

Peripheral Neuropathy under Infliximab Therapy: About One Case

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Abstract

A-TNF inhibitors are increasingly used in various inflammatory disorders. Multiple side effects have been reported in recent years, particularly peripheral neuropathies. We report a case of axonal neuropathy occurring after the start of treatment with Infliximab. This is a 47 years old patient, followed for Crohn's disease requiring treatment with Infliximab. Twenty-two weeks later, the patient presented a grade 4 of axonal neuropathy. We concluded to a medicinal sensitive neuropathy after elimination of other etiologies. Given the severity of the neurological symptoms, we decided to change the therapeutic class.

Keywords

Crohn's Disease, Infliximab, Peripheral Neuropathy

1. Introduction

A-TNF inhibitors treatments are commonly used for the treatment of several inflammatory disorders such as inflammatory rheumatism (spondyloarthropathies, rheumatoid arthritis or psoriatic arthritis) and gastroenterological inflammatory diseases [1]. Among the different therapeutic classes available, there are chimeric or humanized monoclonal antibodies such as infliximab or adalimumab [1]. Among the adverse effects related to the use of these treatments, demyelinating events of the nervous system central [2] and demyelinating peripheral neuropathies [3] were reported. One study estimated that peripheral demyelinating complications could be more frequent than expected compared to central ones [4]. The occurrence of these events poses the problem of the ulterior management in the absence of clear guidelines.

2. Objective

The aim of this work is to highlight related peripheral nerve complications of a-TNF inhibitors, especially peripheral demyelinating and to underline the difficulty of management in the absence of clear guidelines.

3. Case Observation

This is a 47 years old patient, without significant neurological history, chronic smoking weaned, followed since 2014 for Crohn's disease with ano-perineal manifestations under combotherapy (infliximab, 6-mercaptopurine) since 2018 at the recommended dose with good clinical answer and great initial tolerance. From the 6th injection of infliximab, the patient began to report the occurrence of dysesthesia with uncomfortable sensations complicated by painful cramps limiting his physical activity and prompting him to stop treatment.

The patient was hospitalized in gastroenterology department. The clinical examination at its admission founds a conscious patient with no fever. Abdominal examination did not reveal any abnormalities including no abdominal tenderness or palpable mass; the digital rectal examination was very painful. The neurological examination showed hypoesthesia in sock reaching the ankles on. Sociodemographic and clinical characteristics of the patient are summarized in **Table 1**.

The biological assessment revealed anemia with 8 g/dl, blood cells with 10,700 elm/mm³, correct platelets, a high CRP at 209 mg/l and a low TP at 56%. The serology of the hepatitis E virus, HIV and hepatitis C virus were requested, given the neurological manifestations, returned normal. Dosage of vitamin B 12 and folic acid were also normal.

The radiological assessment (**Figure 1**) showed a thickening that extends from the rectum to the left colic angle without individualisation of collection. The proctological examination revealed the presence of large external fistulous orifices placed at 1 o'clock on the anal margin with pus, sphincteric hypotonia and

Table 1. Sociodemographic and clinical characteristics of the patient.

Characteristics	
Age	47 years
Clinical history	<ul style="list-style-type: none"> • Chronic smoking weaned • followed since 2014 for Crohn's disease with ano-perineal manifestations
Admitted for	Sensitive neuropathy
Current treatment	Combotherapy (infliximab, 6-mercaptopurine)
Clinical	<ul style="list-style-type: none"> • dysesthesia • painful cramps
Physical examination	<ul style="list-style-type: none"> • no fever • Digital rectal: very painful, sphincteric hypotonia • Hypoesthesia in sock reaching the ankles on

perception at 12 o'clock of a loss of substance. Anoperineal magnetic resonance imaging (**Figure 2**) showed rectal thickening and sclerolipomatosis, loss of substance at 12 o'clock communicating with a perianal abscess and individualization of 2 fistulas.

