

Case

PRESENTATION

Post-Sclerotherapy Hypertrichosis

Two case reports, a local survey of incidence and a discussion of pathogenesis*

A LIM¹ AND K PARSI²

¹Department of Dermatology, St George Hospital, Kogarah, NSW, Australia and ²Skin and Cancer Foundation Australia, Darlinghurst, NSW, Australia.

CASE REPORTS

Case One. A 57 year old post-menopausal Caucasian female, Gravida3, Para3, presented for compression sclerotherapy of bilateral varicosities of the lower limbs. She had no significant medical or surgical history other than recent onset of non-insulin dependent diabetes mellitus for which she was taking metformin hydrochloride 500 mg daily. She was not on any hormone replacement or iron supplements and there was no history of smoking or regular alcohol consumption. She had no previous recorded problems in relation to excess body hair. She did complain of previous allergies to shellfish.

Clinically, she had trophic skin changes on both medial ankles, bilateral varicosities of the long saphenous veins [LSV], prominent varicosities of the antero-lateral thigh veins, and tortuous varices of the lateral thigh, lateral calf, and infra-patellar veins.

She also had prominent vulvar varicosities, and widespread venulectases and telangiectases (C4s EpA 1R, 2R, 3R, 5R, 17R PR)¹. Doppler examination revealed a bilateral Hach grade IV incompetence of LSVs with gross Saphenofemoral junction [SFJ] reflux. She also had bilateral incompetence of the perforators of popliteal fossae. Both Saphenopopliteal junctions [SPJ] were competent.

Echosclerotherapy procedure was performed treating the right SFJ followed by the trunk of LSV and its distal tributaries. The right anterolateral thigh vein was treated a week later. She remained in a class II graduated compression stocking for a period of two weeks. Two weeks later a similar procedure was repeated on her left leg.

ABSTRACT

Hypertrichosis is a very rare complication of sclerotherapy. There have been only seven documented cases in three separate reports in the literature. We report two cases of localised hypertrichosis following compression sclerotherapy. We also present the results of a telephone survey of 30 practising sclerotherapists in New South Wales, Australia. The pathogenesis of this condition remains unknown. Recent advances in molecular biology have demonstrated a role for various inflammatory mediators, growth factors, neuropeptides and cytokines in the stimulation of hair follicle growth. We review recent work in this area in an attempt to reconcile our current understanding of the effects of inflammatory mediators with the pathogenesis of post-sclerotherapy hypertrichosis.

The patient progressed satisfactorily and reported no adverse effects in the post-treatment period other than a patch of hair growth in the left anterior thigh eight weeks after the treatment. On examination, there was a 10 x 5cm patch of terminal body hair measuring 1 cm in length occurring over the recently treated left antero-lateral thigh varicosity on a background of mild hyperpigmentation. The appearance of hypertrichosis was striking in that it occurred over a minimally hair bearing area of the thigh. The corresponding area of the contra-lateral thigh revealed some mild hemosiderin staining but showed no evidence of excessive growth of terminal hair. Repeat Doppler examination showed that the truncal and axial varicosities of both legs were well sclerosed with no evidence of reflux over the area affected by hypertrichosis.

Three months later, the hypertrichosis had completely resolved. The underlying varicosity was no longer present with normal vellus hair growing on the overlying skin, similar to the contralateral thigh.

Address correspondence and reprint requests to: Dr Kurosh Parsi, P0 Box 419, Wentworth Building, University of Sydney NSW 2006 Australia. Tel: +61 2 9386 0211 Fax: +61 2 9386 0258

* English translation reprinted with permission from *Phlebologie, Annales Vasculaires* 1999; 52(3):335-339

Case Two. A 43 year old woman of Chinese background Gravida 3, Para 2 presented with a 21 year history of varicose veins present since her first pregnancy. She had no significant medical or surgical history. She was taking no medications and was not on any hormonal contraception. There was no history of smoking or alcohol consumption. However, as in case one, she complained of previous allergies to shellfish in the form of generalized pruritis. She had no previous recorded problems in relation to excess body hair.

