Histopathological Findings of Uncomplicated Hair Transplant for Male Androgenetic Alopecia: Can Lichen Planopilaris Features Be Present?

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Keywords

Alopecia · Autologous transplant · Donor site transplant · Histopathology

Abstract

Introduction: Insufficient hair growth after hair transplant, as well as erythema and perifollicular scaling, may be diagnosed as lichen planopilaris and treated as such based on clinical and histopathological findings. The purpose of this study is to observe graft biopsies of patients after uncomplicated hair transplants and to discuss if histological findings are enough to diagnose lichen planopilaris. **Methods and Results:** Eight patients diagnosed with androgenetic alopecia who were submitted to hair transplant were enrolled. In each of the participants, a scalp biopsy was performed in the receptor area and in the adjacent area. Biopsies were performed between 6 months and 1 year after surgery. Exams were analyzed by 3 pathologists. The *t* test was performed

for paired observations, comparing the transplanted and the nontransplanted area for lymphocytic infiltrate and fibrosis. The significance level was considered as 5% ($p < 0.05$). Four of 8 participants had perifollicular lymphocytic infiltrate, from moderate to dense intensity in the recipient area. Fibrosis was seen in 6 patients. These findings were not seen in the control area. **Conclusions:** It is questioned whether lymphocytic infiltrate and fibrosis may be expected in patients who are submitted to normal hair transplants.

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Introduction

Androgenetic alopecia (AGA) is a noncicatricial type of hair loss with progressive miniaturization of the hair follicle resulting in an insufficient coverage for a bald area. It is the most common type of hair loss in men and women [1].

Color version available online

Fig. 1. Lymphocytic perifollicular infiltrate around isthmus.

Color version available online

Fig. 2. Perifollicular fibrosis.

Different types of treatments have been used over the decades, including minoxidil and finasteride, but only a hair transplant is able to recover the area where hair has already been lost. Nowadays, the main techniques for hair transplant are follicular unit transplantation (FUT), when hair is extracted from a strip in the occipital area, and follicular unit extraction (FUE), when follicular units are extracted one by one using a small punch from the donor area. In both situations, hair is implanted into the recipient area with small forceps or implanter devices [2]. The results vary according to surgeons' experience and individual characteristics of patients [3].

Even though it is a very popular procedure, normal findings on clinics, trichoscopy, and scalp biopsies after hair transplant are scarce in the literature so far. Some aspects of its evolution may mimic primary cicatricial alopecia (PCA) and confuse even experienced professionals.

Frontal fibrosing alopecia (FFA) and lichen planopilaris (LPP) are post transplant complications that have been reported by Kossard and Shiell [4] and Crisóstomo et al. [5]. Diagnoses in these cases were made by clinical presentation, with diffuse coalescing areas of hair loss, diffuse hair thinning, and perifollicular erythema, and mainly confirmed through histopathology [5–7].

Considering that histopathological findings of normal hair transplants are not described, this study aims to analyze biopsies of scalps with implanted hair grafts after hair transplant for AGA in patients who have had a normal outcome of their surgeries. We compare these histology findings with the adjacent area of the same patient, not

submitted to the procedure, and discuss features of LPP biopsies in order to make an accurate diagnosis of this possible complication.

Materials and Methods

This is a prospective study developed at the hair transplant department of Hospital do Servidor Público Municipal de São Paulo. All patients agreed to participate and signed an informed consent form. Terms of good practice were observed, and ethics approval was received from the Institutional Review Board (No. 2.810.198).

Patients were included after being diagnosed with AGA through a clinical exam by dermatologists experienced on hair diseases. No clinical signs or trichoscopy findings of LPP were observed in any of the cases previously to the procedure. They were submitted to hair transplant using FUE (patients 1–6) or FUT (patients 7 and 8) techniques from 6 to 12 months prior to the described biopsies.

After local anesthesia with lidocaine 2% with adrenaline, biopsies with a 4-mm punch were taken from a normal aspect hair graft on the recipient site and from an androgenetic area of the same patient, not submitted to the procedure. Specimens were cut in transverse sections and stained with hematoxylin/eosin (HE). Histopathologic criteria analyzed were inflammatory lymphocytic infiltrate and fibrosis.