Taking into account the findings of the neurological examination, an electromyogram was performed and revealed grade 4 of lower limb sensory neuropathy.

The patient was put on strong analgesic as well as vitamin complexes and benefited from fecal diversion to let the rectum rest.

Given the neurological findings and the activity of the disease, the TNF was discontinued at neuropathy onset. We proposed a therapeutic alternative to anti TNF alpha treatment to manage the inflammation on one hand and on the other hand not to further aggravate sensory neuropathy. Hence, we decide to start the Methotrexate. The treatment and its side effects were explained to the patient. The switch to Methotrexate was made with no further neurological complications. The patient was followed up for 14 months. The evolution was marked by improvement in neurological signs after 5 months with partial improvement on the digestive level.



Figure 1. CT image showing inflammatory thickening that extends from the rectum to the left colic angle (at the neuropathy onset).



Figure 2. Image of MRI showing thickening and sclerolipomatosis, loss of substance at 12 o'clock communicating with a perianal abscess and individualization of 2 fistulas (at the neuropathy onset).

4. Discussion

The occurrence of peripheral neurological adverse effects under anti-TNF alpha is a problem which prescribers may be increasingly confronted with because of the growing use of this therapeutic family [5]. The estimation impact of peripheral neuropathy during Infliximab therapy is difficult and the time to onset is often less than two years after the beginning of anti TNF alpha [1]. S. Fernández-Menéndez *et al.* [6] report a case of multifocal-motor-neuropathy-like disease associated with the use of Infliximab in a patient with Crohn's disease, that occurred 3 years after beginning of the anti TNF. In Singer's study [7] and Rodriguez-Escalera's study [8], the sensory neuropathy of both lower limbs began after the 4th month in patient with chronic inflammatory bowel disease. In our case, the manifestations were observed after the 6th cure. In our case, the patient began to report the occurrence of peripheral neuropathy from the 6th injection of infliximab.

The risk of neuropathy and other neurological complications varies from one anti TNF to another [5]. The decision to continue treatment with anti TNF alpha should be discussed on a case by case. Our patient has developed a grade 4 of lower limb sensory neuropathy under infliximab thing that pushed us to change this therapeutic class. In the Stubgen study's and Tsouni study's [9] [10], specific management of neuropathy by intravenous corticosteroids and immunoglobulins was necessary despite a spontaneous improvement in the symptomatology when anti TNF alpha was stopped and when there was no response to stopping anti TNF in Tsouni study's. In the case reported by Zinebi *et al.* [5], the evolution is partially favorable with regression almost complete of symptoms after three months of reduction in the dosage and a complete electrical recovery at the 10th month. In our case, we observed the disappearance of the neurological symptoms after 5 months from stopping the anti TNF.

Summary of patient characteristics, neuropathy, and outcome are shown in **Table 2**.

Table 2. Summary of patient characteristics, neuropathy, and outcome.

	Our case	Tsouni <i>et al.</i> [10]	Zinebi <i>et al.</i> [5]	Rodriguez-Escalera <i>et al.</i> [8]
Age at the presentation	47 years	49 years	60 years	34 years
Underlying inflammatory disorder	Crohn's disease	inflammatory disorders	hemorrhagic rectocolitis	rheumatoid arthritis
A-TNF agent used	infliximab	Infliximab/Adalimumab	infliximab	Infliximab
A-TNF onset to neuropathy	6 th injection	19 months	3 months	4 th injection
Treatment	a-TNF stopped	a-TNF stopped +/-intravenous immunoglobulin	reduction of the dose to half	a-TNF stopped
Neuropathy outcome	Recovered at 3 months	3 months	10 months	6 months

5. Conclusion

The effectiveness of Infliximab is indisputable in gastroenterological inflammatory diseases. The reduction of the dose or the change of therapeutic class to the occurrence of an adverse effect, particularly peripheral neuropathy, must be discussed on a case-by-case.

Conflict of Interest

None of the authors has any conflict of interest, financial or otherwise.

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