

Case Report

Gingival Overgrowth Induced by Sirolimus in a Patient with Kidney Transplant

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Abstract: Drug-induced gingival overgrowth due to immunosuppressant is a side effect of this, however, is not completely known the cause. Furthermore, patients that undergo kidney transplant must enter to an immunosuppressive therapy forever, so one of the alterations presented are gingival overgrowth. The following case shows a female patient of 20 years old with a kidney transplant 4 years ago, under treatment with Sirolimus and Mycophenolate Sodium; who presents gingival overgrowth in anterior section of maxillary superior due to immunosuppressive therapy. It was indicated a gingivectomy and gingivoplasty, which had a good evolution and healing after 15 days of post-operative period.

Keywords: Gingival overgrowth, immunosuppressant, kidney transplant, gingivectomy, gingivoplasty.

INTRODUCTION

Kidney transplant is indicated to patients who have chronic or terminal renal diseases [1-3]. Therefore, in order to prevent rejection of the new organ in the organism, the subjects must undergo in an immunosuppressive therapy throughout their entire life. Initially, nephrologists started with Cyclosporine-A, calcineurin inhibitors and tacrolimus; however, over time it showed nephrotoxicity [1]. So, nowadays, it has been used combined immunosuppressant in the maintenance therapy, such as Mycophenolate Mofetil or Sodium and Sirolimus, because it is known that it improves the long-term graft survival and reduces the side effects that causes the drug itself[1-3]. Some of the side effects that can produce this drugs are: gastrointestinal alterations such as diarrhea, vomiting, dyspepsia; acne, moon facies, buffalo hump, and gingival hyperplasia[2].

Concerning to gingival hyperplasia or gingival overgrowth, as it is known, this is an alteration of the gingiva, in which increases its volume and size of the tissue. The cause of gingival overgrowth by immunosuppressive drugs its not yet known or established [4]. However, its hypothesized the presence of a fibroblast profile with abnormal susceptibility[5]; which is characteristic of the gingival enlargement, where the histopathological lesion shows a great amount of fibroblasts, abnormal amount of connective tissue stroma with overproduction of collagen, plasma

cell infiltration, increased number of inflammatory cells and increased degree of vascularization cells[6].

Nevertheless, it produces aesthetical alterations, which the patient doesn't like, and want a solution to this problem. Then, there are some non-surgical treatments that can be done in order to avoid surgery, for example: improving the oral hygiene, changing the medication the patient is taking, prophylaxis, root scanning and planning and watch how the inflammation decreases or responds to it [7, 8]. But, when the non-surgical treatment doesn't resolves completely the gingival overgrowth, it is necessary a surgical approach, which is gingivectomy and gingivoplasty [7].

Anyway, transplanted patients cannot stop taking the immunosuppressive drugs and then, they have an immune system that isn't able to respond completely which may contribute to the proliferation and colonization of bacteria and the increment of the plaque accumulation, but its not yet established completely. Then, it's important to share these findings to the science and academic community in order to have further studies in this theme.

CLINICAL CASE DESCRIPTION

Female patient of 20 years old which attends to the Faculty of Dentistry in the University of Cartagena because of esthetically non-conformity with the size of her teeth. During the examination, it is found the

presence of thickened gum in the anterior section of the oral cavity, from tooth 15 to 25; and presence of plaque accumulation especially in the anterior section. The subject refers to have neither pain at all, nor bleeding during brushing. (Fig-1.) She informs to have a kidney transplant 4 years ago from a clinically dead donor, and is under immunosuppressive therapy with Sirolimus 1mg in the morning every 24 hours, and Mycophenolate Sodium (Myfortic) 360mgs every 12 hours. Also, refers to have been intervened with a gingivectomy and gingivoplasty 2 years ago but now realizes the teeth smaller than that time. The possible diagnose is drug-induced gingival overgrowth. Its then submitted to the nephrologist in order to see if the medication can be changed but the response was negative because that was the best pharmacological therapy since 2011 that can reduce risk factors and have less side effects.

Therefore, it was done a prophylaxis and root scanning and planning but the inflammatory response stood the same, no changes where observed. So, a surgical approach is necessary in order to solve this alteration. A gingivectomy and gingivoplasty was performed in the gingiva of teeth 15 to 25, with previous informed consent signed. The procedure was done under local anesthesia; initially it was performed internal bevel incision with manual scalpel and took a tissue sample of the gingiva for further histopathological study, then it was done an outer bevel incision performed with an electrosurgical unit until the excess of gingival tissue was removed. The procedure was performed without complications and only few bleeding was presented which was easily controlled, and some stitches where placed to prevent the interdental papilla to fold. (Fig-2.)

