Background

Ipilimumab (Yervoy®) is a new monoclonal antibody (anti-CTLA4) approved since 2011 by Swissmedic for treatment of unresectable melanoma. It promotes the activation of cytotoxic T lymphocytes by stopping their inhibition, at the price of autoimmune side effects. 35% of patients treated with Ipilimumab will develop colitis, in which 10% of these can be complicated by a colonic perforation requiring surgical management (1,2). Ipilimumab induced colitis has immune and histological patterns similar to that of Crohn’s disease (3). Steroids or anti-TNF alpha drugs are generally used to treat this colitis (4).

Presentation of a case

A 74 year old woman was treated with Ipilimumab during one month for a multi metastatic melanoma. She developed an Ipilimumab induced rectocolitis proven by colonoscopy and biopsies and was admitted for steroid therapy. Symptoms of colitis disappeared but she developed total fecal incontinence as a result of a wide posterior anorectal fistula (fig 1.). Clinical examination and anoscopy revealed multiple rectal ulcerations. A deroofing fistulectomy (Fig. 3 and 4) under local anesthesia was performed: the tissue bridge forming the top of the fistula was ligated and removed. Histologic examination didn’t find any malignancy. The surgery allowed a better coaptation of the anus and an improved continence. Due to delayed wound healing and persistence of rectal ulcers, an anti-TNF alpha therapy (Infliximab®) was introduced. After two injections, the patient developed pancycopenia and the therapy was discontinued. The patient died a few months later due to the natural evolution of her oncologic disease and complete fistula healing was not achieved by this time point.

Discussion

This case is the first description of an Ipilimumab induced anorectal fistula and its management by surgery and anti-TNF alpha therapy. The deroofing procedure restored anatomy of the anus and was successful in improving continence. However, the healing of the wound was delayed. This was the result of the poor general condition of the patient, steroid impregnation and persistent autoimmune inflammation, as a result of Infliximab discontinuation.

Conclusion

Most patients treated with Ipilimumab are in a palliative situation and fragile. Management of an Ipilimumab induced fistula should be focused on patient comfort and thus symptoms of anal discharge or incontinence. In this particular case, deroofing fistulectomy was successful in relieving symptoms. Anti-TNF therapy, used to treat the colitis, might be an option for rectal lesions. However, in this case, the patient never reached this endpoint as she discontinued therapy and as a confounding factor impaired the local healing.

Because of the expanding use of Ipilimumab, we expect to see an increasing number of these anorectal complications.

References