CASE REPORT

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Lung parenchima changes in neurofibromatosis type 1

Promene parenhima pluća kod neurofibromatoze tipa 1

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Abstract

Introduction. Neurofibromatosis type 1 (NF1), also known as von Recklinghausen disease, is one of the most common single-gene disorders (mutation on chromosome 17q) and usually associated with cutaneous, musculoskeletal and neurological disorders in humans. NF1 is generally complicated with one or more neurobehavioral disorders or tumors located in the peripheral nervous system such as neurofibromas, peripheral nerve sheath tumor, pheochromocytoma, etc. In the available medical literature, the thoracic manifestations of NF1 have been rarely described in these patients. There are few reports about intrathoracic neurogenic tumors, kyphoscoliosis, pneumonitis and pulmonary fibrosis in patients with NF1. **Case report.** A 65-year-old female was admitted to the Intensive Care Unit at the Lung Clinic of Belgrade University Clinical Center of Serbia. The patient's general condition was poor with shortness of breath and present cyanosis. At the same time, the skin changes similar to NF1 were noticed, which were additionally documented by her medical history and diagnosed as NF1. After the application of noninvasive mechanical ventilation and other emergency respiratory medicine measures, the patient soon felt better. The parenchymal changes were viewed by subsequent X-rays and CT scanning of the thorax. **Conclusion.** This is a case report presenting the NF1 associated with the abnormality of lung parenchyma established during diagnostic procedures at the Intensive Care Unit, Clinic of Pulmonology.

Key words:
neurofibromatoses; diagnosis; lung fibrosis; radiography; tomography, x-ray computed.

Apstrakt

Uvod. Neurofibromatoza tipa 1 (NF1), takođe poznata kao fon Recklinghauzenova bolest, jedan od najčešćih poremećaja pojedinačnih gena (mutacija na hromozomu 17q), obično je povezana sa kožnim, mišićnoskeletnim i neurološkim poremećajima kod ljudi. Takođe, NF1 obično je povezana sa jednim ili više neurobihejvioralnih poremećaja ili tumora lociranih na perifernom nervnom sistemu, kao što su neurofibromi, plašt tumori perifernih nerava, feohromocitom, itd. Kod istih bolesnika torakalne manifestacije NF1 opisane su retko u sadašnjoj medicinskoj literaturi. Postoji nekoliko izveštaja o intratorakalnim neurogenskim tumorima, kifoskoliozi, pneumonitisu i plućnoj fibrozi kod bolesnika sa NF1. **Prikaz bolesnika.** Bolesnica, stara 65 godina, na prijemu u Jedinicu intenzivne nege Klinike za pulmologiju Kliničkog centra Srbije bila je u lošem opštem stanju, kratakog daha i sa prisutnom cijanozom. U tom trenutku primećene su i promene na koži. Nakon dobijanja informacije kao i podataka iz medicinske istorije bolesnice, utvrđeno je da je u pitanju NF1. Posle primene neinvazivne mehaničke ventilacije i drugih mera hitne respiratorne medicine, bolesnica se ubrzo osećala bolje. Na kasnije učinjenom RTG snimku i CT skenu grudnog koša uočene su promene parenhima. **Zaključak.** U ovom prikazu opisana je NF1 povezana sa abnormalnostima plućnog parenhima, utvrđena tokom dijagnostičkih procedura u Jedinici intenzivne nege Klinike za pulmologiju.

Ključne reči:
neurofibromatoza; dijagnoza; pluća, fibroza; radiografija; tomografija, kompjuterizovana, rendgenska.

Introduction

Neurofibromatosis belongs to the group of diseases called phakomatoses. Neurofibromatosis type 1 (NF1) is caused by gene mutation on chromosome 17q which encodes a protein known as neurofibromin, a negative regulator of Ras oncogene [1]. NF1 has a number of possible signs. The presence of *café-au-lait* maculas and multiple neurofibromas, usually 5–15 mm in diameter was a key sign of diagnosis [2]. Chest manifestations may be different: kyphoscoliosis, ribbon deformity of the ribs, intrathoracic neoplasms, and interstitial lung disease such as diffuse interstitial fibrosis and bullous lung disease either alone or in combination, sometimes called fibrosing alveolitis [3].

