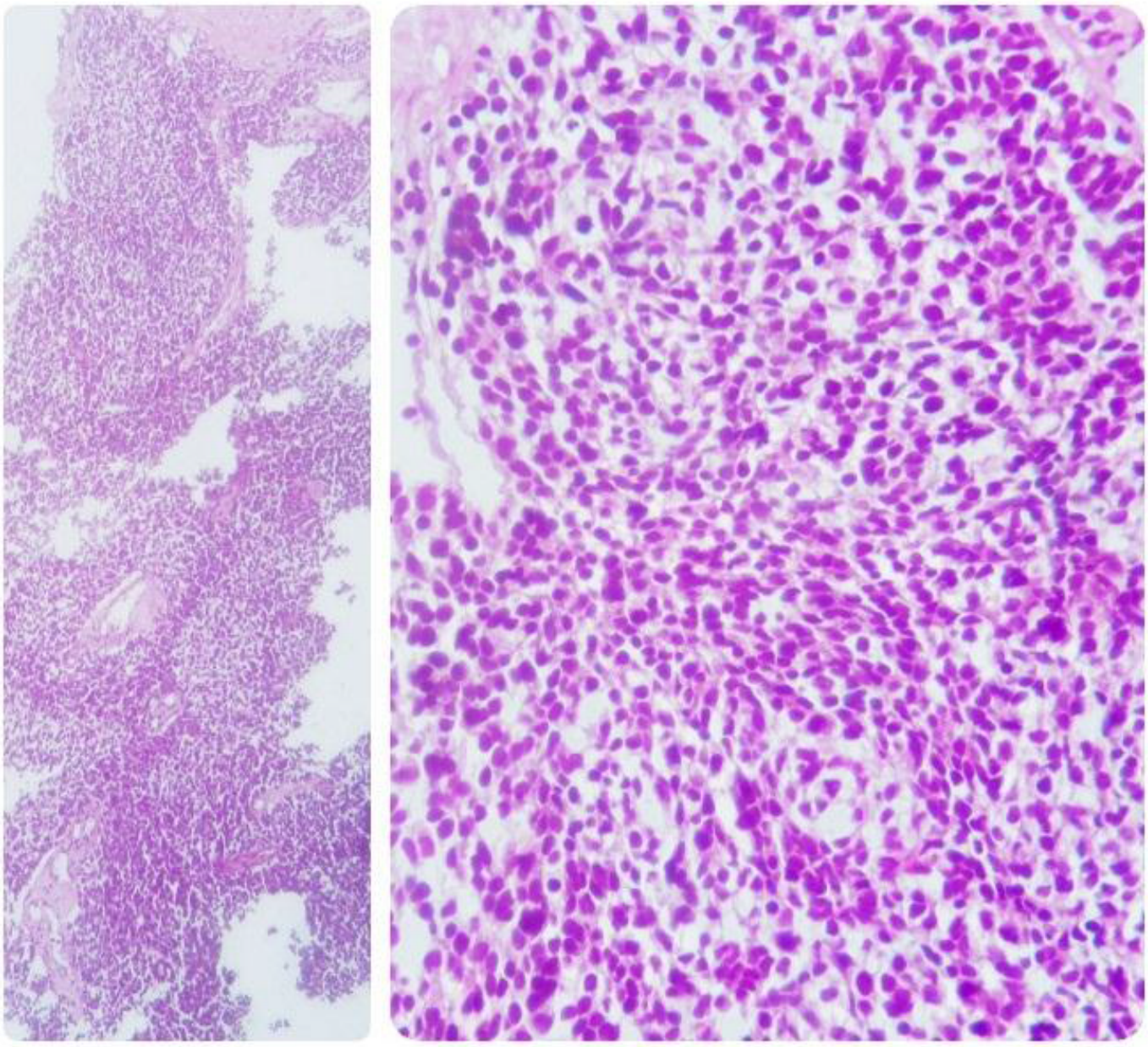

FIGURE 9: Small undifferentiated cell carcinoma: basophilic cytoplasm and dense hyperchromatic nucleus ,downhill with atypia and mitosis

17. Shepherd FA, Laskey J, Evans WK, Goss PE, Johansen E, Khamsi F. Cushing's syndrome associated with ectopic corticotropin production and small-cell lung cancer. J Clin Oncol 1992; 10: 21–27.;.

18. Winquist EW, Laskey J, Crump M, Khamsi F, Shepherd FA. Ketoconazole in the management of paraneoplastic Cushing's syndrome secondary to ectopic adrenocorticotropin;.

19. Toi-Scott M, Jones CL, Kane MA. Clinical correlates of bombesinlike peptide receptor subtype expression in human lung cancer cells. Lung Cancer 1996; 15: 341–54.;.

20. Kanaji N, Watanabe N, Kita N et al. Paraneoplastic syndromes associated with lung cancer. World J Clin Oncol 2014; 5: 197–223.;.

