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PARA-NEOPLASTIC LIMBIC ENCEPHALITIS EDIFYING A SMALL CELL CARCINOMA OF THE LUNG – TWO CASE STUDIES

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Abstract :

Paraneoplastic encephalitis that is limbic a rare condition, often related to small cellular lung cancer.

Case report: We report in this book the cases with various age brackets, which presented with various signs which can be neurological as repetitive seizures or anterograde amnesia. Cerebral CT-scan, cerebral MRI and anti onco-neural paraneoplastic antibodies were suggesting the diagnosis of paraneoplastic encephalitis that is limbic.

Etiological exploration triggers the diagnosis of locally advanced cell that is little of this lung. We began rapidly a curative protocol associating chemotherapy and sequential radiotherapy that is thoracic.

We insist on the variety of the imaging findings, immunological analyses and conclude on therapy of this entity. Prognostic impact remains also uncertain.

Keywords: *Paraneoplastic: Limbic encephalitis; Small cell carcinoma; Antibodies; MRI*

Abbreviations

MRI	Magnetic Resonance Imaging
CT-scan	Computer Tomography Scan
LE	Limbic Encephalitis
MoCA	Montreal Cognitive Assessment
PNS	Paraneoplastic Neurological Syndromes
CSF	Cerebro-Spinal Fluid
GABA	Gamma-Aminobutyric Acid Receptor
VGCC	Voltage Gated Calcium Channels
VGKC	Voltage Gated Potassium Channels

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INTRODUCTION:

LE (Paraneoplastic limbic encephalitis) is a scarce neurologic syndrome which is complicated to identify. This entity is clinically classified by a cognitive disorder, amnesia, humor troubles, psychiatric signs or seizures. It is characterized in patients exhibiting with lung cancer (50%), genital cancer (20%) and breast cancer (8%). To be accredited as paraneopastic, prognosis of the underlying neoplasia should imperatively be accomplished within just a four year period (Bolster et al., 2015). While there is presently no well-established cures for LE, therapeutic administration of the malignant tumor is the first choice if no metastases were discover. Symptomatic treatment consists of corticosteroids which are the most usually used, followed by high-dose immunoglobulins. We describe two cases of paraneoplastic LE related with small-cell lung carcinoma in two male patients with different ages (Alamowitch, 2016).

Case 1

A male person with 53 years of age, working as a taxi driver, active smoker, and hypertensive for ten years, introduced to the emergency department with a condition epilepticus with generalized tonicoclonic seizures linked with anterograde amnesia. The patient has been smoking for thirty years at a rate of 10 cigarettes per day. Neurological evaluation discovered a bradypsychia, with preserved motricity and sensitivity. The personal examination of cognitive function via the Montreal Cognitive Assessment (MoCA) score was 21/30. The brain scan revealed a right para-sagittal meningioma of the superior sagittal sinus, determining 8 mm. Lumbar puncture and the electroencephalogram were normal. Cerebral MRI with T1, T2 and FLAIR sequences displayed no abnormalities (Figures 1a and 1b) (BOWYER et al., 2016).

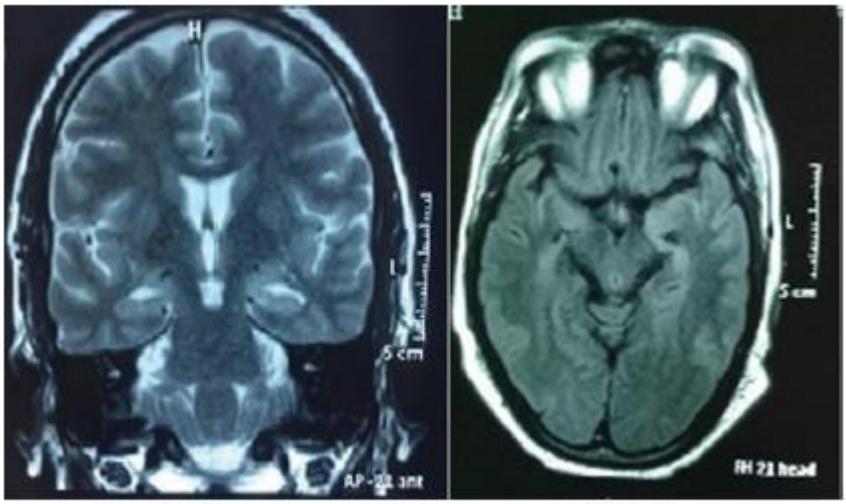

Figure 1a Figure 1b

Figure 1: Cerebral MRI (T2 + FLAIR) shows no abnormal signal within the limbic regions.

