To the Editor

Paraneoplastic Anti-HU Syndrome Associated with Uterine Tumor

The spectrum of neurological manifestations described with anti-Hu antibodies (anti-neuronal nuclear antibody type 1) is vast. The most frequent paraneoplastic syndromes with anti-Hu are subacute sensory neuronopathy, limbic encephalitis and paraneoplastic cerebellar degeneration[1]. Anti-HU paraneoplastic syndrome is most frequently associated with small cell lung carcinoma[1]. There are only two cases in the literature describing patients with anti-Hu Ab and gynaecological tumors (a cervix and a uterine tumor).[2,3] We thus want here to present a third case supporting this association.

Case Report

Initial presentation

A 54-year-old woman presented at the emergency room, in February 2009, for *de novo* partial complex seizure with secondary generalisation. She also had a one-month history of right hearing impairment, vertigo and right facial numbness, superimposed to a three-week complaint of cognitive slowing and memory loss. Moreover, she reported pain and paresis of the left arm progressing over the last few days before presentation, along with progressive visual blurring and involuntary loss of several pounds in weight over a few months.

Examination revealed impaired memory with relative sparing of other cognitive spheres, bilateral acute Adie's pupils, severe right sensorineural deafness and vestibular deficit and finally proximal paresis of the left upper extremity (MRC 4/5 for deltoid, 3/5 for biceps, 4/5 wrist extensors) with diminished left bicipital reflex. Right upper extremity and lower extremities strength were normal at that time.

Initial investigations demonstrated abnormal cerebral magnetic resonance imaging (MRI), which showed increased T2/FLAIR signal in the left lateral neocortical temporal region (Figure 1A). Electro-encephalographic recordings displayed periodic lateralized epileptiform discharges (PLEDs) in the left fronto-temporal region. Lumbar puncture results were unremarkable. Screening for a paraneoplastic etiology, abdominal computed tomogram (CT) scan was consistent with a high grade malignant uterine tumor, with FDG-PET scan revealed uterine captation suggestive of neoplastic mass without any other foci of hypermetabolism. Nerve conduction studies were normal. There was chronic denervation in the left biceps and brachioradialis, with unremarkable cervical MRI.

Exhaustive laboratory workup displayed nothing relevant except for positive anti-Hu antibodies in the blood.

Treatment and evolution

Two months after presentation, the entire tumor was surgically removed. Pathology showed a high grade malignant uterine tumor, with unspecified histological type, either high grade sarcoma versus mixed müllerian tumor. This prompted preventive radiotherapy and curietherapy.

Unfortunately, despite curative treatment of the tumor, weakness continued to progress temporarily after surgery in both her proximal upper extremities (MRC 0/5 for deltoids and biceps, MRC 1/5 for wrists extension) essentially evolving into a man-in-the-barrel syndrome. Both bicipital, styloradial and left tricipital reflexes were abolished. Lower extremities' strength and reflexes remained normal.

