

Pneumocystis Jirovecii Pneumonia During Treatment of Autoimmune Hepatitis with Oral Budesonide.

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Abstract

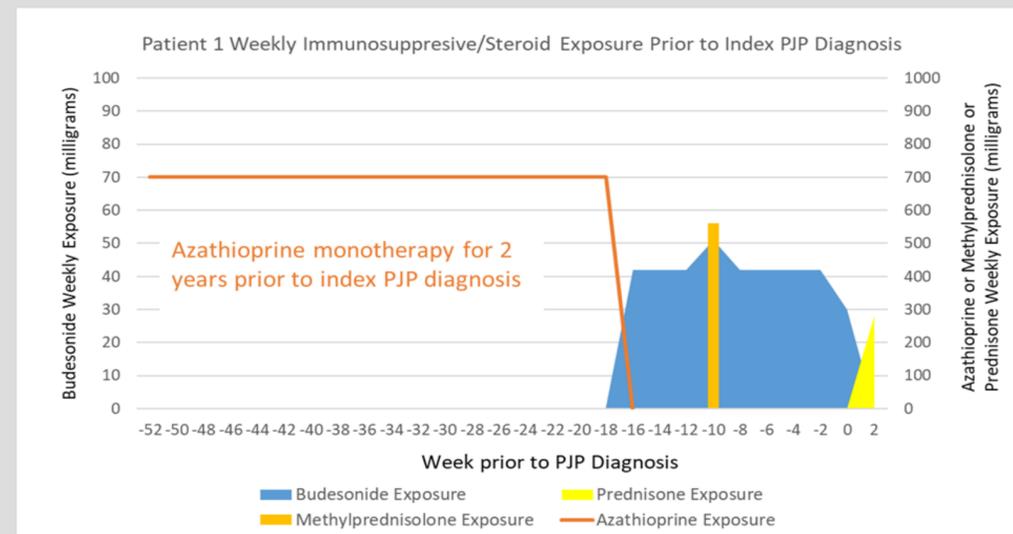
- Oral budesonide is an effective therapy for autoimmune hepatitis with fewer side effects compared to oral prednisone. Clinical trials and observational studies of its use in autoimmune hepatitis and Crohn's disease have reported no increase in the incidence of infection, consistent with its first-pass inactivation in the liver. In particular, the opportunistic infection *Pneumocystis jirovecii* pneumonia (PJP) has not been reported with budesonide, a status unique among oral steroids. We herein report two cases of PJP that occurred during budesonide treatment of autoimmune hepatitis. Both patients were started on budesonide despite the presence of cirrhosis and portosystemic shunting, conditions where budesonide use is contraindicated. We hypothesize that PJP infection occurred due to minimal first-pass metabolism of budesonide due to cirrhosis and portosystemic shunting, allowing sufficient systemic drug levels to increase PJP risk. These cases illustrate the importance of identifying signs of developing cirrhosis and/or portosystemic shunting in patients with autoimmune hepatitis while on therapy and substituting other steroids or steroid-sparing agents with the provision of PJP prophylaxis when indicated.

Background

- Autoimmune hepatitis (AIH) is a rare liver disease for which lifelong immunosuppression is often indicated.
- Oral budesonide is an effective steroid in AIH treatment based on evidence showing less steroid-related side effects.
- Budesonide is particularly appealing as a therapy secondary to its anti-inflammatory effects being exerted almost exclusively in the liver following gut absorption, after which it is largely inactivated to inert metabolites before leaving the liver.
- Cirrhosis is associated with less first-pass inactivation of budesonide and 13-fold higher blood budesonide levels, and is thus considered a contraindication to budesonide use.
- Portosystemic shunting leads to a further decrease in first-pass liver metabolism and should prompt discontinuation of oral budesonide and substitution of a steroid with more predictable pharmacokinetics.