Source: (BOWYER et al., 2016)

An immunological test for anti-neuronal antibodies showed the presence of anti-Hu antibodies, anti-SOX 1 antibody and anti-GABAr B1/ B2 antibodies (Table 1).

Antibodies	Results	Antibodies	Results
Anti Cv2	-	Anti Titin	-
Anti PNMA	-	Anti Amphiphysin	-
Anti Ri	-	Anti AMPA1/AMPA2	-
Anti Yo	-	Anti CASPR2	-
Anti Hu	+	Anti LG11	-
Anti Recoverin	-	Anti GABAr B1/B2	++
Anti SOX1	++		

Table 1: Serum immunoassay for anti-onco-neuronal and anti- membrane antibodies.

(Source: (M et al., 2018)

Chest X-ray revealed retro-cardiac opacity with erratic limitations. Bronchial fibroscopy demonstrated a budding placement entirely hindering the left lower lobe. Bronchial biopsies determined to a small cell carcinoma. The body scan objectified a tumor mass obstructing the left lower lobe with left hilar and sub carinal adenomegalies, and a dubious retro-esophageal lymph node. The tumor would be categorized T2bN3M0. By using clinical, biological and radiological data, we built the analysis: paraneoplastic limbic encephalitis exposing a locally complex small cell carcinoma of the lung. Chemotherapy linking carboplatin and Etoposide was established quickly. Anticonvulsant therapy was also administered: A blend of oral corticosteroid (prednisone 40 mg/day), phenobarbital 50 mg three times daily and levetiracetam 500 mg in the morning and 1000 mg at night. Regardless of the treatment, the patient had a seizure every two weeks (Chan, Rangaswamy and Peng, 2017).

The onset of chemotherapy had a constructive effect with disappearance of the seizures. Throughout chemotherapy sessions, the patient was still bradypsychic but with a more maintained memory. The MoCA score was 25/30. After 4 cycles of chemotherapy based on carboplatin and etoposide, we noted a stability of the tumor. Therefore, consecutive thoracic radiotherapy was recommended (M et al., 2018).

Case Two

A 73 years old man, earlier smoker, was admitted to pulmonology department for investigation of a continual dry cough. The patient has been smoking for 42 years at a rate of 10 to 20 cigarettes a day. He had past medical background of a remedied gastric ulcer. He was whining of increasingly promising cough with retrosternal burn sensation. His family members signaled anterograde amnesia with neither humor difficulty nor suicidal tendency. Physical evaluation revealed a normal cardio-pulmonary status, normal sensitivity and motricity. Chest X-ray unveiled a right hilar opacity with presumed margins. Bronchial fibroscopy revealed a budding enhancement mostly preventing the right upper lobar bronchus. Bronchial biopsies determined to small cell carcinoma. The thoracic CT scan objectified a tissue mass stretching from the hilus to the right upper lobe, computing 59 mm of diameter, linked with sub-pleural speculated nodules of the right lower lobe, mediastinal lymph nodes in the zones 4R, 7 and 10 (Figure 2) (M et al., 2018).

