Eosinophilia during natalizumab treatment: Incidence, risk factors and temporal patterns

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Abstract

Eosinophilia is common during natalizumab treatment for multiple sclerosis but risk factors are unknown. We aimed to identify demographic, clinical and laboratory characteristics predicting eosinophilia. Sustained eosinophilia occurred in 16.8%. Risk factors for sustained eosinophilia included baseline pre-treatment eosinophilia, medical conditions potentially associated with eosinophilia including allergies, and suboptimal compliance. One temporal profile was associated with the highest and most rapidly developing eosinophilia, and was less likely to resolve: in one such case, eosinophilia was symptomatic. Changes in eosinophil and lymphocyte counts were only weakly correlated, suggesting factors other than Very Late Antigen-4 (VLA-4) inhibition drive eosinophilia. The concept of neuroinflammation in multiple sclerosis (MS) includes several components of both adaptive and innate immune responses as well as inflammatory responses of brain and spinal cord cells. The main inflammatory processes involve: infiltrating lymphocytes and myeloid cells; activated microglia, astrocytes, oligodendrocytes; alterations of blood–brain barrier integrity; cytokine/chemokine signaling. Most of these events remain compartmentalized within the CNS of MS patients possibly mediating the persistence of chronic inflammation and the accumulation of motor and cognitive disability. The current special issue has the purpose to examine and discuss recent insights into MS neuroinflammation cell and molecular mechanisms and the identification of potential, new MS-specific inflammatory biomarkers in order to provide a comprehensive overall view of MS neuropathology and neuroimmunology. Multiple sclerosis (MS) is a neurodegenerative and inflammatory disease usually presenting with acute demyelinating events that can start as, or progress to, chronic damage. The development of animal experimental models, specific for each stage of MS will aid in the design of new drugs specific for the different forms of the disease. Animal models of experimental autoimmune encephalomyelitis successfully reflect the pathophysiological mechanisms of the early phases of MS. However, few models resemble the features of the progressive forms of MS such as cortical demyelination and meningeal inflammation. Recently, a few auspicious animal models recapitulating many of the characteristics of progressive MS, aimed at a better understanding of the Pathology of these forms of the disease, have been developed. In this review, we will summarize the latest developments in animal models reflecting the cortical and meningeal pathological features of progressive MS, as well as their response to drugs specifically targeting these forms. Prenatal opioid exposure is associated with significantly adverse medical, developmental, and behavioral outcomes in offspring, though the underlying mechanisms driving these impairments are still unclear. Accumulating evidence implicates gut microbial dysbiosis as a potential modulator of these adverse effects. However, how opioid exposure during pregnancy alters the maternal and neonatal microbiome remain to be elucidated. Here, we utilize a murine model of brief hydromorphone exposure during pregnancy (gestation day 11–13; i.p.; 10 mg/kg) to examine its impact on the maternal and neonatal microbiome. Fecal samples were collected at various timepoints in dams (4 days post hydromorphone exposure, birth, and weaning) and offspring (2, 3, and 5 weeks) to interrogate longitudinal changes in the microbiome. Stomach contents at 2 weeks were also collected as a surrogate for breastmilk and microbial analysis was performed using 16S rRNA sequencing. Alongside alterations in the maternal gut microbial composition, offspring gut microbiota exhibited distinct communities at 2 and 3 weeks. Furthermore, functional profiling of microbial communities revealed significant differences in microbial community-level phenotypes gram-negative, gram-positive, and potentially pathogenic in maternal and/or neonatal hydromorphone exposed groups compared with controls. We also observed differences in stomach microbiota in opioid-exposed vs non-exposed offspring, which suggests breast milk may also play a role in shaping the development of the neonatal gut microbiota. , the main focus of ischemic stroke research was on the central nervous system (CNS) aiming to rescue the damaged neurons on site of ischemic stroke. However, failure of neuroprotective treatments in clinical trials strongly suggests ischemic stroke is rather a sophisticatedly systemic disorder involving not only the nervous system. In fact, stroke exhibits multiphasic processes, including the progression of ischemic brain injury associated with intense and long-lasting innate and adaptive immune responses in the periphery and CNS. These immune responses are biologically distinguishable, providing a time frame for intervention and also represent a novel therapeutic target.