On examination, she had bilateral varicosities of the anterolateral thigh vein along with tortuous varicose tributaries communicating with the LSV below the knee. Scattered areas of venulectases and telangiectases were also present (C2aEpA1R, 3R, 5R, 17R, 18R PR)¹.

The initial Doppler examination done at our practice suggested bilateral SFJ incompetence. Subsequently, a color duplex examination was performed at the local radiology practice. Despite our Doppler study, the duplex examination reported competent bilateral SFJ and SPJ.

This patient's treatment was started with sclerotherapy of the left anterolateral thigh vein followed by the left posterior arch vein. She remained in a class II graduated compression stocking for a period of two weeks. Retained blood was evacuated a week later. A similar procedure was then repeated on the right lower limb.

Three months later she developed localized hypertrichosis affecting her left lower leg over the sclerosed posterior arch vein. On examination, there was a 10 x 2cm patch of terminal body hair measuring 1 cm in length (photos 1-4). This occurred over a segment of a partially sclerosed anterolateral varicosity with deep haemosiderin staining of the overlying skin. Doppler and duplex examination showed left SFJ incompetence with incompletely sclerosed anterolateral thigh vein.

A SURVEY OF NSW SCLEROTHERAPISTS

Due to the apparent rarity of this complication, a screening survey was considered appropriate. A telephone survey was conducted amongst full-time practising sclerotherapists in Sydney, Australia (table 1). The listing of sclerotherapist was obtained from the 1998 registry of members of the Sclerotherapy Society of Australia [SSA]. Participants were asked whether they had encountered any cases of localised hypertrichosis post-sclerotherapy.

Table 1: Summary of survey results

Total number of sclerotherapists contacted	36
Total number of respondents	30
Percentage of respondents	83 %
Number of cases of localised hypertrichosis encountered	0

The rarity of post-sclerotherapy localised hypertrichosis is underlined by the absence of any anecdotal reports amongst full-time practicing sclerotherapists in New South Wales, Australia (SSA registry). Of the 36 registered members of SSA, 30 responded to the survey. Of the six members who were unavailable, three were not practicing in New South Wales, giving an effective response rate of 91%. Of those who responded, only one was aware of previous reports of post-sclerotherapy hypertrichosis and none had personal experience with this particular complication.

DISCUSSION

Commonly encountered medium term complications of sclerotherapy include hyperpigmentation and telangiectatic matting. Post sclerotherapy hyperpigmentation is the result of haemosiderin deposits² and its incidence has been reported any where from 11% to 80%^{3,4}. The incidence of telangiectatic matting is around 16% in a retrospective analysis involving a patient sample of 7200⁵. There are only seven documented of hypertrichosis as a post-sclerotherapy complication^{6,7}. STD was the sclerosant used in 4 cases while an iodine-based sclerosant was used in the remaining 3 cases. In all cases, the acquired hypertrichosis was transient and resolved within a period of four months after its onset. Accordingly, warning of post-sclerotherapy hypertrichosis is not a routine feature in patient information and consent documents.

The development of localised or diffuse excess hair may be determined genetically as a normal familial trait, or may occur in association with many inherited syndromes as well as in association with the use of certain medications. It is well known that localised hypertrichosis can occur at sites of trauma, scar and occupation-related sites of irritation⁸. There have been sporadic examples of documented localised hypertrichosis following the application of plaster cast in the treatment of fractures^{9,10}. Reports of transient circumscribed hypertrichosis following small pox and chicken pox vaccinations also exists in the literature^{11,12}. Peripheral nerve damage from major thoracic surgery can be followed by unilateral hypertrichosis that occurs in the absence of increased blood flow¹³. Of more relevance to phlebologists, localised hypertrichosis has also been reported in patients following superficial thrombophlebitis and deep venous thrombosis [DVT], as well as in patients with chronic venous insufficiency following surgical treatment^{14,15}.

