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Double Synchronous Primary Tumors: Metastatic Melanoma and Advanced Pulmonary Adenocarcinoma in a 32-Year-Old Adult: Case Report and Literature Review

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ABSTRACT

Introduction: The presence of multiple primary malignant neoplasms is an unusual finding during the diagnostic approach of patients with cancer. The coexistence of melanoma with lung adenocarcinoma is extremely rare according to some cohort studies since a prevalence of 0.05% is estimated in this group of patients. The most relevant risk factors for the development of multiple malignant tumors are genetic, environmental exposures to carcinogenic substances, and treatment of a preexistent cancer.

Case description: Male, 32 years old who denies family history of malignant neoplasms, drug addiction, chronic degenerative diseases, allergies, surgeries, and hospitalizations. His main symptom was a progressive weakness of the right upper and lower limb which, over a period of days, made it impossible to walk. During his hospitalization, MRI revealed metastatic lesions associated with vasogenic edema. For this reason, an evaluation was requested by the neurosurgery service, who performed a decompressive craniectomy with a biopsy that reported malignant cells consistent with metastatic melanoma. As part of the diagnostic approach, a thoracoabdominal CT with IV contrast was performed, which revealed another tumor at the lung level in the left lower lobe that obliterates the bronchus, not suggestive of metastatic activity, for this reason a lung biopsy was performed, which reported findings of poorly differentiated adenocarcinoma with angiolymphatic invasion present and extensive necrosis. The patient was discharged home with the palliative care measures due to the poor prognosis of both stage IV cancers reported synchronously.

Conclusion: The coexistence of 2 primary different cancers in the same patient is an unusual phenomenon which represents a challenge for the multidisciplinary team that treats the patient. Likewise, the coexistence between melanoma and lung adenocarcinoma is exceptionally reported in the literature, which in advanced phases confers a poor prognosis and few therapeutic options.

KEYWORDS: Melanoma; Lung cancer; synchronous tumors, Metastasis.

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INTRODUCTION

The presence of multiple primary malignant neoplasms is an unusual finding during the diagnostic approach of patients with cancer, since it is reported in the literature mostly in 2% of the cases, but some reports have published it up to a 17%.[1] This clinical condition is subclassified into two groups: synchronous when there is a time frame of less than 6 months between the diagnosis of one tumor and another; and metachronous, when this diagnostic window is longer than 6 months.[2] In a cohort of 1785 patients with multiple solid neoplasms, it was reported that up to 70% of the cases belonged to the group of synchronic neoplasms, reporting that

the most recurrent combination was uterine cancer and ovarian cancer. The coexistence of skin tumors with lung tumors occurred in only 1 patient from this same cohort of 1785 subjects, being 0.05% of the registered cases.[3] The following case has the distinction of being a young adult, which makes the discovery of lung cancer even more exceptional, since it occurs in adults under 35% in only 1.37% of the recorded cases.[4]

CASE DESCRIPTION

We present the case of a 32-year-old male, born in Monterrey, Nuevo León, Mexico, technical career education, occupation: driver, personal history of smoking with a smoking rate of 0.5 pack/year, as well as social alcoholism, denies drug abuse, and he is right-handedness. Prior to his first admission, he denied chronic degenerative diseases, allergies, surgeries, and hospitalizations.

The patient began his current condition in August 2023, describing a progressive weakness of the right upper and lower limb which, over a period of days, made it impossible to walk. Upon his admission to the emergency department, the physical examination revealed symmetrical right hemiparesis 2/5 on the Daniels scale, as well as ipsilateral facial asymmetry, the rest of the examination without relevant findings. The medical team at the moment decided to perform a simple CT scan of the head in order to rule out stroke. In this study, it was evident a frontal lesion without signs of ischemia or hemorrhage. The following study was a contrast-enhanced magnetic resonance study, with suggestive finding of diffuse metastatic tumors associated with vasogenic edema. The patient was evaluated by the Neurosurgery service who decided to perform decompressive Craniectomy and resected the tumoral lesion located in the frontal region with an abdominal subcutaneous bone flap (10/22/23). A sample was sent to pathology, and they reported malignant cells consistent with metastatic melanoma.

