Secondary Autoimmune Diseases Following Ocrelizumab Therapy for Multiple Sclerosis

Elands S[1] , Lemmers A[2], Delhaye M[2], Franchimont D[2], Liefferinckx C[2], Pezzullo M[3] and Perrotta G[1]
1. Department of Neurology, Erasmus Hospital, Brussels; 2.Department of Gastroenterology, Erasmus Hospital, Brussels;
3. Department of Radiology, Erasmus Hospital, Brussels.

Introduction

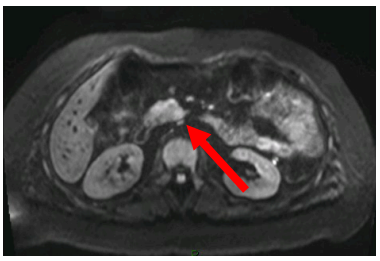
Ocrelizumab is an anti-CD20 monoclonal antibody (mAb) recently approved for the treatment of multiple sclerosis (MS), both in relapsing-remitting (RR) and in primary progressive (PP) forms. The main known side effects are infusion-related reactions and the increased risk of infections, although the long-term safety profile has yet to be evaluated. During the randomised controlled trials, there were five reported cases of acute pancreatitis, two of which had no predisposing risk factors. Since then, there has been one other case report of an acute pancreatitis, and another of a refractory colitis. We here present two further cases followed by a literature review:

Case 1: 25 year-old woman with RRMS (2014)

- Previously treated by Interferon beta (Rebif) and Dimetyl Fumarate (Tecfidera) before initiating Ocrelizumab therapy.
- Following 2nd dose of Ocrelizumab : Nausea, epigastric pains, loose stools and a panniculitis.
    - Abdominal CT and MRCP: Auto-immune pancreatitis
    - PET-CT: Highly suggestive of inflammatory origin.
    - Biopsy: Inflammatory Bowel Disease (IBD) akin to ulcerative colitis.
- She was treated conservatively without the use of corticosteroid therapy.

Case 2: 44 year-old woman diagnosed with PPMS (2019)

- No previous disease-modifying therapies given.
- Following 1st dose of Ocrelizumab: Abdominal pain, diarrhea.
    - CT and MR Imaging: Right-sided colitis
    - Biopsy: Inflammatory Bowel Disease (IBD) akin to ulcerative colitis.
- She was treated with a course of intravenous Augmentin and now remains stable off treatment at 1-year follow-up.



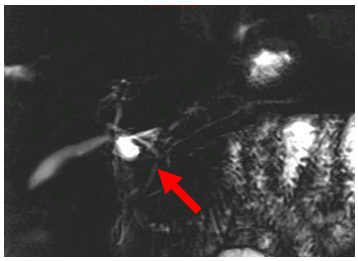
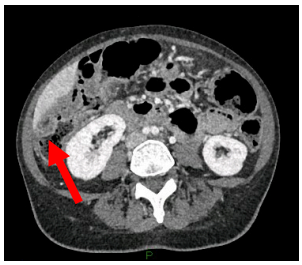


Figure 1: MRCP (Magnetic Resonance Cholangio-Pancreatography) images showing radiological features of autoimmune pancreatitis, i.e. focal inflammatory swelling of pancreatic head with diffusion restriction and ductal narrowing without upstream dilatation nor periglandular fat infiltration.



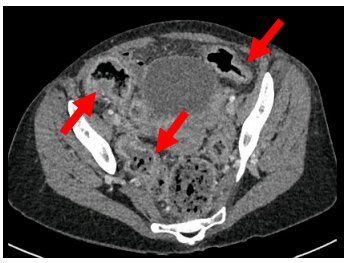


Figure 2: Computed tomography images showing diffuse stratified inflammatory thickening of colonic wall showing mucosal hyperhemia and submucosal oedema.

Discussion

The temporal association between Ocrelizumab administration and the development of symptoms is suggestive of an anti-CD20-induced effect, especially given the lack of other causes after exhaustive diagnostic workups. In both cases Ocrelizumab was discontinued. Rituximab, another anti-CD20 mAb, has also been reported to have pancreatitis and colitis as side-effects, and Ofatumumab has been associated with diarrhea/colitis-like symptoms. The underlying mechanism of action is still not understood, although an immune dysregulation causing visceral organ inflammation has been suggested, for example by means of an upregulation of pro-inflammatory cytokines. Further study is needed to better understand the pathogenesis and those patients who may be at greater risk.

Conclusion

Acute pancreatitis and colitis may present as secondary autoimmune diseases following Ocrelizumab therapy. As an increasing number of MS patients are now being treated with anti-CD20 therapies, it is important to counsel them appropriately and monitor them closely for these potential side-effects.

References

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