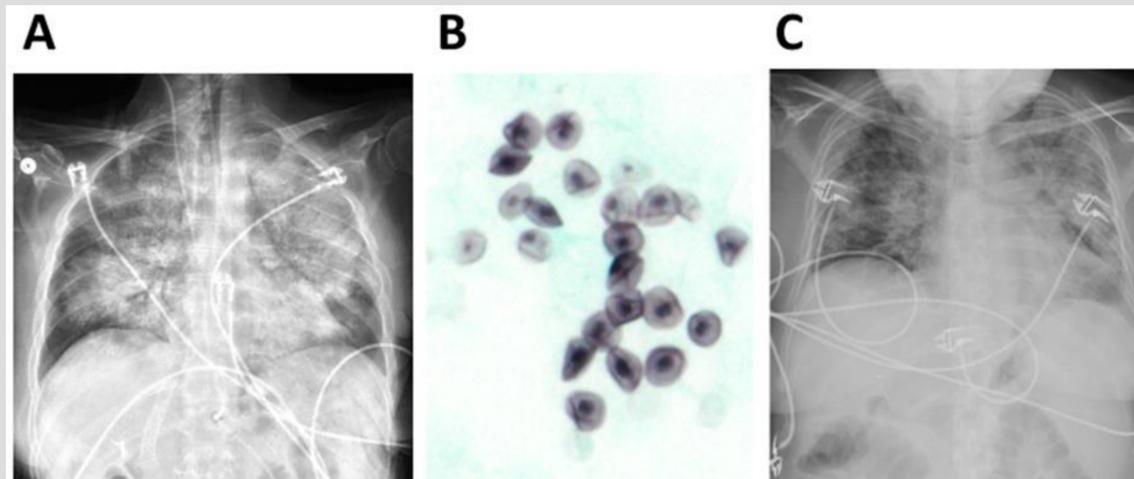
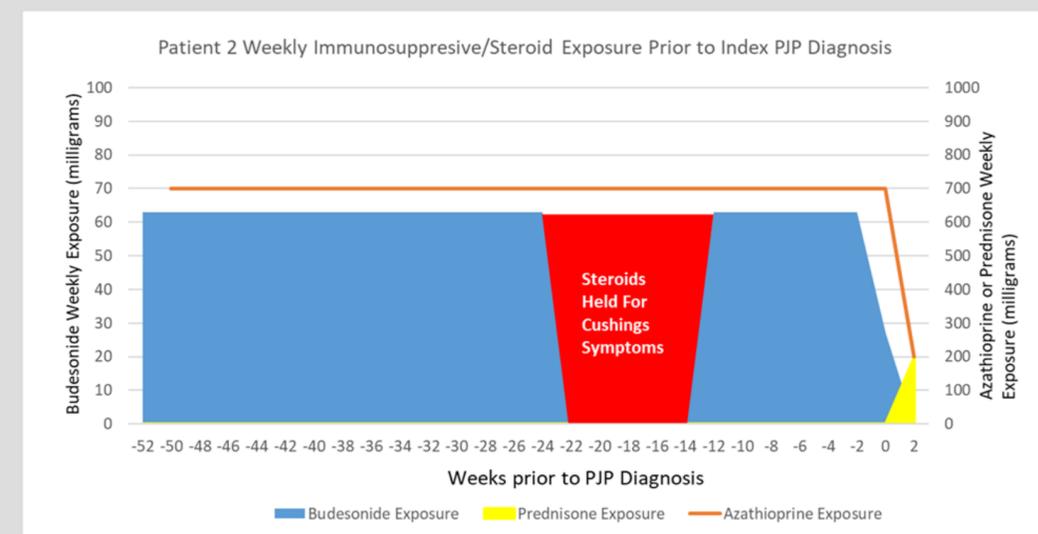
Case 1

- A 48 year-old woman was diagnosed three years before admission with AIH by liver biopsy. Initial treatment was with mercaptopurine but later switched to azathioprine. Thirteen months prior to admission a TIPS was placed and oral budesonide started with two subsequent hospitalizations for hepatic encephalopathy.
- During the hospitalization of interest, the patient was admitted for hepatic encephalopathy. On hospital day 6 she developed dyspnea, cough, and the SpO2 was 64% on room air. A chest radiograph showed bilateral alveolar infiltrates. She was moved to an intensive care unit due to increasing oxygen needs and was intubated shortly after transfer. The acute respiratory distress syndrome (ARDS) was diagnosed. Empiric broad spectrum antibiotics were started. Bronchoalveolar lavage (BAL) revealed PJP by direct fluorescent antigen (DFA) testing and Intravenous trimethoprim-sulfamethoxazole (Bactrim) was added. She was extubated three days later and discharged on hospital day 16 on oral Bactrim, prednisone 40 mg daily, and minimal oxygen.



Case 2

- A 51 year-old woman was diagnosed with AIH-PBC overlap 14 months before admission. EGD at that time showed varices. In addition to ursodiol, budesonide and azathioprine were started for initial induction therapy.
- She was referred to our facility for a liver transplant evaluation and was admitted that day for hepatic encephalopathy. On hospital day 4 she developed respiratory distress. A chest radiograph showed bibasilar consolidation. Empiric broad spectrum intravenous antibiotics and PJP prophylaxis with thrice weekly oral Bactrim was started. On hospital day 7 a chest CT scan revealed bilateral alveolar infiltrates. BAL was performed on hospital day 11 which revealed a positive DFA for PJP. Oral Bactrim at treatment doses was administered. On hospital day 14 she was transferred to an ICU and intubated. Due to refractory shock and worsening ARDS her family withdrew care. She died on hospital day 15.



- Chest radiograph from the first PJP case showing bilateral alveolar infiltrates. Note that the TIPS is visible in the right upper quadrant.
- Silver stain of bronchoalveolar lavage cytology preparation from this patient showing pneumocystis organisms (gray).
- Chest radiograph from the second PJP case showing bilateral alveolar infiltrates.

Conclusions

- In summary, these cases illustrate that vigilance is required during oral budesonide therapy of AIH such that treatment is halted and switched to a more predictable and titratable steroid (such as prednisone or prednisolone) as soon as signs of cirrhosis or portosystemic shunting are clinically apparent. Appropriate PJP prophylaxis should commence if steroid exposure risk thresholds are met.