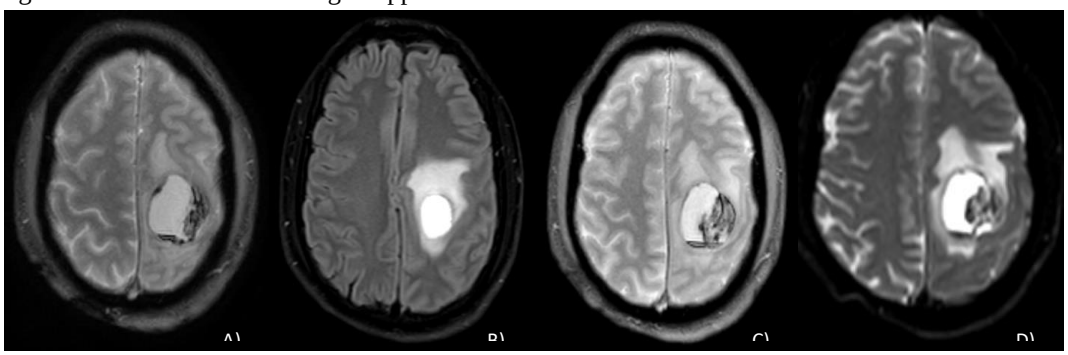

Figure 1. Brain Contrast enhanced MRI: intra-axial lesions, oval, circumscribed at the level of the left precentral gyrus and ipsilateral lingual gyrus, and large cystic portions which show fluid-liquid levels, without diffusion restriction after the administration of intravenous contrast with avid ring enhancement as well as the mural nodules, the largest measuring 44.5 x 41.8 x 36.0 mm. Vasogenic edema that causes compression of the left lateral ventricle and ipsilateral atrium as well as deviation of the midline of up to 4.4 mm. Intra-axial lesions in the left frontal and occipital lobes, highly suggestive brain metastases. A) T1 Weighthed Gadolinium enhanced. B) T2/Flair Weighted Gadolinium enhanced. C) Gradient Echo sequence. D)Diffusion Weighted Imaging.

As part of the diagnostic approach, a thoracoabdominal CT with IV contrast was performed, which revealed another tumor at the lung level in the left lower lobe that obliterates the bronchus, accompanied by a small pleural effusion and subcarinal and paratracheal lymph node conglomerates. The patient underwent a lung biopsy, where pathology reported poorly differentiated adenocarcinoma with angiolymphatic invasion present and extensive necrosis. This study was complemented with an immunophenotype, consistent with primary pulmonary origin, due to the following positive biomarkers: CK7+, TTF-1+, P63+.

Figure 2. Thorax and abdomen CT with IV contrast 04/09/23: irregular mass in the left inferior lobe, irregular borders, with heterogeneous reinforcement after IV contrast. 9.4 cmx8.3 cm axial cut. Left bronchial with obstruction, and small pleural effusion. Mediastinal enlarged lymph nodes. A) Coronal View, chest sequence. B) Axial View, chest sequence.

Afterwards, the patient was hospitalized with a suspected abdominal bone flap infection, and during his approach, a CT scan was requested, with a marked increase in the left pleural effusion reported previously. Therefore, the patient submitted for the infected bone flap removal, and an intrapleural chest tube was placed for drainage, with cytochemical results compatible with paraneoplastic cause without infection. It was completely drained without complications and the patient was discharged home with the palliative care measures due to the poor prognosis of both stage IV cancers reported synchronously.

DISCUSSION

The existence of multiple malignant tumors was reported for the first time in the literature in 1921 and until today, the presence of two neoplasms of different histological strains continues to be considered a rare and lethal clinical condition. This condition is estimated to occur in up to 2-3% of patients with newly diagnosed cancer and has even been observed in 17% of cases during follow-up 20 years after the diagnosis of a primary malignant neoplasm. This has been increasing in recent years due to advances in cancer screening protocols and the great progress in research and technology in Oncology. Still, in most cases, this tends to be an accidental finding.[5]

The most relevant risk factors for the development of multiple malignant tumors are genetic, environmental exposures to carcinogenic substances, and treatment of a preexistent cancer. The following figure displays commonly associated risk factors:

Figure 3. Risk factors associated with multiple malignant tumors.[1]

