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CLINICAL CASE
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CEREBRAL METASTASES IN LUNG CANCER OF NON-SMALL CELLS WITH EGFR MUTATION

METÁSTASIS CEREBRALES EN CÁNCER DE PULMÓN DE CÉLULAS NO PEQUEÑAS CON MUTACIÓN EGFR

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ABSTRACT

Lung cancer is one of the tumors that have the ability to metastasize in the brain and have the ability to penetrate the blood-brain barrier, the clinic is varied depending on the affected site, as well as the associated risks of seizure. Therefore, the choice of treatment is complex, considering the primary, the number of metastases and the affected sites. Radiotherapy has long been the choice of patients who are not candidates for surgery. The presence of mutations have allowed targeted therapies such as tyrosine kinase inhibitors that penetrate the blood-brain barrier and have been key to therapeutic management.

Key words: Lung cancer; Brain metastases; EGFR; Mutation EGFR. (source: MeSH NLM)

RESUMEN

El cáncer de pulmón es uno de los tumores que tienen la capacidad de metastatizarse en el cerebro y tienen la capacidad de penetrar la barrera hematoencefálica, la clínica es variada dependiendo del sitio afectado, así como los riesgos asociados de convulsión. Por lo tanto, la elección del tratamiento es compleja, considerando el primario, el número de metástasis y los sitios afectados. La radioterapia ha sido durante mucho tiempo la elección de los pacientes que no son candidatos a la cirugía, La presencia de mutaciones han permitido brindar terapias dirigidas como los inhibidores tirosin kinasas que penetran la barrera hematoencefálica y han sido clave para el manejo terapéutico.

Palabras clave: Cáncer de pulmón; Metastasis cerebral; EGFR; Mutación EGFR. (fuente: DeCS BIREME)

CLINICAL CASE

INTRODUCTION

Lung cancer is the first cause of death all over the world, both in men and in woman. In Peru it is the fifth neoplasm detected with a prevalence of 6 X 100,000 inhabitants of age average age of 60 years and the prevalence of males 2,074 (67.1%) women 1,015 (32.9%) and their relationship (H / M) 2.5 / 1 where the main risk factor that was found, smoked in 75% of the cases, of which clinical stages stage I 3.5%, stage II 4.4%, stage III 32.4% and stage IV 59.7%.

(Source: Cancer Registry of Metropolitan Lima Research Inst. Maes Heller. INEN-2013).

Lung cancer can be classified as non-cellular Small NSCLC and small cells (SCLC). As the histological point of view we find a variety among which adenocarcinoma predominates. The NSCLC represents approximately 85 % of lung cancers, and the rest as small cell lung cancer SCLC[(1)]. The NSCLC carrier patients with histology adenocarcinoma have molecular mutations: Activation of the mutation in the factor receptor of epidermal growth (EGFR) that occurs in non-smoking patients, female and of Asian ethnicity. The presence of the fusion oncogene anaplastic lymphoma kinase (ALK) that are more frequent in non-smokers or ex-smokers and produces at a younger age. There are other less frequent mutations such as BRAF, HER2, β-catenin, DDR2 and MEK. The expression of the tumor PD-L1 predicts response to certain immunotherapies and can guide the choice of treatment both in the

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first-line treatment as in the line subsequent[2,3]. Brain metastases are a common complication in a wide range of cancers, but they are particularly common among patients with lung cancer. Patients with metastases brain, lung cancer is the primary tumor in 40 to 50 % of cases and approximately 10 % of newly diagnosed patients with advanced NSCLC cancer have brain metastases[3,4].

Brain metastases are a cause common morbidity and mortality in patients with NSCLC. Patients with EGFR mutation have a better prognosis due to survival prolonged use of targeted systemic agents[5]. In 2016 a study revealed that the median overall survival (OS) of a carrier population of NSCLC with brain metastasis that was divided into 2 groups: EGFR- not mutated and one EGFR mutated, ranged from 3 to 15 months[6]. OS in patients with NSCLC and brain metastasis and mutated EGFR is observed that it ranges from 19-58 months[7,8]. However, the previously published studies describing the use combined therapy of Cisplatin and Pemetrexed they present good tolerability[9,10]. During the last decade, EGFR-tyrosine kinase inhibitors (TKI) have been used successfully in patients with NSCLC based on identification of mutations of the EGFR gene[11,12].

Other studies showed that combination of RT and EGFR-TKI produced results superiors for patients with metastatic NSCLC brain and EGFR mutations[13,14].

CASE REPORT

54 year old female patient, born in Huancayo, coming from Lima and go to

emergency of the Central Military Hospital on september 12, 2015 with a time of one month disease characterized for tonic-clonic seizures. Personal and family history: Exposure to firewood for more than 20 years. Denies allergy to medications. Surgical history: Cholecystectomized 14 years ago.

Physical Exam: ECOG 3-4. Skin and mucous membranes: paleness + / +++, jaundice (-), dry mucous membranes ++ / +++, no edema. Bloated fascies. Cardiopulmonary auscultation: Vesicular murmur passes well through both hemithorax; no added noises. Abdomen: water noises (+), soft, depressible, no masses, no visceromegaly. Genitourinary: Lumbar percussion fist (-) no hematuria, no dysuria, no bladder balloon. Neurological: disoriented with a tendency to sleep and walk unstable.