The histopathological study showed hyperplasia of the lining epithelium, at the level of the lamina propria its observed chronicle inflammation and fibrosis of the connective tissue. (Fig-3.) The final diagnosis is fibrous gingival hyperplasia, which in clinical context may be in relation to induction by drugs.

Furthermore, after 15 days of post-operative period, the stitches were removed and not only it was observed a good healing and response to the surgical therapy, but also it was evidenced a bigger size in the teeth.



Fig-1: Initial teeth of the patient, which can be observed the small size of them.



Fig-2: The antero-superior teeth after the gingivectomy and gingivoplasty in the tooth 15 to 25, with the presence of stitches in the interdental gingiva to prevent them from folding upwards. It can be noticed bleeding control and bigger size of the teeth.

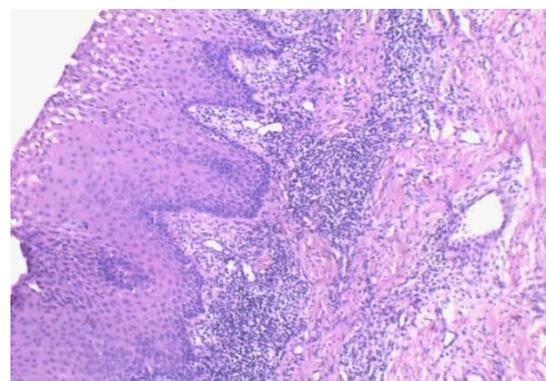


Fig-3: The histopathological study shows hyperplasia of the lining epithelium, and at the level of the lamina propria its observed chronicle inflammation and fibrosis of the connective tissue

DISCUSSION

Different types of drugs produce drug-induced gingival overgrowth, however, the ones that had showed the most prevalent and important gingival enlargement are due to anticonvulsants, antihypertensive and immunosuppressants [6, 7]. Bondon *et al* found that most drug-induced gingival enlargement occurs in men (58,5%) or people older than 40 years (71,4%), which then doesn't happens with

the patient shown below because in this case its a 20 year old woman [4].

However, in the present case its evidenced a gingival overgrowth induced by Sirolimus, which is a rapamycin type inhibitor immunosuppressive [3] used as a maintenance therapy in kidney transplants. Therefore, studies have showed that gingival overgrowth associated with renal factors, independently of the immunosuppressive regimen used has a prevalence rate of 47% [1]. Nevertheless, studies have shown that drug-induced gingival overgrowth frequently occurs after 1 or 3 months after initiating the immunosuppressive therapy [4], which then agrees with this case because the patient have been under immunosuppressants during 4 years.

However, studies have shown that Sirolimus is a immunosuppressive drug that has the least cases found to produce gingival overgrowth in comparison with Tacrolimus or Cyclosporine-A, which are the most commonly used drugs that can reduce the greater amount of risk factors [1]. But, Sirolimus is not the only drug the patient is taking, then, Mycophenolate sodium and Sirolimus may, combined, could produce gingival enlargement. Also, some researchers have found no link between the serum level and dosage of the immunosuppressant and the severity of the gingival overgrowth [1].

In this case, it can be noticed that the teeth of the patient at first sight didn't appeared to have gingival enlargement, it was mostly thought that the size of the teeth were small since eruption. However, after it was clinically examined and treated non-surgically it was observed that the diagnosis could possibly be gingival overgrowth.

Although, several investigators have found a relationship between the amount of plaque found in oral cavity and the presence of gingival overgrowth, which then immunosuppressive drugs could be secondary or exacerbate the gingival enlargement already produced by the plaque-induced inflammation [1, 6, 8]. This could be supported by Mishra et al and Tejnani et al, that said having good oral hygiene and significant plaque control will reduce gingival inflammation and may help the evolution in the increase of gingival overgrowth [9, 10].

Furthermore, Moffit et al in 2012 observed that the average recurrence rate in their cases were of 34% after 18 months of post-operative period from the gingivectomy[7]; which then agrees with this case because the patient have had gingivectomy and gingivoplasty 2 years ago but it occurred again.

In conclusion, drug-induced gingival overgrowth, specially, by immunosuppressive drugs can be unnoticed clinically but tends to enlarge in a long period of time using the drugs. Preferably, its

recommended to change the medication but if its strongly necessary upon the patient life then surgical treatment is by far the best solution to it, taking into account that it may reoccur several years later. However, patients with transplants must be treated multidisciplinary along with different professional because they need special attention and the best solution with the least invasive treatment. Nevertheless, studies upon Sirolimus and Mycophenolate side effects should be started so the association between gingival overgrowth and immunosuppressant therapy with Sirolimus and Mycophenolate can be clearly defined and explained.

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