

# Limbic Encephalitis Driven by a Pleural Mesothelioma: A Paraneoplastic Complication

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## Abstract

Paraneoplastic neurological syndromes have only been described with pleural mesothelioma in five cases. We have described a 72-year-old man who developed anterograde amnesia 27 months after diagnosis of epithelioid pleural mesothelioma. Investigations revealed a limbic encephalitis with no alternative causes identified. Limbic encephalitis is a classical paraneoplastic syndrome and presentation within five years of a cancer with no other causes identified is sufficient to diagnose a paraneoplastic etiology. This is the first case of isolated paraneoplastic limbic encephalitis driven by a pleural mesothelioma.

**Keywords:** Mesothelioma, Paraneoplastic syndromes, Limbic encephalitis

## Introduction

Limbic encephalitis (LE) refers to inflammation of the limbic system which causes characteristic symptoms such as short term memory loss, confusion, seizures, and psychiatric symptoms.<sup>1</sup> It has a number of causes such as viral, vasculitic, and autoimmune.<sup>2</sup> Paraneoplastic limbic encephalitis (PLE) refers to an autoimmune LE that is the result of the presence of a tumor but not due to direct invasion or metastases. The most frequently implicated underlying tumor is small cell lung cancer but other cancers include non-small cell lung, testicular,

and breast cancers.<sup>3,4</sup> To the best of our knowledge, mesothelioma has been previously implicated in paraneoplastic neurological diseases in only five cases. None describe an isolated LE syndrome.<sup>4-8</sup> We discuss the case of a man with mesothelioma who presented subacutely with a pure amnesic syndrome, likely from a paraneoplastic cause.

## Case Report

A 72-year-old man with a history of pleural mesothelioma of the epithelioid type was referred to the Memory Clinic following a 2-3 week profound decline in memory which

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then stabilized. His wife noticed that he was repeatedly discussing the same familiar topics and could only retain memories for a few minutes. There was no preceding infectious prodrome, associated seizures, or psychiatric symptoms. He was found to have a predominantly anterograde amnesia with an otherwise normal neurological examination. Addenbrooke's Cognitive Examination-Revised score was 77/100 with the majority of marks lost in the memory domain (13/26, with 0/7 in delayed recall). Routine blood tests that included serum neuronal antibodies (Hu, Ri, Yo, Ma1, Ma2, CV2/CRMP5, amphiphysin, Sox-1, Zic4, Tr, VGKC, NMDA receptor, GAD, Purkinje cell) were normal. Cerebrospinal fluid (CSF) analysis revealed 3 lymphocytes/mm<sup>3</sup>, a mildly elevated protein level (0.53 g/L), and paired oligoclonal bands in the CSF and serum. An MRI of his head showed focal symmetrical high signal in the anterior and medial temporal lobes that predominantly involved the white matter (Figure 1).

This confirmed the diagnosis of LE. He received empirical immunotherapy – initially a high dose of steroids followed by intravenous immunoglobulin (IVIg) against a presumed paraneoplastic etiology which had no effect on his memory. He has remained clinically stable with neither improvement nor further decline in his neurological status. He requires more frequent pleural aspirations for control of his malignant effusion but is no longer a candidate for indwelling pleural catheter given his cognitive impairment.

## Discussion

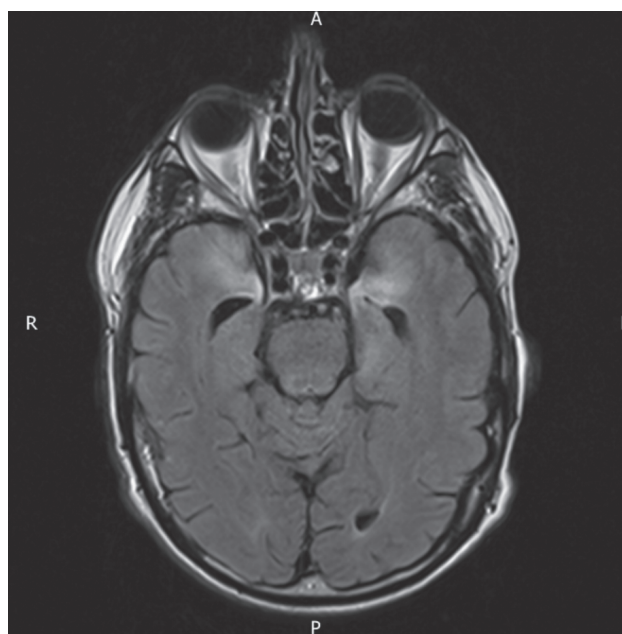
According to the Graus criteria, the presence of a tumor within five years of development of a classical paraneoplastic syndrome is sufficient to define a definite paraneoplastic syndrome, even in the absence of neuronal antibodies.<sup>1</sup> Limbic encephalitis is a classical paraneoplastic syndrome which our patient developed two years after diagnosis of his mesothelioma and thus fulfils these criteria. Other causes of LE include infections, vasculitis, and non-paraneoplastic autoimmune LE. Our patient's clinical course

was most suggestive of an autoimmune cause. There was no evidence of alternative explanations on CSF or MRI analyses. The presence of a malignancy makes a paraneoplastic cause most likely. There was no evidence of alternative tumors on CT thorax-abdomen-pelvis imaging. The lack of response to immunotherapy is not unusual in paraneoplastic LE.<sup>9</sup>

Mesothelioma rarely causes paraneoplastic neurological syndromes; there are only five previous cases reported. Two of these described paraneoplastic cerebellar degeneration,<sup>4,7</sup> one reported opsoclonus and cerebellar signs<sup>5</sup> and another showed a biphasic pattern of LE followed by sub-acute myeloroicopathy.<sup>6</sup> The final case described sensorimotor peripheral neuropathy.<sup>8</sup> No previous cases reported an isolated LE.

## Conclusion

We describe a patient with a paraneoplastic LE driven by a pleural mesothelioma. This is the first case that describes an isolated LE in association with mesothelioma, which broadens both the clinical spectrum of paraneoplastic LE and the complications of pleural mesothelioma.



**Figure 1.** T2/FLAIR MRI image that shows focal symmetrical high signal in the anterior and medial temporal lobes.

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## Conflict of interest

No conflict of interest is declared.

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