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CASE REPORT

Suicidal thoughts in a patient after administration of infliximab

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ABSTRACT

Infliximab (IFX) is a chimeric monoclonal antibody biologic drug that works against tumor necrosis factor alpha (TNF- α) and is used to treat autoimmune diseases. This is case of a 45-year old female patient who had suicidal thoughts after receiving infusions with IFX. She did not report any family psychiatric history. She was diagnosed with ulcerative colitis. She had many relapses and she was treated with azathioprine and prednisolone. After many incidents of diarrhea, she started therapy with infliximab infusions. She had totally 13 infusions during a period of 13 months. The last year and in particular during the time of Infliximab intake, she reported suicidal ideation. Due to lack of improvement in her physical symptoms, she voluntarily discontinued medication and resorted to a nutritionist and a mental health counselor, where she followed cognitive and behavioral interventions. Treatment of autoimmune disorders with infliximab raise an awareness among medical and paramedical staff involved in the care of these patients about the psychiatric side effects of the drug.

KEYWORDS: infliximab, Side effects, suicidal ideation, depression, ulceral colitis

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Introduction

Infliximab (IFX) is a chimeric monoclonal antibody biologic drug that works against tumor necrosis factor alpha (TNF- α) and is used to treat autoimmune diseases. Infliximab exerts its influence by binding to TNF- α . TNF- α is a chemical messenger (cytokine) and plays an integral part in autoimmune reaction. It was originally developed as a mouse antibody in mice. As humans have immune reactions to mouse proteins, the mouse common domains were replaced by similar human antibody domains.¹ IFX is as second line therapy in patients with ulcerative colitis who fail to respond in intravenous steroids.² Psychiatric side effects are rare.³ We present a case of a female patient who had suicidal thoughts after receiving infusions with IFX.

Case Presentation

This is case of a 45year old female patient who attended a community mental health center due to depressive mood. She did not report any family psychiatric history. Ten years ago she was diagnosed with ulcerative colitis. She had many relapses and she was treated with azathioprine 100-150mg p.o., prednisolone 30mg p.o. After many incidents of diarrhea, she started therapy with infliximab infusions. She had totally 13 infusions during a period of 13 months. The patient reported considerable psychological burden from the early days of the disease; however, with good adaptation in the ensuing years. Mild symptoms of irritability and sleep disturbances were reported. Her clinical condition worsened in 2010 after a new relapse of the disease when she manifested decreased mood and energy, fatigue, generalized anxiety and irritability. The intensity of the symptoms was hand in hand with her physical condition and was consonant with the exacerbations and remissions of the disease. In addition, for a considerable time period she described reduced functionality in her work, social withdrawal, and strenuous gastrointestinal symptoms, feeding fear, anxiety and avoidance behaviors (distant parts, control of the toilet - agoraphobia). She endeavored to regulate and control her defecation before leaving for her work on a daily basis in the form of a ritual. During the last year and in particular during the time of infliximab intake, she reported suicidal ideation. She had thoughts that she wanted to hurt herself and specifically she started thinking that she wanted to fall out the window but he never got to try it. Suicidal ideation occurred almost two months after starting treatment with infliximab and appeared suddenly. She had no symptoms of depression before starting treatment. The patient had also cognitive disorders and specifically she forgot thing more often, important events such as appointments or social engagements and also, she become more impulsive or showed increasingly poor judgment. Due to lack of improvement in her physical symptoms, she voluntarily discontinued medication and resorted to a nutritionist and a mental health counselor, where she followed cognitive and behavioral interventions. Since then both her physical and mental well-being were significantly improved one month after the discontinuation of the treatment, restoring thus a large part of her functionality, undertaking and fulfilling family responsibilities, mobilizing with greater autonomy, improving mood and alleviating suicidal ideation. Irritability, impatience, cognitive disorders, avoidance behaviors, and pre-morning preparation rituals ("waking up two hours earlier, drinking a large amount of coffee, using toilet and leaving for work") remain. The patient has provided informed consent for this report and her anonymity has been preserved.

Discussion

In our patient there was a time interrelation between the IFX therapy and the suicidal thoughts. The patient was not receiving any other treatment during IFX infusion. In the