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Case report

A 65-year-old woman was admitted to the Intensive Care Unit, Clinic of Pulmonology, University Clinical Center of Serbia, Belgrade, due to crisis of consciousness, shortness of breath and very pronounced cyanosis. The patient's medical history, dating back as far as 30 years, showed that the patient had been treating for chronic obstructive pulmonary disease (COPD) all the time. The last few years, the patient experienced more frequent exacerbations.

Moreover, the patient had manifested NF1 disease since childhood in the form of *café-au- lait* maculae and multiple neurofibromas covering almost the entire skin; she had also had positive family medical history of some manifestations of the disease presented in her mother and grandfather. Since 2011, the patient had been suffering from verified tachyarrhythmia, high blood pressure and chronic cardiomyopathia. During that period, thoracic computed tomography (CT) scanning revealed, for the first time, abundant sequelae of specific process and fibrothorax in the left lung. The patient was skinny with almost child constitution: height of 152 cm, weight 45 kg, body mass index (BMI) 19.48 kg/m^2. She was a non smoker. Physical examination showed multiple maculae on the entire skin (Figure 1) and deformity of the spine in the form of kyphoscoliosis. Respiratory findings were as follows: lower airway sounds and polyphonic wheezing. Cardiac findings were: tachycardia, and cardiac arrhythmic action with occasional extrasystoles; blood pressure: 130/100 mmHg; heart rate: 121/min. Abdomen and limbs were clinically normal. Laboratory analysis showed mild positive inflammatory syndrome, anemia and thrombocytopenia, hypoproteinemia and electrolyte imbalance. Arterial blood gas analyses were in favor of acidosis and global respiratory insufficiency. Spirometry results were: forced vital capacity (FVC) 1.23 L (56%); predicted forced expiratory volume in 1 second (FEV1) 0.67 L (37%); predicted ratio FEV1/FVC 54.92%; mixed ventilatory pattern, dominantly obstructive and reduced diffusing capacity of the lung; diffusing capacity of the lung for carbon monoxide (DLCO) 31%; transfer coefficient (KCO) 54%. The chest x-ray showed an increased transparency from the apex to the base, pleuropericardial and pleurobasal adhesions, with fibrous changes in parenchyma on both sides (Figure 2). Computed tomography scan revealed solid emphysema and bullous changes viewed in the apical left, right and posterior areas (Figure 3). Fibroindurative chronic changes with the interstitial inflammation and hilar traction were observed in bilateral the upper medial lobes. Bullous changes with bronchiectasis were present basally on the left side. Paratracheal lymph nodes, 18 mm in diameter, were also evident. Bilateral pleural effusion was basally organized. Diffuse lung reduction was recorded (Figure 4).

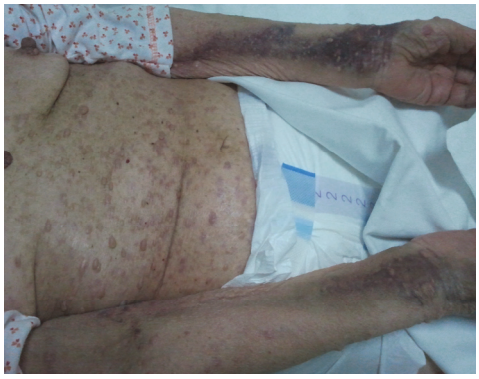

Fig. 1 – Physical examination showed multiple *maculae* on the entire skin.

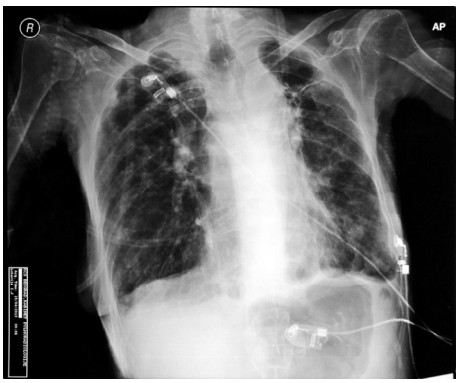

Fig. 2 – Chest x-ray showed on both sides an increased transparency from the apex to the base as well as pleuropericardiac and pleurobasal adhesions, with fibrous changes of parenchyma.