Factors	Category	Primary tumor	Secondary tumor	Prevention/testing
Virus	HPV	Gynecological	Oral and anal	HPV screening
	SV40	Brain, bone and lymphoma	Mesothelioma	PCR/ELISA
	EBV, HHV-8	Nasopharynges	Lymphoma	PCR/ELISA
	Hepatitis B and C	Hepatocellular		Serology
Exposition	Therapy (Chemotherapy/radiation)	Non-Hodgkin's lymphoma, breast and cervical cancer.	Leukemia, kidney, and bladder	
	Smoking	Lung and gastrointestinal	Lung, gastrointestinal, and genitourinary	Smoking cessation
Genetics	BRCA 1 and 2, PTEN, TP53, CDH1	Non-Hodgkin's lymphoma, breast, cervical and pediatric cancers ovarian cancer, and oral cancer	Gynecological, genitourinary, lung, and breast cancers Ovarian cancer	Genetic testing
	Lynch syndrome (MLH1, MSH2, MSH6, PMS2 or EPCAM genes)	Digestive cancers Breast Colon Breast and ovary	Gastrointestinal, liver, kidney, brain, and skin cancers	Genetic testing
	MEN1, and MEN2	Endocrine, and thyroid Lung	Pancreas, prostate adrenal cortical tumors, carcinoid tumors, facial angiofibroma's,	Genetic testing

			collagenomas, and lipomas	

Figure 3. HPV: Human Papilomavirus, SV40: Simian Virus 40, EBV: Eppstein Barr Virus, HHV: Human Herpes Virus, MEN: Multiple Endocrine Neoplasia.

Melanoma is defined as a malignant tumor that arises from melanocytes, cells that produce the pigment melanin and are mainly found in the skin, eyes, ears, leptomeninges, gastrointestinal tract, and oral, genital, and sinonasal mucous membranes. Its incidence is approximately 25 new cases per 100,000 inhabitants in Europe, 30 cases per 100,000 inhabitants in the USA and 60 cases per 100,000 inhabitants in Australia and New Zealand.[6] Clinically, they tend to be dark, pigmented lesions in different shades of tan, brown and black. However, they can also be the color of the patient's skin or pink (amelanotic), which can make an early detection more difficult.[7] It is estimated that up to 60% of all melanoma patients will develop brain metastases during the progression of melanoma.[8]

The diagnostic approach, should include CT or MRI with IV contrast to identify CNS lesions in patients with a recent diagnosis of melanoma.[8] Treatment options for melanoma brain metastases remain limited, however, neurosurgery is a viable option for patients with single or solitary brain metastasis and for those who desire symptomatic relief.[9] Despite advances in targeted therapy, immunotherapy, and radiation therapy, survival in patients with metastatic melanoma in the central nervous system have a life expectancy less than 9 months.[10]

Whereas our patient, lung cancer has the highest number of deaths related to cancer worldwide. The average diagnosis of non-small cell lung cancer is 70 years, and only between 1-10% of these are diagnosed in people under 40 years of age, with the particularity that 50%-60% already have advanced disease and a poor prognosis.[11] In contrast to the typical presentation in older adults, young adults have a higher incidence in women compared to men, and it is more frequent the adenocarcinoma pathology finding. It has been shown in cohorts that there are genetic mutations in EFGR and ALK associated with an earlier age of presentation of lung cancer, however the main risk factor continues to be the history of smoking and followed by the biomass exposure.[11, 12]

Regarding treatment, the strategy differs compared to the usual management in the elderly. A study conducted at Tokyo Medical University suggests that young adults with lung cancer undergo more aggressive multimodal management, reporting better tolerance and a better prognosis. Although despite such management, survival in stage IV at one year is 50%, 3 years is 8.4% and 5 years is 5.6%.[13] In our patient, we have 2 different late staged malignant tumors with both a poor survival rate, but the one that has the poorest prognosis is the CNS metastatic melanoma.

CONCLUSION

In conclusion, the coexistence of 2 primary different cancers in the same patient is an unusual phenomenon which represents a challenge for the multidisciplinary team that treats the patient. On this occasion, the case presented is exceptional, since lung and skin cancer are reported synchronously in less than 1% of cases, and even more unusual is the fact that they are both in an advanced stage even though this is a young patient, conferring a worse prognosis and few treatment alternatives.

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