Paraneoplastic Motor Neuron Disease in a patient with a Natural Killer cells leukemia.

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Case report. A 79-year-old man presented with several months-history of rapidly progressive weakness of the upper limbs, which quickly spread to the lower limbs. Onset occurred in June 2016. In September 2016 the patient underwent a first neurological examination, which disclosed a severe weakness and atrophy of the shoulder girdle, of the right arm and lower limbs. Reflexes were present only in the left arm. EMG showed widespread polyphasic MUP and fibrillation potentials, with normal sensory and motor conduction velocities. A brain and cervical MRI were within normal range. A diagnosis of MND was made, with ALSFRS-R score of 18/48. However, a blood test showed a marked increase of WBC (76050/μL), with a high prevalence of lymphocytes. A routine blood test performed a few months before the clinical onset was reported normal.

Early November 2016, he was admitted to the Hematology Unit at our Hospital. Blood cytofluorimetric analysis and bone marrow biopsy showed a marked infiltration by immature NK and NK-T cells, while CT scans showed an isolated involvement of small bowel. A CSF analysis showed increased proteins and 360/μL NK-T-cells. A diagnosis of NK/T-cell leukemia/lymphoma was made. A systemic chemotherapy according to HyperCyVAD schema was started (High Dose Dexamethasone; Hyperfractionated Cyclophosphamide; Oncovine and Doxorubicine) along with repeated intrathecal injections with Methotrexate, Ara-C and Dexamethasone was performed. A search for paraneoplastic antibodies was negative. In the following days, the patient showed a transient improvement of muscle strength and function, and ALSFRS-R increased to 27/48. Unfortunately, the general health status deteriorated besides the chemotherapy, and in late December 2016, the patient was referred to a Hospice.

Discussion. We have described a paraneoplastic MND associated to an aggressive NK leukemia/lymphoma. Although rare, the association between MND and leukemia/lymphoma has been reported (Younger et al.,1991). Recent reports suggest increased number of NK and NK-T-cells in the blood of ALS patients, suggesting an immune system activation (Rentzos et al.,2011; Murdock et al.,2016). Furthermore, a reduction of circulating NK-cells leads to a significant life span prolongation in the ALS SOD1G93A mouse (Finkelstein et al., 2011).

Conclusion. We have reported a novel case of an aggressive paraneoplastic MND in a patient with NK-cell leukemia. These data adds to the growing literature on the putative role of the immune system, with particular reference to NK-T-cells, in the pathophysiology of motor neuron degeneration.

Table 1

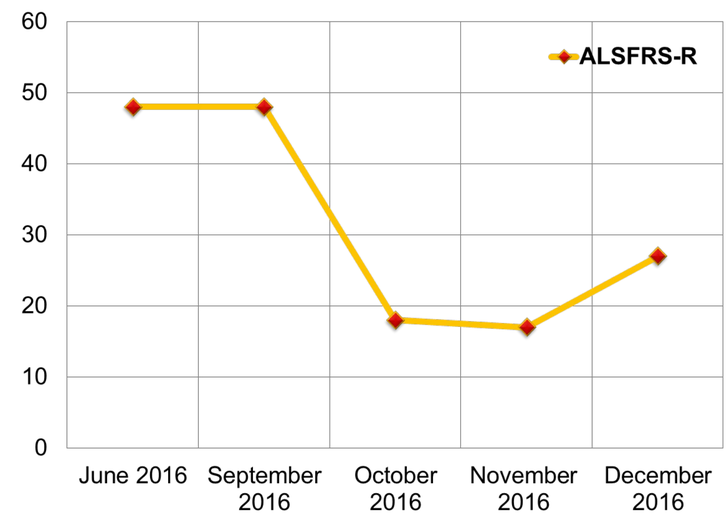
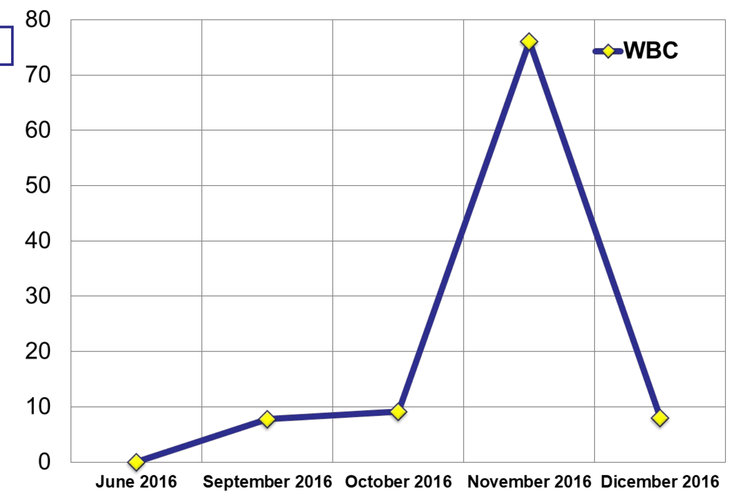


Table 2



The tables show the temporal correlation between the worst level of ALSFRS-R (Table 1) and the hightest white bloodcell count (Table 2).

Table 3

Bone marrow aspiration and cytofluorimetric analysis			
CD45	100%	CD16+CD56+CD3+	60%
CD3+	80%	CD16+CD56+CD3(-)	13%
CD7+CD3+	70%	CD57+CD3+	Neg
CD8+CD3+	8%	CD57+CD3(-)	Neg
CD4+CD3+	8%	TCR-ab+CD3+	77%
CD2+CD3+	77%	TCR-gd-CD3+	Neg

The histopathologic analysis of the bone biopsy was matched with cytofluorimetric analysis (Table 3). Immunohistologic staining disclosed a lymphoproliferative disorder with NK cell differentiation.

References

1. Rentzos M, Evangelopoulos E., Sereti E, et al. Alteration of T cell subsets in ALS: a systemic immune activation? Acta Neurol Scand 2012; 125: 260-264

2. Murdock BJ, Backus C, Goutman SA, Feldman EL. NK and NKT Cells are increased in the peripheral blood of ALS patients. Ann Neurol 80; 2016:S155

3. Finkelstein A, Kunis G, Seksenyan A, et al. Abnormal changes in NKT cells, the IGF-1 axis, and liver pathology in an animal model of ALS. PLoS one 2011; 6:e22374