Alterations were only considered when these findings were perifollicular and in isthmus level mainly. Values of 0, 1, 2, and 3 were attributed to each outcome as none, mild, moderate, and severe, respectively, based on comparison among biopsies and pathologists' personal experience. The results were analyzed by 3 different experienced pathologists (NV, CH, and NM), 2 of them were blind (NV and CH) and the third, non-blind (NM).

After that, a consensus of the 3 pathologists for each of the 4 outcomes was taken. Since it was not a completely objective scale, if all 3 did not agree on a case, the majority of the opinions were

Table 1. Findings of the study

Patient	Gender	Age, years	Time between transplant and biopsy, months	Transplanted area			Nontransplanted area (control)		
				Pat 1 (NV)	Pat 2 (CH)	Pat 3 (NM)	Pat 1 (NV)	Pat 2 (CH)	Pat 3 (NM)
1	M	29	12	0	0	+	0	0	0
Inf Fib				0	++	0	0	0	0
2	M	36	7	0	0	0	0	++	0
Inf Fib				+	++	0	0	+	0
3	M	36	7	+	+	+	0	++	0
Inf Fib				+	+	0	0	+++	0
4	M	39	7	+	+++	0	0	0	0
Inf Fib				+	+++	0	0	++	0
5	M	61	12	++	0	0	0	+	0
Inf Fib				+	++	+	0	0	0
6	M	46	6	++	+++	+++	0	0	0
Inf Fib				+	+++	0	0	++	+
7	M	46	6	+	+	++	0	0	0
Inf Fib				++	++	+	0	0	+
8	F	50	9	+	++	++	0	0	0
Inf Fib				+	++	0	0	+	0

M, male; F, female; Pat, pathologist; Inf, inflammation; Fib, fibrosis; 0, none; +, mild; ++, moderate; +++, intense.

considered (2 out of 3). Statistical analyses were performed, and we evaluated whether the distribution could be considered normal by using the Shapiro-Wilk test for normality. If they were normally distributed, we performed the *t* test for paired observations, comparing the transplanted and the nontransplanted area for lymphocytic infiltrate and fibrosis. The significance level was considered as 5% ($p < 0.05$).

Results

Seven male patients and 1 female patient, between 29 and 61 years (mean age 42.9 ± 10.0), phototypes II–V, Hamilton-Norwood II–VI, were selected. All of them were transplanted at the frontal area.

In 4 of the 8 patients (4, 6, 7, and 8), moderate to intense lymphocytic inflammation was seen after hair transplant in the designated area, shown in Figure 1. In the control area, not submitted to the procedure, these findings were not observed. Moderate to intense fibrosis was seen in 6 of the 8 patients (2, 4, 5, 6, 7, and 8) after hair transplant, and in the majority of them (2, 4, 5, 7, and

8), shown in Figure 2, fibrosis was not detected in the control area.

In one of the patients (3), mild lymphocytic inflammation and fibrosis were also seen by at least 2 pathologists in the transplanted area. In the control area, 2 of them did not see any alterations. All findings are shown in Table 1.

Discussion

Successful hair transplants are usually not submitted to biopsy. Clinical aspects, considering erythema and scaling, are not usually described even though they may be seen in normal patients due to recent surgical trauma (authors' experience) and other conditions, such as AGA and seborrheic dermatitis. It may cause an erroneous diagnosis of LPP.

Our cases for this study were chosen based on the absolute lack of any clinical signs of erythema and scaling in the biopsied site. Considering histopathological exams, in a previous study, inflammation, mainly lymphocytic, and

fibrosis were found in 70% of normal AGA cases with moderate and intense inflammation appearing in 36% of the patients [8].

