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Case Report

Multiple primary tumors in a young adult female (Li-Fraumeni syndrome)

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Abstract

The objectives of this study was to describe the occurrence of multiple primary tumors in a young adult as an example of the Li-Fraumeni syndrome and emphasize the difficulty and complexity of treatment. Young adult patients with multiple tumors are rarely reported. In our case, a 23-year-old female presented over a period of 14 months with primary tumors in the right adrenal, lung, breast and brain. She had a family history of lung cancer, breast cancer and astrocytoma grade II of the brain. The patient underwent resection of tumors of the right adrenal and left lower lung segment as well candidates for preventive bilateral mastectomy. Family history of cancer and the occurrence of multiple tumors at a young age should lead to suspicion of Li-Fraumeni Syndrome.

Keywords: Brain tumor, Breast tumor, Li-Fraumeni syndrome, Lung adenocarcinoma, Pheochromocytoma

INTRODUCTION

Li Fraumeni Syndrome (LFS), first described in 1969, is a rare hereditary autosomal dominant cancer syndrome, due to germ cell TP53 (tumor suppressor gene) mutation, a gene located on chromosome 17(17p13.1). This syndrome is most commonly associated with a tendency to develop a wide range of certain, rare, cancers such as brain, bone and soft tissues sarcomas, leukemia, and adrenocortical carcinoma as well as breast cancer (Kim et al., 2001; ASCO, 2017; Miroslav et al., 2014; Max et al., 2018).

LFS affects females more than males, this syndrome is characterized by inheritance and early appearance of multiple tumors.

Classic LFS criteria are as follows:

-A proband diagnosed with a sarcoma before age 45 years and

-A first-degree relative with any cancer diagnosed before age 45 years and

-Another first- or second-degree relative with any cancer diagnosed before age 45 years or a sarcoma diagnosed at any age (Max et al., 2018; Michael and George, 2018).

A pheochromocytoma is a rare neuroendocrine tumor of the adrenal medulla of which about 30% are caused by hereditary syndromes. About 85% are located within the adrenal glands and 98% are within the abdomen (Michael and George, 2018).

Breast cancer is the most common malignancy in adult patients with LFS in which the median age at first breast cancer diagnosis is 32 years (Amara et al., 2017; Payal et al., 2018).

Gene mutations in inherited syndromes lead to increased risk of brain tumors (Rick et al., 2017).

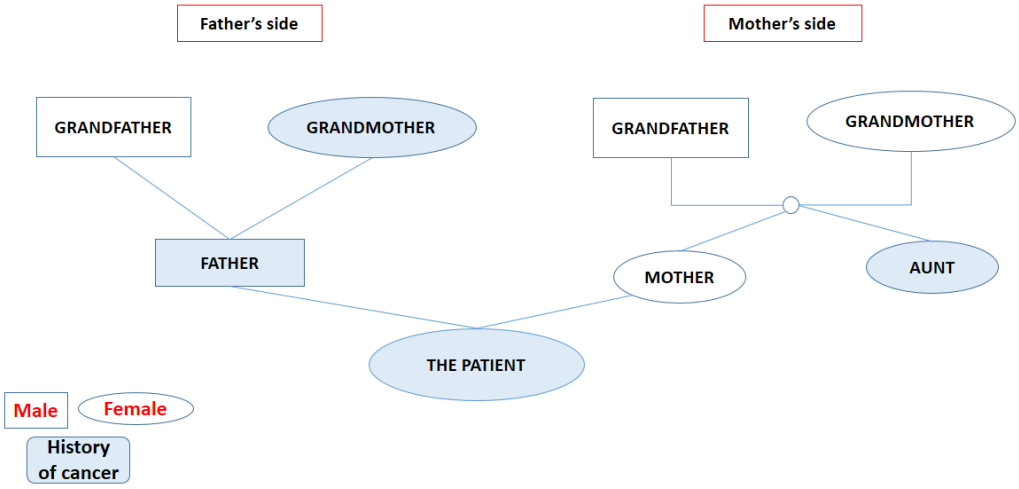

Figure 1. The following diagram showing cancers in the family: a father with astrocytoma, grandmother metastatic breast carcinoma and an aunt with lung cancer.

Figure 2. showing a PET-CT scan for the patient before and after the removal of the right adrenal pheochromocytoma per PET-CT.

Approximately 8% of lung cancers are inherited or occur as a result of a genetic predisposition and increase the risk among first-degree relatives (Madiha et al., 2017).