21. G R, S G, N LR, Jp L, E B, J C. [Small Cell Bronchial Cancer in a 17-year-old Young Man]

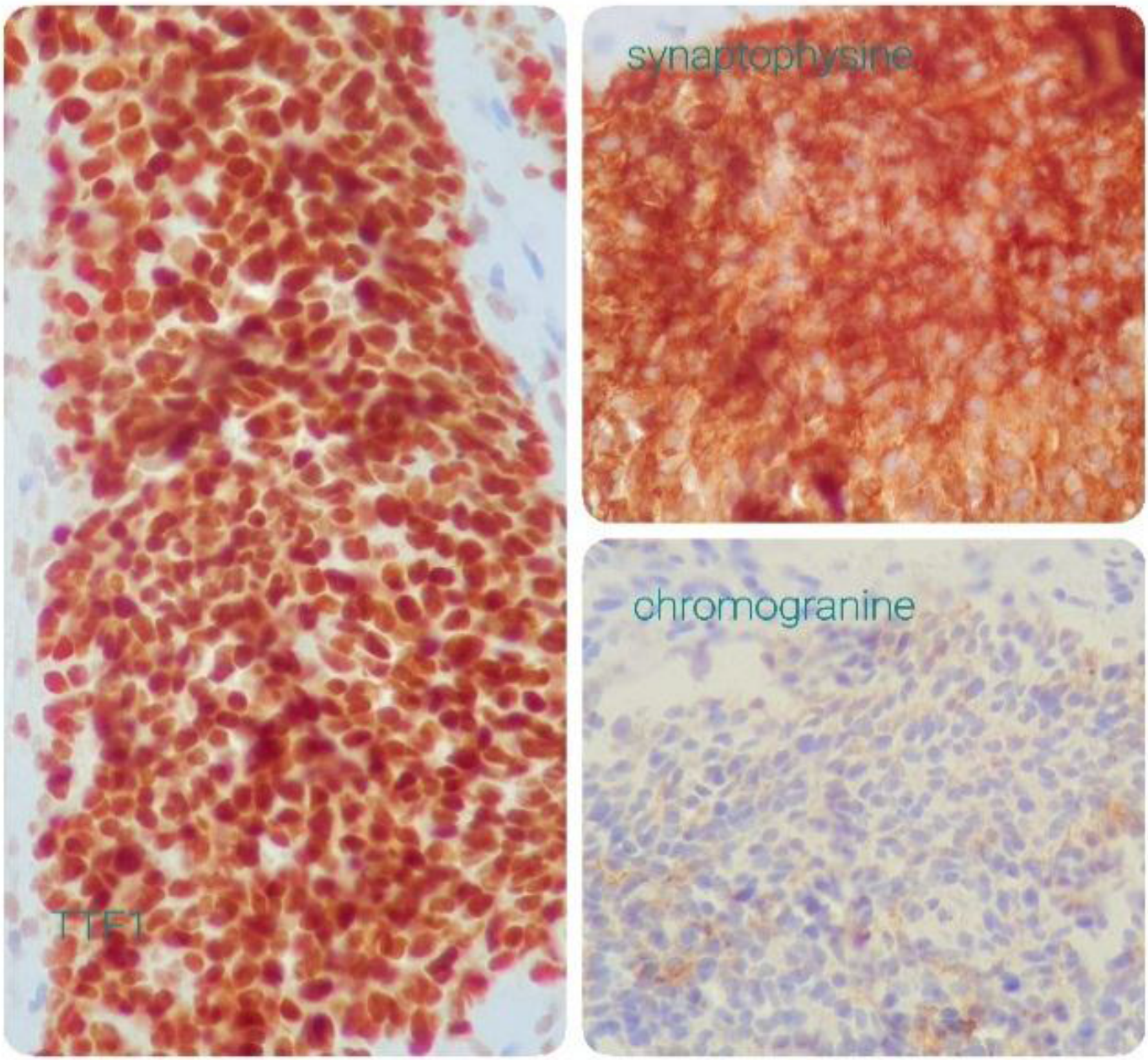

FIGURE 10: Immunohistochemistry:intense and diffuse manner of chromogranin synapotphysin and TTF1

[Internet]. Vol. 11, Revue des maladies respiratoires. Rev Mal Respir; 1994;.

22. Post GR, Lewis JA, Hudspeth MP, et al. Disseminated neuroendocrine carcinoma in a pediatric patient: a rare case and diagnostic challenge. J Pediatr Hematol Oncol. 2012;34: 200–203.;.
23. Barbour M, Bujold KE, Tjarks BJ, Jassim AD. A Case of Small Cell Lung Carcinoma in a 15-Year-Old Boy and Literature Review: J Pediatr Hematol Oncol. oct 2018;40(7):563-6.;.

How to cite this article: F.J., M.A., S.M.H., K.A. Small cell carcinoma with paraneoplastic Cushing's syndrome in a 23 -Year-Old. A New Observation And Literature Review. Journal of Medical Case Reports and Reviews. 2021;1037–1047. https://doi.org/10.52845/JMCRR/2021/4-12-2