In our cases, these characteristics were not related exclusively to AGA or seborrheic dermatitis because we have seen lymphocytic perifollicular inflammation and fibrosis in the transplanted area but not in the control area, with AGA but not submitted to hair transplant. Thickening of the dermal sheath and a denser vascular network were seen in a previous study, 2 and 5 years after FUT in 2 normal hair transplants. Anti-CD31 and anti-collagen I staining were positive in immunohistochemistry, showing increase in vascularization and size of grafted follicles [9].

In FUE performed in 2 patients with a normal outcome, a significant infiltration of B and T lymphocytes as well as macrophages could be observed in the infundibulum of transplanted hair 6 months after the procedure. Anti-CD20, anti-CD3, and anti-CD68 staining were positive [10].

After surgical trauma, inflammation was present in the whole process of wound repair. Neutrophils, macrophages, and lymphocytes can be found. Lymphocytes enter the wound relatively late, most of them are T cells, and the number of T cells can regulate wound repair [11].

Our results reinforce that lymphocytic perifollicular inflammation at isthmus level and fibrosis may also occur in uncomplicated hair transplants for AGA since they were present in about 50–60% of our cases in histopathology. Peri-infundibular inflammation was also seen in some cases and may be useful in future studies considering the difference between post-inflammatory infiltrate and LPP, but until now we cannot assume that since nothing has been described in the literature.

Thirty patients have been described so far with the diagnosis of LPP or FFA after hair transplant, even though several procedures are being performed everyday throughout the world [4–7]. Diagnosis was suspected by symptoms such as itching in 9 patients and burning and pain in 2 patients. Recess of the frontal line was observed in 5 patients, one of them also presenting loss of the eyebrows. Diffuse areas of hair loss were present in 12 patients, including the recipient and donor areas. Loss of follicular ostia was seen in 8 cases. Nineteen patients did not achieve expected density after the procedure, and the majority of them had clinically < 50% of implanted hair growth.

Erythema, perifollicular scaling, and miniaturization were the only findings in 18 patients. All of them had their diagnosis of LPP confirmed only by biopsy and clinical aspects. Our cases differ from the reported ones mainly because of its clinical presentation, especially because no

loss of follicles was observed in 6 months to 1 year of follow-up, even though it is a short period of time for definitive conclusions. In some cases, erythema and scaling were seen, but the good outcome of these hair transplants showed that they might be due to the other conditions described above, such as seborrheic dermatitis. The 18 cases described in the literature that were only diagnosed by these particular aspects may show overestimation of the LPP after transplant.

Considering the time between hair transplant and biopsies, in cases described in the literature, signs of LPP appeared from 3 months to 9 years after the procedure. In our case series, biopsies were taken from 6 to 12 months after hair transplant. This fact may favor the presence of the infiltrate. Further studies with biopsies after longer periods of follow-up will be needed to study for how long these findings will be present. All of our patients had normal outcomes of their surgeries so far, even when abnormal findings were seen in histopathology.

Conclusions

Gold standard confirmation for cases with clinical suspicion of LPP is histopathology. However, this exam may be very similar to the findings on post-uncomplicated hair transplant biopsies, especially in the first year. Clinical aspects are fundamental, especially if diffuse areas of hair loss are present. Excess of biopsies on discrete erythema and perifollicular scaling may be avoided to prevent false diagnosis of LPP. Further studies with a larger number of cases and considering biopsies of patients more than 1 year after the procedure may be necessary in order to determine if the inflammatory infiltrate is still present and may help in the diagnosis of post transplant LPP, along with clinical features such as graft loss.

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Statement of Ethics

All patients agreed to participate and signed an informed consent form. Terms of good practice were observed, and ethics approval was received from the Institutional Review Board (No. 2.810.198).

Disclosure Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Andressa Silva Alcântara: conducted the study. Aline Donati: analyzed data and involved in critical review. Maria Victoria Suárez: designed the research study. Ivan José Netto Pereira: performed surgeries and collected materials. Neusa Yuriko Sakai Valente, Nilceo Schwery Michalany, and Cristiano Luiz Horta de Lima Jr.: biopsy interpretation. Leticia Arsie Contin: wrote the paper, performed surgeries, collected data and exams, and analyzed the data.

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