Case Story

A 23- year old female generally healthy on no medication, non-smoking, she was referred to the emergency department in September, 2017 by a primary care physician due to red urine (hematuria). Family medical history showed her father with a brain tumor- astrocytoma grade 2, grandmother (mother's father)with metastatic breast carcinoma and an aunt (mother's sister), a smoker, with lung cancer (Figure 1).

To evaluate the hematuria, routine laboratory investigations (complete blood count, and Coagulation Profile) didn't show any pathological findings (Table 1), physical examination, cardiovascular examination including electrocardiogram and auscultation were normal. The patient underwent computed tomography

Table 1. Patient's Complete Blood Count (CBC) and Coagulation.

Parameter	Lab Reference	Result
WBC (10^3 cells/ul)	4.8-10.8	7.28
Eosinophil's	1-3%	1.9%
Basophils	0-1.5%	0.4%
Blasts	%	0.73
Platelets (10^3/ul)	130-400	231
Hemoglobin (g/dL)	12-16	13.8
PT-INR	0.89-1.16	0.93
PT-SEC (sec)	10-13.5	11.1
APTT-sec (sec)	26-39	30.9
Neutrophils.(10^3 cells/ul))	1.9-8	4.53

Table 2. Patient's Endocrinology and Markers laboratory tests.

Parameter	Lab Reference	Result
Calcitonin (pg\ml)	0-5	<2
Dopamine (ug\24h)	65-400	577
Epinephrine (ug\24h)	>20	27
Norepinephrine (ug\24h)	15-80	189
Metanephrine (ug\24h)	<301	1710
Normetanephrine (ug\24h)	< 527	3363

(CT) of the abdomen that showed a lesion 3.5X3.8X5 cm in the right adrenal. A hypo-dense lesion in segment A4 in the liver was suspected to be a hemangioma.

She was admitted to the hospital for further evaluation laboratory investigations of endocrinology and markers blood tests (Table 2). She underwent removal of the lesion in the right adrenal, pathologic examination showed: pheochromocytoma with single infiltrated to blood vessel, large nests positive more than 10% of tumor cells, and positive for chromogranin, synaptophysin, GATA3, S100 and Ki67-positive for 10% of tumor cells.

Genetic investigation was negative for the whole panel for the known mutations of pheochromocytoma. After operation tests showed: Metanephrine –88ug\24h and Normatenprin- 175ug\24h.

During follow up abdominal CT showed-a suspicious finding (nodular) in the left lower lung (LLL) field. For further investigation she underwent CT of chest which showed: nodular finding in LLL with diameter of 1.4 cm**.** an additional nodule 6 mm diameter with surrounding ground-glass opacity (GGO) and multiple pulmonary nodules with largest diameters up to 3 mm in the right lower lung (RLL) and a nodule in the right breast 1.2 cm.

She had then undergone breast ultrasound which showed a 1.2 cm benign nodule (BIRADS2).

Because of requiring further investigation combined positron emission tomography-computed tomography (PET-CT) test showed – absence of signs of malignancy for the findings.

In November, 2018 she had LLL segmental resection. Pathologic examination showed: adenocarcinoma of lung origin, clean margins, positive for CK7 (cytokeratin-7), TTF-1 (thyroid transcription factor-1) and NAPSIN A, and focally reactive for p63 (tumor suppressor protein).

Two months later magnetic resonance imaging (MRI) of the brain showed: a lesion in the deep right temporal lobe with triangular shape that was consistent with structural dysplasia, PET-CT of body showed: no changes. After Consultation with an endocrinologist the diagnosis of Li-Fraumeni syndrome was made, also a liquid biopsy was done and showed a mutation in TP53 and the diagnosis of Li-Fraumeni was also confirmed. An option of preventive bilateral mastectomy was suggested.

DISCUSSION AND CONCLUSION

We have described a rare case of Li-Fraumeni syndrome, although it is known as a rare disease it should be considered to be seen with different primaries and also possible being diagnosed in young patient such as our case in which onset in pheochromocytoma and lung adenocarcinoma and preventive indications was suggested as serious and which she was treated surgically. We should remember that a family history of cancers in first and second degree relative within different types of cancers should be taken as serious problems and family members need close follow up also screening imaging is very important for trying to improve the prognosis and discovering of the pathological finding and associated tumors. Also because of the risk related to this syndrome the family member should be informed

also physical examination and annual clinical review should be done for prevention of missing it.

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