AUXILIARY TEST:

• Tumor Markers:

MARKERS	14/09/15	15/03/16	21/06/216	25/08/16	22/11/16	23/2/17	23/05/17
CEA	81.6	4.9	1.9	1.9	2.9	7.9	38.2
CA125	83.8	-	-	-	-	-	-

Images:

- **BRAIN MST (09/12/15):** Intracerebral aspect formations nodules associated with edema perilesional vasogenic located in the left frontoparietal region and right occipital. The last of they 25mm.
- **BRAIN MNR (09/14/15):** Three focal lesions. Two of them of cortico-subcortical location involving the right occipital lobe and the left parietal lobe and a third, that it involves the left lenticular nucleus. Injury larger located in the occipital lobe right shows intense enhancement and is associated with edema perilesional vasogenic. The other two, show area necrotic in appearance.
- **THORAX MST (09/18/15):** Solid mass with an proliferative of irregular appearance into right segment 10 of 37mm x 29mm. Mediastinal and axillaries nodes up to 8mm.

MEDICAL PROCEDURE:

• PULMONARY NODULE BIOPSY (11/5/15):

PA: Lung parenchyma infiltrated by nests ofmalignant of glandular epithelial neoplasm appearance with areas of necrosis. IHC: TTF-1: (+) NAPSIN: (+) CYTOKERATIN 7: (+) PRIMARY

ADENOCARCINOMA PULMONARY.

Mutation is made: EGFR EXON 19 (+)

DIAGNOSIS DX: LUNG CANCER CLINICAL STAGE IV FOR BRAIN METASTASIS

TREATMENT:

HOLOCRANIAL RADIOTHERAPY for intracranial hypertension syndrome.

10 SESSIONS 300cGY total dose: 3000cGY from (12/2/15 to 12/15/15).

Start treatment with ITK 12/2015 at doses of 150 mg. / day from ERLONITIB.

10 SESSIONS 300cGY total dose: 3000cGY from (12/2/15 to 12/15/15)

Start of treatment with ITK December 2015 at a dose of 150 mg. / day of ERLONITIB.

INTERCURRENCES:

03/15/16: temporarily suspends treatment ITK for presenting herpes zoster. 03/22/16 resume ITK.

FIRST REEVALUATION OF DISEASE:

THORAX / ABDOMEN / PELVIS MST (04/09/16) (-) NEOPLASIA.

BRAIN NMR: Focal lesions with small peripheral edema in size on the left lenticular nucleus and frontal cortex of the same side, others greater size in the right side occipital lobe.

DIAGNOSIS: PARTIAL RESPONSE.

TREATMENT:

He continues treatment with ITK ERLOTINIB 150 mg / day.

SECOND REEVALUTION OF DISEASE:

THORAX MST (11/11/16): In the central portion between the right segment 7 and 9, 13 and 16 mm solid nodular image.

MST ABDOMEN / PELVIS: (-) NEOPLASIA

BRAIN MRI 11/14/16: In the right medial or sagittal lobe area, two images that decrease the cortical volume, dependent on surrounding edema to two small lesions that stand out in the periphery of 8 mm the largest.

DIAGNOSIS: PARTIAL RESPONSE

3.- TREATMENT:

Continuous treatment with ITK ERLOTINIB 150 mg. / day.

THIRD REEVALUATION OF DISEASE:

MST TORAX 02/19/17: apical segment lung mass LID measuring 42mm x 37mm x 36mm in defined borders of sub pleural location.

DIAGNOSIS RESPONSE: PROGRESSION OF DISEASE.

4.- TREATMENT:

External radiation therapy to the right lung at anterior and posterior field.

16 SESSIONS 250cGY total dose: 4000cGY from (02/28/17 to 03/27/17)

INTERCURRENCES:

Radiodermatitis VS contact dermatitis, both controlled by dermatology.

Hospitalization (05/02/17): headache, hemiparesis of left side and asthenia.

FOURTH REEVALUATION OF DISEASE:

MST THORAX (05/05/17): Posterior basal segment of the LID solid irregular nodulation of 21x22x 20 mm. Irregular edges, remain unaltered.

MST ABDOMEN / PELVIS: (-) NEOPLASIA

BRAIN MNR (05/06/17): Occipital lesion 25x28x 24 mm right. Extensive areas are associated with altered perilesional signal of distribution subcortical with midline displacement 15 mm and decreased ventricular volume right.

DIAGNOSIS RESPONSE: PROGRESSION OF BRAIN DISEASE - SINGLE INJURY.

5.- TREATMENT:

Continuous treatment with ITK ERLOTINIB 150 mg. / day. Initiation of Radiotherapy re-irradiation of single lesion. Radiotherapy 12 sessions from June 16/2017 - June 30/2017.

CONCLUSION

Brain metastases is a common complication in lung cancer. For patients with NSCLC, with brain metastasis without mass effect or risk of herniation at the brain level and has a mutation EGFR positive, targeted therapies should be initiated with ITK. In the case that was presented, there is evidence that resistance to TKI (erlotinib), this patient developed both intracranial and extracranial progression where a biopsy was requested from the most accessible (for extra-medical reasons it was not carried out). The therapeutic recommendation is to start osimertinib already that has achieved higher intracranial concentrations and has been shown to have intracranial activity significant against brain metastases at standard dose of 80 mg daily, even against leptomeningeal carcinomatosis and those with a resistance mutation T790M.

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