literature two other cases have also demonstrated suicide attempts after IFX therapy.^{4,5} Side effects with psychological or psychiatric implications are rare during infliximab therapy; while in relevant clinical trials the following side effects have been documented: amnesia, confusion, somnolence depression and apathy.⁶ In another case report a 16-year-old male with a 2-year history of disabling symptoms and complications of Crohn's disease was initiated on a trial of infliximab. Within days of the first infliximab infusion, he experienced symptoms of depression, which intensified over weeks and resulted in a serious suicide attempt.⁷ In a cohort study analyzing data from the French national hospital higher risks were observed for certain pairs of adverse events and underlying pathologies: psychotic disorders in patient treated for ulcerative colitis, manic episodes in patients treated for severe psoriasis, and suicide attempts in patients treated for rheumatoid arthritis.⁸ Infliximab neutralizes the biological activity of TNF- α by binding with high affinity to the soluble (free floating in the blood) and transmembrane (located on the outer membranes of T cells and similar immune cells) forms of TNF- α , and inhibits or prevents the effective binding of TNF- α with its receptors. Infliximab and adalimumab (another TNF antagonist) are in the subclass of "anti-TNF antibodies" (they are in the form of naturally occurring antibodies), and are capable of neutralizing all forms (extracellular-, transmembrane-, and receptor-bound) TNF- α .⁹ A large body of evidence corroborates an association among tumor necrosis factor α (TNF- α), inflammation and depression. Immune activation and the concomitant upregulation of TNF- α is usually followed by a series of physiological, behavioral and motivational changes including fever, increased slow wave sleep, hyperalgesia, anorexia, anhedonia, disturbed mood and impaired concentration.¹⁰ Childhood abuse has been associated with increased TNF- α mRNA consistent with extant studies of increased inflammation in subjects with history of childhood abuse.¹¹ TNF- α mRNA also continued to be increased in SA even after controlling for childhood abuse. Similar to HCC, TNF- α mRNA was also associated with perceived stress; however, TNF- α mRNA was associated with several clinical predictors of suicidal behavior of increased severity of depression and anxiety symptoms, impulsivity, aggression, hopelessness, and sleep disturbances. TNF- α is a potent pro-inflammatory cytokine and is one of the cytokines that can cross the blood brain barrier (BBB) without BBB disruption and affect brain function.¹² In this case, in addition to being at increased risk for depression due to the medical history of Crohn's disease, our patient had no previous psychiatric history and suicidal ideation came late after the start of treatment compared to other incidents in the literature and the escape time of suicidal ideation in the literature usually is withdrawn after discontinuation of treatment.¹³

Conclusion

Considering that infliximab remains a highly effective standard treatment of autoimmune disorders, there is an imperative need to raise awareness among medical and paramedical staff involved in the care of these patients about the psychiatric side effects of the drug. Psychiatrists and gastroenterologists must liaison on inflammatory bowel disease therapy, so as to ensure success, reduce side effects and minimize the likelihood of relapse.

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ΠΑΡΟΥΣΙΑΣΗ ΠΕΡΙΠΤΩΣΗΣ

Αυτοκτονικός ιδεασμός σε ασθενή ύστερα από χορήγηση ινφλιξιμάμπης

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-----ΠΕΡΙΛΗΨΗ-----

Η ινφλιξιμάμπη (infliximab) (IFX) είναι ένα βιολογικό φάρμακο χιμαιρικού μονοκλωνικού αντισώματος που λειτουργεί ενάντια στον παράγοντα νέκρωσης όγκου άλφα (TNF-α) και χρησιμοποιείται για τη θεραπεία αυτοάνοσων ασθενειών. Περιγράφεται η περίπτωση ασθενούς 45 ετών που είχε αυτοκτονικές σκέψεις μετά από λήψη εγχύσεων με IFX. Δεν ανέφερε κανένα οικογενειακό ψυχιατρικό ιστορικό. Διαγνώστηκε με ελκώδη κολίτιδα. Είχε πολλές υποτροπές και υποβλήθηκε σε θεραπεία με αζαθειοπρίνη και πρεδνιζολόνη. Μετά από πολλά περιστατικά διάρροιας ξεκίνησε θεραπεία με εγχύσεις infliximab. Είχε συνολικά 13 εγχύσεις για μια περίοδο 13 μηνών. Τον τελευταίο χρόνο και ιδιαίτερα κατά τη διάρκεια της πρόσληψης ινφλιξιμάμπης, ανέφερε αυτοκτονικό ιδεασμό. Λόγω της έλλειψης βελτίωσης των σωματικών της συμπτωμάτων, διέκοψε οικειοθελώς τη φαρμακευτική αγωγή και κατέφυγε σε διατροφολόγο και σύμβουλο ψυχικής υγείας, όπου ακολούθησε νοητικές και συμπεριφορικές παρεμβάσεις. Η θεραπεία αυτοάνοσων διαταραχών με ινφλιξιμάμπη αυξάνει την ευαισθητοποίηση του ιατρικού και παραϊατρικού προσωπικού που εμπλέκεται στη φροντίδα αυτών των ασθενών σχετικά με τις ψυχιατρικές παρενέργειες του φαρμάκου.

ΛΕΞΕΙΣ ΕΥΡΕΤΗΡΙΟΥ: ινφλιξιμάμπη, παρενέργειες, αυτοκτονικός ιδεασμός, κατάθλιψη, ελκώδη κολίτιδα

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