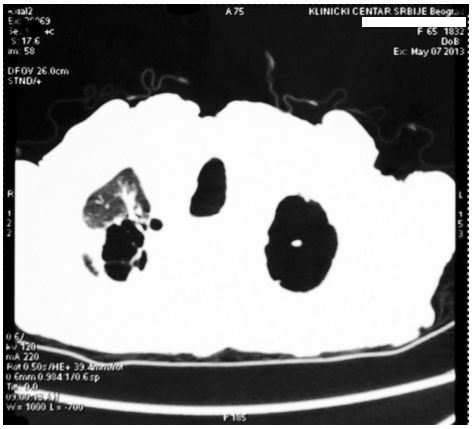

Fig. 3 – CT scanning showing apical left, right and back solid emphysema and bullous changes.

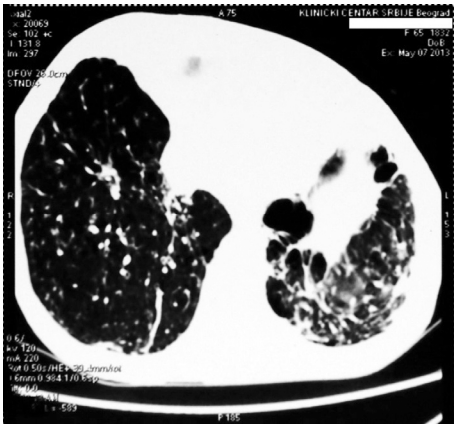

Fig. 4 – CT scanning showing bullous changes with bronchiectasis to the basal left. paratracheal lymph nodes 18 mm in diameter, bilateral pleural effusion, basal, organized, as well as diffuse lung reduction.

Discussion

The condition of the presented patient fully fits in the clinical picture of NF1. At least two criteria have to be recognized for establishing the diagnosis of NF1: the presence of minimum six *cafe-au-lait* spots of more than 5 mm in diameter in children and 15 mm in adults; no less than two neurofibromas or one plexiform neurofibroma; freckles and/or discoloration in the sun-protected areas (armpits, pubic area); optic glioma; the presence of at least two iris nodules (Lisch nodules); specific skeletal abnormalities; hereditary high blood pressure [4]. Appropriate diagnostic procedures confirmed the presence of lung changes. Although pulmonary fibrosis, bullae or other interstitial abnormalities are uncommon findings with neurofibromatosis, the parenchyma lung involvement has been reported in 1.9–20% of NF1. The first cases of chest abnormalities in NF1 were described in 1963 [5]. Some studies show that the increased sensitivity of the lung to cigarette smoke causes an early development of emphysema-like changes [5, 6]. Since the identification of the NF1 gene, great advances in understanding the role of the NF1 gene in molecular pathogenesis of NF1-associated clinical abnormalities have been achieved [5]. Clinical studies have begun to define specific subpopulations of patients at risk for cancer and have identified targeted therapies for NF1-associated tumors, based on science research advances [7]. Quality of life in NF1may be different and it depends on many factors: sex, age, emotions, physical symptoms, functioning, and other associated diseases. Patients with more severe NF1 reported more effects on the physical function, general health perception and vitality [8]. Patients with neurofibromatosis and respiratory symptoms need to be checked for possible changes in the lung parenchyma, and they require a multidisciplinary approach [1, 9].

Conclusion

We presented a patient, non-smoker, whose changes in the lung parenchyma were most likely not caused by COPD for which the patient was treated over 30 years. The impairment of pulmonary function was the result of kyphoscoliosis and emphysema changes in the lung parenchyma. Only a few available references on the association between NF1 and changes in pulmonary parenchyma indicate that this problem has been rarely recorded. Well documented NF1 case reports indicate that the routine tests (X-ray, CT scan, spirometry, diffusion) can detect pulmonary changes in the early stages of the disease, which is certainly important for better prognosis.

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