Poster # DP06

PML and IRIS: Between a Rock and a Hard Place

Joshua D. Katz, MD[1]; Ellen S. Lathi, MD[1]; Lauren M. Heyda[1]; and David Titelbaum, MD[2]

[1]The Elliot Lewis Center for Multiple Sclerosis Care, Brighton, MA; [2]Shields MRI, Brockton, MA

The Elliot Lewis Center For Multiple Sclerosis Care

Background

- Progressive multifocal leukoencephalopathy (PML) is a well recognized complication of natalizumab treatment.
- The clinical course of PML is frequently complicated by immune reconstitution inflammatory syndrome (IRIS).
- Distinguishing between PML and IRIS is challenging and treatment of these 2 conditions potentially opposes one another.
- While there are no established treatment protocols for PML or IRIS, various medication regimens have been tried.

Objective and Methods

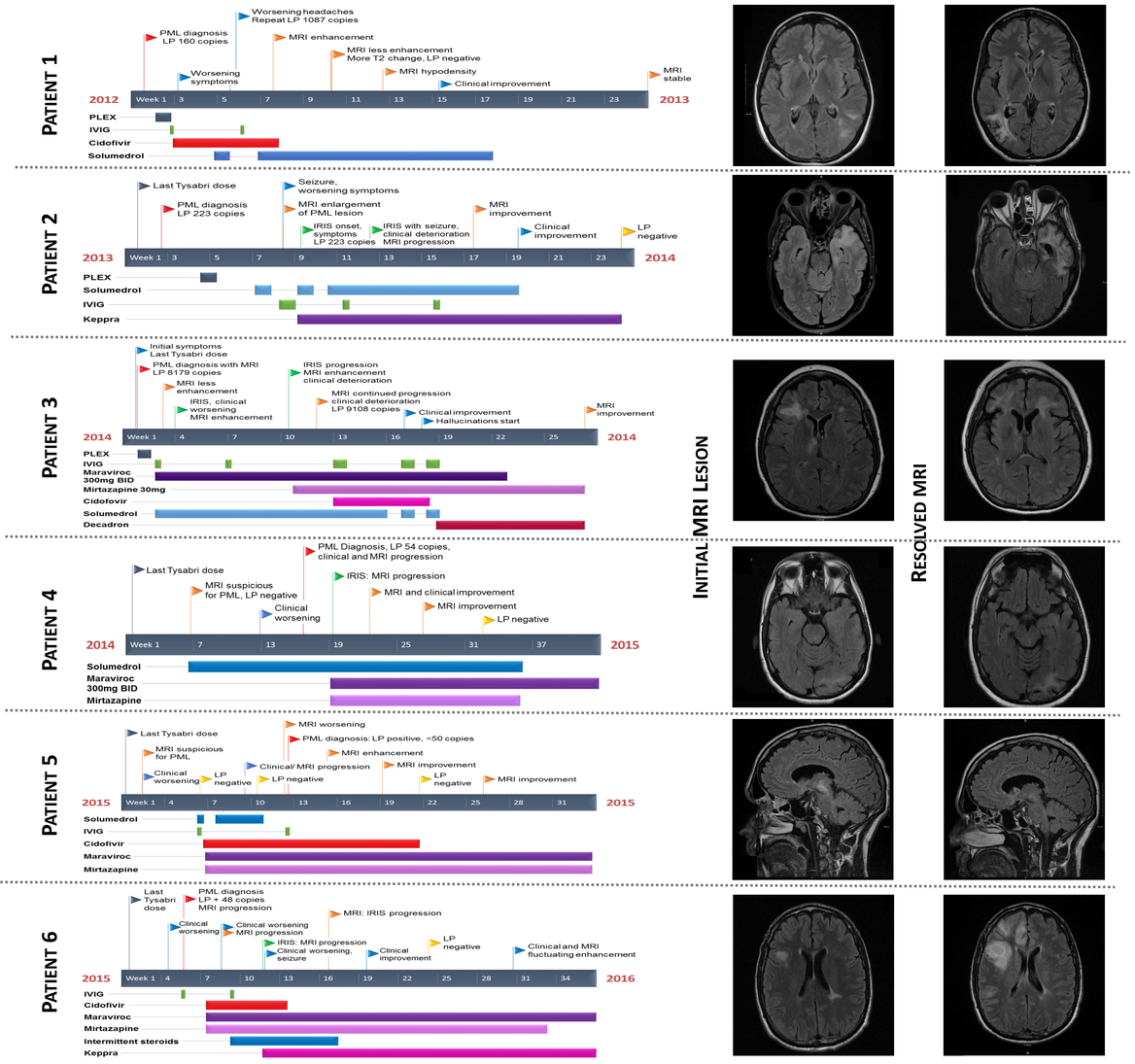
To describe the clinical course, radiologic findings, treatment, and outcomes of 6 patients with natalizumab-associated PML and IRIS treated at The Elliot Lewis Center from 2012 to 2016.