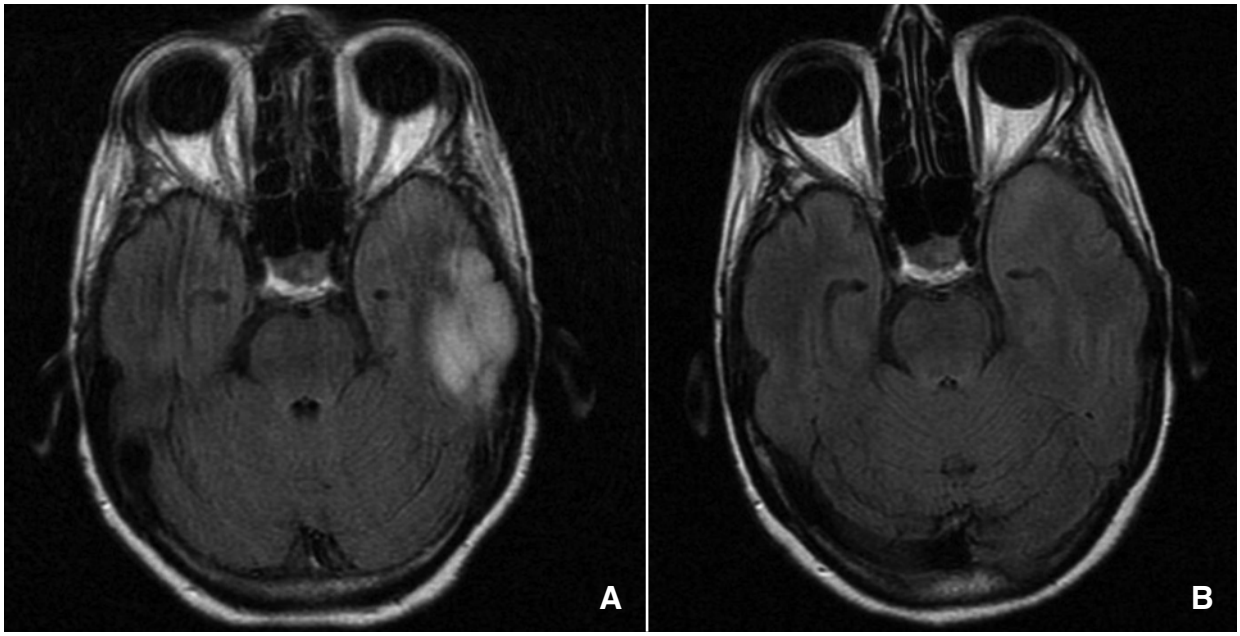

Figure: *A) Head MRI without contrast. In axial FLAIR, cortical and subcortical hyperintensity are seen in the left lateral temporal region. B) Repeat head MRI without contrast five months later. Axial FLAIR, showing complete resolution of the cortical and subcortical hyperintensity in the left lateral temporal region.*

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One month after surgery, intravenous immunoglobulin was given biweekly for eight weeks, without clinical improvement, and five months after surgery, seven plasma exchanges were tried, again without clinical improvement. At this point, a second EMG showed severe chronic denervation in C5-C6-C7 territories bilaterally symmetric. The abnormal MRI signal in the left temporal region completely regressed (Figure 1B).

She had a complex partial seizure despite phenytoin. Last EEG showed left subcontinous slow activity with occasional fronto-centro-temporal sharp waves without PLEDs.

Anti-Hu Ab remained positive seven months after tumor removal.

Mild motor improvement was seen two years after the initial presentation, along with no tumor recurrence.

Discussion

According to the criteria published by the "Paraneoplastic Neurological Syndrome Euronetwork"[4], this case qualifies as a definite paraneoplastic neurological syndrome. The patient had a non classical neurological syndrome with well characterised onconeural Ab and a cancer that was found within few months of the neurological disorder.

The patient had some characteristic clinical manifestations described with anti-Hu syndrome, as limbic encephalitis[5]. She also had rarer features of the syndrome. Bilateral tonic pupils have been described in association with anti-Hu Ab, but seem relatively rare. Unilateral presentation is more common. Autonomic failure at large, including abnormal pupillary responses, has been described in 28% of patients, but the prevalence varies between different series[5]. Our patient had a man-in-the-barrel syndrome attributable to her paraneoplastic syndrome. Lower motor neuron involvement, with progressive proximal upper arm weakness spreading distally, has been reported in 14 % of patients with anti-Hu Ab[5].

There is one case in the literature of a malignant mixed müllerian tumor (carcinosarcoma) associated with anti-Hu paraneoplastic sensory neuronopathy[2] resistant to pharmacological and surgical treatments, with another case of cervical cancer with anti-Hu Ab, cerebellar ataxia and sensory neuropathy having been reported[3].

This case exemplifies once again that the spectrum of cancers associated with anti-Hu can be enlarged to include gynaecological tumors.

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To the Editor

Spontaneous Occlusion of the Temporal AVM Associated With Tinnitus

Arteriovenous malformations (AVMs) of the brain were traditionally considered congenital abnormalities. However, there have been a fair number of case reports describing a de novo origin and an eventual spontaneous regression of the AVMs suggesting a dynamic nature to some of these lesions. These lesions can be occult at the early stages, grow over time and later regress. According to Lasjaunias[1], the origin of AVMs might be explained by continuous vascular remodeling which is triggered by a provocative event altering the normal vascular development. Pulsatile tinnitus is a recognized clinical presentation of cerebral AVMs. The spontaneous occurrence of tinnitus in patients, with an otherwise clinically silent AVM, supports the fluctuating growth of these malformations. These malformations can further lead to more critical changes in the cerebral hemodynamics. To our best knowledge, the spontaneous regression of an AVM causing a transient tinnitus has not been reported previously.

Case report

A 21-year-old female presented with a six month history of left sided pulsatile tinnitus and was diagnosed with a 3 cm superficial left temporal AVM on magnetic resonance imaging (MRI). She was consequently evaluated with a conventional angiogram which demonstrated a solitary feeding artery arising from one of the M2 branches of the left MCA (Figure 1A) and three cortical veins draining the malformation into the left inferior petrosal and sigmoid sinuses (Figure 1B). An elective embolization was chosen as the method of treatment. Two months later, on the day of the procedure, the repeat angiogram failed to demonstrate patency of the nidus of the malformation. Several segmental areas of stenosis of the feeding artery and occlusion of the proximal segment of the largest draining vein were observed (Figure 2A and 2B). The patient's symptoms resolved, and a follow up MR performed one month later confirmed the thrombosis of the malformation.

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