FINGOLIMOD AND NON-HODGKIN LYMPHOMA : TWO CASES AT MULTIPLE SCLEROSIS CENTER OF FIDENZA

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Introduction

We reported two cases of non-Hodgkin lymphoma derived from peripheral B cells in two patients with MS-RR treated with Fingolimod 0.5 mg observed at Multiple Sclerosis Center of Fidenza. Despite literature data do fall cases described in the series of general patients with RRMS treated with fingolimod we show the need, in our view, to a close monitoring of the patient during therapy with Fingolimod.

Materials and methods

We described the adverse events through the use of clinical data available at the Multiple Sclerosis Center of Fidenza (histological data, radiological data, laboratory data), investigating the patient's medical history, previous treatments, the familiar, the mechanism of action of Fingolimod, and comparing the collected material with literature data.
We reported two cases of non-Hodgkin lymphoma derived from peripheral B cells (in a case follicular lymphoma with bone marrow infiltration, in the other case marginal lymphoma without bone marrow infiltration) occurred in patients with RRMS followed at our Multiple Sclerosis Center on a total of 42 patients treated with Fingolimod 0.5 mg. We have investigated and verified that there were any risk factors associated with the development of lymphoma earlier in both patients.

Case Report 1

Male, Caucasian, 55 years.
Diagnosis of MS-RR in 1984. Prior treatments: Interferon Beta 1a i.m. from February 2004 to February 2007.
From July 2007 the patient receveid Fingolimod inside CFTY720D2302 and CFTY720D2399 study; the drug was suspended on 1st Agoust 2014.
During the period of treatment the patient showed clinical stability (EDSS 1.5) and MRI.
In October 2013 appears painless laterocervical lump; the patient has performed ultrasound and needle-biopsy that diagnosed a reactive lymphadenitis.
The patient performed blood tests (normal), thyroid and neck ultrasound made in July 2014 (thyroid was normal in size and shape, but there was in the back seat right mandibular a pathological hypoechoic, not homogeneus expanded to irregular margins, very vascularized).
On 30th July 2014 neck MRI was performed compatible with retroparotidea cervical adenopathy and PET was carried out on 19th September 2015 which showed lesions with high metabolic activity in right laterocervical lump, and in thoracic, abdominal, splenic and bone area. The 23th September 2014 the patient was operated and on removed sample was performed histological that diagnosed non-Hodgkin lymphoma derived from B lymphocytes in the peripheral type of Grade 1-2 follicular lymphoma (with metastasis) confirmed by bone marrow biopsy. The patient received from October 2014 to March 2015 six cycles of Immuno-chemo-therapy with Rituximab-Bendamustine.
The last PET, performed on 7th April 2015 was negative for lesions with high metabolic activity. The patient is continuig immunotherapy maintenance with Rituximab every two months for two consecutive years.

Case Report 2

Female, Caucasian, 50 years
Diagnosis of MS RR in 1998, NOR debut in 1983
The patient received Beta Interferon 1a i.m. from 1998 to October 2000, suspended by the patient for side effects intolerable.
In May 2008 the patient was recruited in ALLEGRO study (Laquinimod-Placebo), discontinued in December to withdraw informed consent; the patient was in the placebo group.
In August 2012 the patient has began treatment with Fingolimod 0.5 mg cp.
To April 2014 the patient had deep abdominal pain and, in the same period, palpable soft tissue lesion appears on the front right leg.
TAC total body with mdc showed multiple soft tissue injuries.
Surgical excision of lesion on the right leg was performed and the histological sample showed location of marginal B Lymphoma of soft tissues, CD20 +, CD3-, Ki67 20%.
Fingolimod was suspended. In July 2014 the patient begins chemotherapy with Bendamustine and Rituximab and that a total of 6 cycles.
On 17 September 2014 the PET was negative; at this time are not new signes of the disease .
The MS is stable: no new lesions at MRI , no new clinical signes.

Results

Although there is no obvious correlation drug / lymphoma from literature data, for us it is important to report these two cases, since both patients had no risk factors for lymphoma, in particular: age <55 years, familiar negative for lymphoma or hematological diseases, EBV negative, they had never done immunosuppressive therapy earlier and had not been exposed to radiation, they were not immunocompromised and in the past they had made immunomodulatory therapy (interferon beta-1a).
In clinical trials and in post-marketing analysis, where there have been reports of lymphoma of different types including a fatal case of B-cell lymphoma positive Ebstein Barr virus.
However, the percentage found in our center is high (4.7%).

Conclusions

Despite cases of lymphoma reported in the literature are all heterogeneous both anatomically and histologically and in no case has been established a causal relationship to Fingolimod, in our opinion it is necessary to keep an attitude of active pharmacovigilance patients considering the possibility of developing lymphoproliferative disorders , having verified by us 2 cases out of 42 treated patients (4.7%).

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