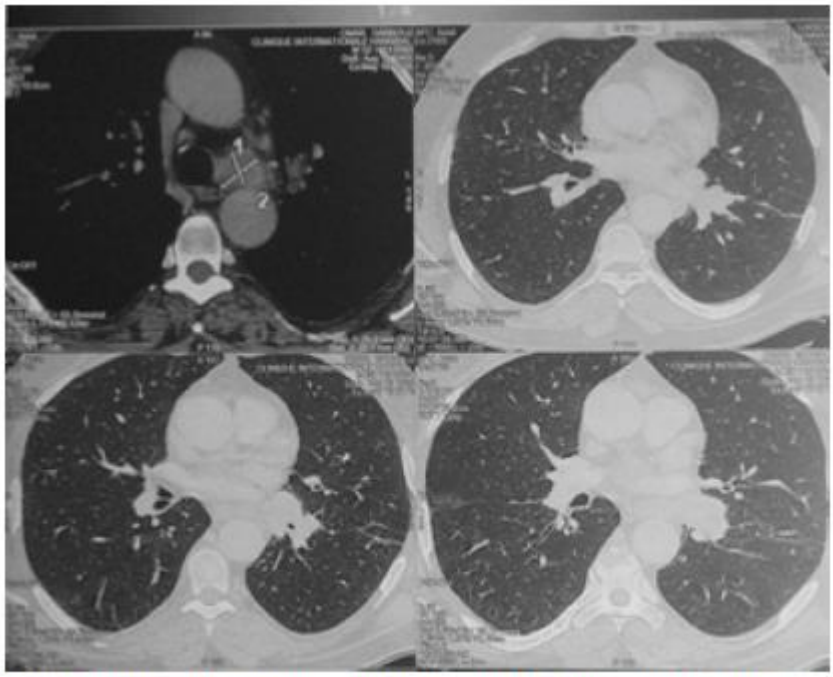

Figure 2: Thoracic CT shows a tumor mass that obstructs the left lower lobe bronchus with left hilar and sub-carinal adenomegalies.

(Source: (M et al., 2018)
Cerebral MRI revealed bilateral high signal intensity on T2-weighted and FLAIR image in the hippocampus (Figures 3a and 3b).

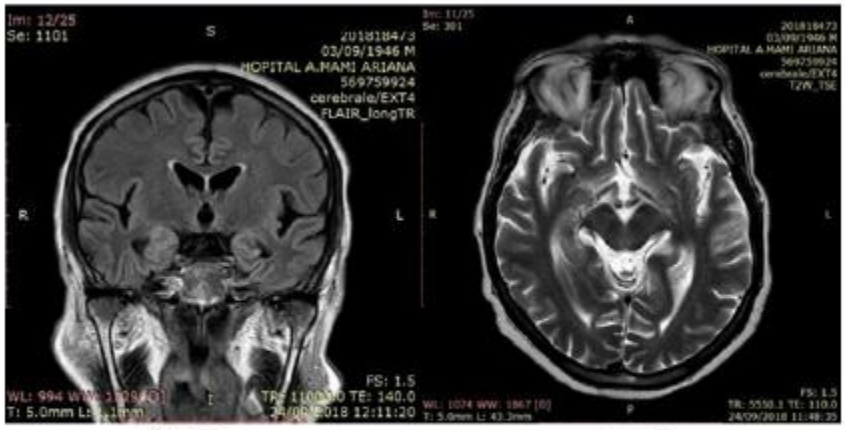

Figure 3a Figure 3b

Figure 3: Cerebral MRI revealing bilateral high signal intensity on T2-weighted and FLAIR image in the hippocampus.

Source: (M et al., 2018)

We determined on paraneoplastic limbic encephalitis. The tumor was organized T4N3M0 according to the 8th edition of TNM classification. No treatment was specifically suggested for the encephalitis. Four cycles of chemotherapy comprising carboplatin and etoposide, then sequential thoracic radiotherapy was proposed (M et al., 2018).

DISCUSSION:

Paraneoplastic neurological syndromes (PNS) are

uncommon neurological disorders related with cancer that are not clarified by a metastatic, metabolic, irresistible, lack or iatrogenic reason. The pathogenesis of this condition isn't totally seen, yet the doubtlessly theory is that of an invulnerable reaction coordinated against the antigens communicated by the sensory system cells like the tumor antigens, bringing about neuronal misfortune with lymphocyte penetration of perivascular and microglial cells. The nearness of circling serum autoantibodies or anomalous cerebrospinal liquid (CSF), explicitly connected with PNS is one of the signs of these disorders (M et al., 2018).

They are found in over 80% of patients with a PNS. Contingent upon the objective of the antibodies found, there are two kinds of PNS. There are intracellular targets (anti-neuronal) and layer targets. Very much described anti-neuronal antibodies, for example, anti-Hu, anti-Ri, anti-Yo, anti-Ma/Ta, anti-amphiphysin, anti-Sox1 and anti-CV-2 are genuine markers of malignancy, by and large little cell lung disease, bosom, ovarian or testicular malignant growth. Clinical information and the explicitness of the anti-neuronal antibodies direct the oncological evaluation. The best portrayed layer targets are ionotropic glutamate receptors: N-Methyl D-Aspartate Receptor (NMDAr) or Gamma-Aminobutyric Acid Receptor (GABAr), either particle channels, for example, voltage-gated calcium channels (VGCC) or voltage-gated potassium channels (VGKC). The clinical introductions differ from case to case. The beginning is for the most part sub-intense. In 65% of cases, paraneoplastic neurological contribution goes before the revelation of malignant growth for a while or years (M et al., 2018).

