Narcolepsy associated with primary temporal lobe B-cells lymphoma in a HLA DR2 negative subject

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Abstract
Narcolepsy and cataplexy began one year before treatment of a left mid-temporal primary B-cells lymphoma in a HLA DR2 negative man. Treatment with radiotherapy and immunosuppression induced regression of the lymphoma and disappearance of narcolepsy and cataplexy.

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Symptomatic or secondary narcolepsy has been described in a number of diseases involving immune system or in CNS diseases such as Multiple Sclerosis head trauma, hypoxic ischaemia and tumours of the midbrain and diencephalon. A recent review, however, suggests that there is no unequivocal association of narcolepsy with other disorders and that some cases of so-called secondary narcolepsy-cataplexy may be examples of the association of separate disorders rather than causally related.

The major element prompting the redifinition of secondary narcolepsy was the finding of very high (99%) narcolepsy association with HLA DR2-DQw1 haplotypes in idiopathic and secondary cases: only a few white and black DR2 negative patients have been found.

We describe a patient affected by "unequivocal" (according to the criteria suggested by the Association of Sleep Disorders Centers) narcolepsy-cataplexy that was secondary to a CNS B-cells lymphoma.

Case report
The patient, a 30 year old white male, presented to us approximately one year after the onset of excessive daytime sleepiness (EDS) and uncontrollable daytime sleep attacks, lasting from 5 to 10 minutes, preceded by a dramatic abolition of voluntary movement. Such attacks interfered with his daily activities and on one occasion caused a minor driving accident.

In the preceding year his friends had noticed that he was often "dozing-off" and only the complaints of his fiancée forced him to visit our out-patient unit. He sometimes fell to the ground or, if sitting, felt his head dropping without loss of consciousness particularly during exciting or unpleasant situations. The patient was alert and orientated and the neurological examination was normal. Three sets of nocturnal EEGs revealed that "sleep" was spent as follows: 6% wake, 4% stage 1, 46% stage 2, 24% stage 3, 4 and 20% REM sleep. REM sleep latency was 3-5 minutes. MSLT was carried out in our sleep laboratory after a quiet night’s sleep, by means of a polygraph recording EEG, EOG, EMG, ECG and nasal airflow. We recorded 5 scheduled nap periods starting 2 hours after awakening from sleep-onset REM (SOREM) Period. Note the sudden appearance from the stage of wake of a low voltage, fast EEG activity accompanied by Rapid Eye Movements, depression of muscular tone at the EMG and mild increase in heart and respiratory frequency (REM sleep). The monitoring of airflow by nasal thermistors shows no abnormality of breathing and excludes the presence of sleep apneas. Vertical calibration is 50 μV for EEG, 100 μV for eye movements, 300 μV for EMG and EKG.

Figure 1: Polygraph recording, performed one year before the appearance of CNS lymphoma, showing a sleep-onset REM (SOREM) Period. Note the sudden appearance from the stage of wake of a low voltage, fast EEG activity accompanied by Rapid Eye Movements, depression of muscular tone at the EMG and mild increase in heart and respiratory frequency (REM sleep). The monitoring of airflow by nasal thermistors shows no abnormality of breathing and excludes the presence of sleep apneas. Vertical calibration is 50 μV for EEG, 100 μV for eye movements, 300 μV for EMG and EKG.
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7 Guilleminault C. HLA-DR2 and narcolepsy: not all narcoleptic-cataplectic patients are DR2. Human Immunol 1986;17:1-2.

Discussion

After the critical reviews by Bonduelle and Degos and Parkes secondary narcolepsy is considered a rare or dubious clinical entity. To our knowledge there are no other reports describing narcolepsy in CNS lymphoma. The course of the disease had furthermore at least three peculiarities differentiating this patient from others reported in the literature: 1) Narcolepsy preceded by one year the appearance of the left mid temporal lobe lymphoma; 2) Narcolepsy disappeared when radiation therapy induced regression of the lymphoma; 3) the patient haplotype was DR2, DQw1 negative.

The typical history of primary brain lymphoma is known to be characterised by behavioural and personality changes or focal neurological signs that precede by several months symptoms due to increased intracranial pressure. We proposed that the unusual clinical picture we describe was due to a focal infiltration of lymphomatous cells in the basal forebrain, in particular the hypothalamus and the area of the third ventricle, which are involved in the regulation of sleep-wake cycle and REM sleep. Immunotherapy and/or radiotherapy may have suppressed the infiltrating lymphomatous cells.