Results

- Of the 6 patients, 4 patients had JCV titers prior to diagnosis:
  - 2 had titers persistently >2.00
  - 2 had titers between 0.4 and 0.7
- 3 patients received plasma exchange (PLEX) shortly after diagnosis.
- Other treatments included various combinations of solumedrol, IVIG, cidofovir, maraviroc, and mirtazapine.
- IRIS developed in all patients, presenting as clinical deterioration and enhancing MRI lesions with onset averaging 2 months after diagnosis.

Discussion

- There is no specific treatment for PML.
- PLEX is currently the de facto standard of care but it can precipitate rebound disease activity and IRIS.
- Our patients had months of mild symptoms preceding their PML diagnosis.
- Clinical deterioration only occurred after natalizumab withdrawal.
- Steroids almost always halted or reversed clinical progression, suggesting IRIS as the cause for clinical deterioration rather than PML.
- Patients who received PLEX deteriorated more rapidly, but time to clinical stability was similar in patients with and without PLEX.
- Treatment with cidofovir, maraviroc, mirtazapine, and IVIG are unproven but have potential benefits that need further investigation.



Patient	Age	Duration of Disease, y	Duration of Tysabri, y	JCV Index	EDSS at Diagnosis
1	43	10-15	6	Not tested	2.5
2	55	12	7	Positive: no index	5.5
3	56	24	5, interrupted	Positive: 0.45 6 months before diagnosis, then 2.19	6.0
4	38	9	7	Positive: 1.77	3.0
5	41	15	8	Positive: 2.6	2.0
6	56	7	2	Positive: 2.1	5.0

Patient	Prodrome	Copy number	PLEX
1	10 days of slurred speech and cognitive clouding	160	Yes
2	Several months of malaise	223	Yes
3	None	8179	Yes
4	1 month of mild hazy vision	Negative: >54	No
5	6 months of fatigue, mild dysarthria, right hand incoordination	Negative: 2x, then <50	No
6	Several months of imbalance and fatigue	48	No

Patient	Onset of Worsening	Onset of Enhancement	Time to Stability, mo	Final EDSS
1	3 wks after PLEX	7 wks after PLEX	2.5	4.5
2	4 wks after PLEX	5 wks after PLEX	3	6.5
3	2 wks after PLEX	3 wks after PLEX	4.5	7.5
4	3 mo after last Tysabri dose	4 mo after last Tysabri dose	5	3.5
5	9 wks	9 wks	3	3.5
6	8 wks after last Tysabri dose	3 mo after last Tysabri dose	4	6.5

Conclusion

IRIS may be a greater cause for short-term disability than PML, but this leads to a dilemma: Treating IRIS may come at the expense of worsening the long-term spread of PML. It may be reasonable to consider withholding PLEX to allow more gradual immune reconstitution for some patients. The benefit of aggressive steroid treatment to preempt IRIS may outweigh the risk of potentially increasing the spread of PML, but more study is needed to make definitive recommendations.