Immune system encephalitis is a standout amongst the most well-known PNS, including predominantly the limbic framework however may likewise include other additional limbic structures. The term immune system encephalitis is liked to LE which is excessively prohibitive. Neurological side effects shift from anterograde memory issue, disarray to dementia and convulsive seizures that may go before the subjective debilitation for a while (fleeting, psychomotor impedance, summed up tonic-clonic seizures). Changes of conduct, identity and mental side effects (touchiness, nervousness, wretchedness, mind flights and aboulia) are additionally depicted. Rest issue (hypersomnia or sleep deprivation, narcolepsy, cataplexy), weight change alongside unsettling influence of the impression of satiety can be found. Further tests are important to make the determination yet in addition to discount the differential findings (irresistible reason, lack, metastatic). The investigation of the cerebrospinal liquid adds to the conclusion by demonstrating the nonattendance of harmful cells (Murata et al., 2016).

Cerebral MRI represents no metastatic lesion. The electroencephalogram demonstrates an undefined feature of epileptic activities in the temporal lobes in 50% of cases. MRI also an important role player while diagnosis a significant position in diagnosis by detecting single or bilateral (60%) amygdalo-hippocampal signal abnormalities. Typically, imaging shows a high-intensity signal on T2-weighting sequences, more visible on the FLAIR and on the diffusion sequences. T1-weighting sequences may show a hyposignal or isosignal with temporal atrophy at a later stage. Augmentation after gadolinium injection can be seen in 15 to 20% of affected cases. MRI may be initially normal, as described in the case study one, therefore the significance of imaging follow-up. FDG-PET scan is productive when the EEG and MRI demonstrate no abnormalities. It represents a hyper-metabolism of the temporal lobes, midbrain, and cerebellum or frontotemporal lobes, indicating an acute phase of the inflammatory process. The existence of anti-neuronal anti-GABAr B1 antibodies is redolent of small cell cancer. The occurrence of anti-Hu antibodies is associated in 94% of cases with small-cell lung carcinoma (Rosenfeld and Dalmau, 2016).

Alamowitch et al. (2015) discovered anti-Hu antibodies in half of patients with limbic encephalitis related with little cell lung carcinoma. Anti-SOX1 antibodies are found in the Lambert-Eaton myasthenic disorder and less as often as possible in patients with anti-Hu disorder or little cell lung carcinoma without neurological indications. GABAr B antibody assay examination ought to be focused in all patients with LE with or without related little cell carcinoma, and in instances of cerebellar dysfunction and opsoclonus-myoclonus without other distinguished antibodies (Rosenfeld and Dalmau, 2016).

The development and prognosis of paraneoplastic LE relies upon the idea of the essential tumor and its treatment. The closeness of anti-neuronal antibodies is regularly connected with poor neurological utilitarian prognosis in spite of the proposed therapeutically arsenal. It is a present thinking regarding that the treatment of the tumor is the just a single ready to balance out the advancement by smothering the antigenic incitement. Within the sight of an antibody membrane, medications focusing on humoral immunity (immunoglobulin IV,

plasmapheresis, and anti-CD20) can be proposed and additionally procedural corticosteroids. Notwithstanding, no remedial convention could be approved by a randomized managed examination in view of the modest number of patients concerned (Rosenfeld and Dalmau, 2016).

CONCLUSION:

The revealed cases feature the decent variety of paraneoplastic disorders, which can be the primary indication of a harmful tumor. The literature review affirms the vital significance of the counter tumor invulnerable reaction that can produce brief or permanent dysimmunitary or endocrine issue. The unpredictability of the pathophysiology clarifies the trouble of treatment. It is likewise hard to depict prescient components of reaction of paraneoplastic neurological signs to the proposed treatments, aside from relapse of the tumor. Tumor control remains superb option.

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