Does the choice of sclerosing agent have a role? We know that hypertrichosis is a well-known complication of certain medications. For instance, generalized hypertrichosis is associated with the use of cyclosporin, corticosteroid therapy and some antihypertensive drugs¹⁶. All cases of reported post-sclerotherapy hypertrichosis follow the use of either STD or iodine based sclerosants. We are unaware of hypertrichosis associated with other sclerosants in the context of sclerotherapy. There is no evidence that either STD or iodine-based sclerosants have an intrinsic effect on

hair growth. Rather, stimulation of hair growth is more likely to be a secondary effect of the inflammatory reaction induced by the sclerosant.

The inflammatory process induced by the sclerosing agent induces endothelial damage. Endothelial damage leads to the release of heparin and other mast cell factors that both promote the dilation of existing blood vessels and stimulate angiogenesis¹⁷. Angiogenesis is mediated by the release of a number of important cytokines such as basic fibroblast growth factor [bFGF] and vascular endothelial growth factor [VEGF]¹⁸. The relevance of angiogenic cytokines in the pathogenesis of hypertrichosis was recently highlighted by Lachgar and colleagues who showed that VEGF serves as a growth factor for hair follicle dermal papilla cells¹⁹. VEGF might contribute to hair growth either by acting directly on papilla cells or by stimulating local vascularisation¹⁹.

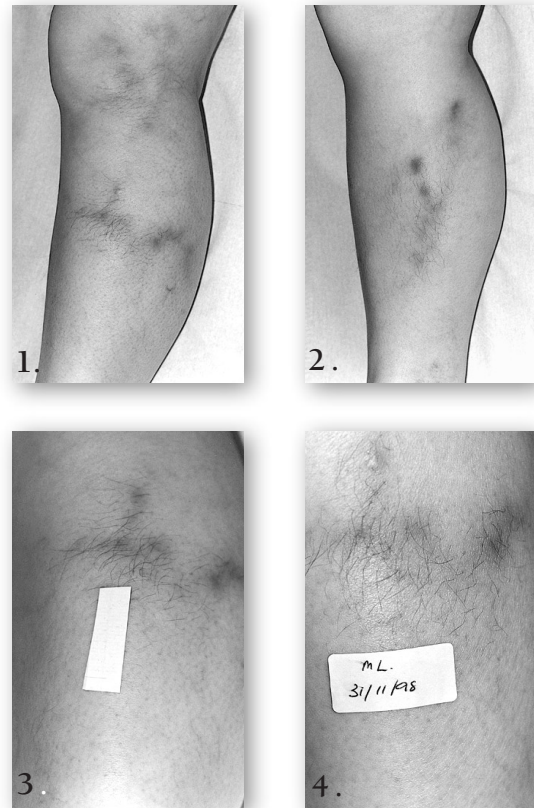
Histamine release from the mast cells may also play a role in the development of post-sclerotherapy pigmentation and hypertrichosis observed in both patients²⁰. Sclerotherapy produces some degree of peri-vascular inflammation which is presumed to promote degranulation of perivascular mast cells²¹. Released histamine leads to endothelial cell contraction, which results in widening of endothelial gaps through which extravasation of red blood cells can occur. This leads to post-sclerotherapy hemosiderin deposition and pigmentation.

Histamine release from the mast cells has also been associated with release of neuropeptides such as Calcitonin Gene Related Peptide [CGRP] and possibly Substance P [SP] from sensory nerve fibres²². These neuropeptides released from afferent nerves in the skin are potent vasodilatory agents and may have a direct effect on the isthmus and bulge region of the hair follicle²². Subcutaneous implanted pellets releasing SP induce anagen²³. Even subnanomolar concentrations of SP significantly stimulate hair follicle keratinocyte proliferation in murine skin organ culture²⁴.

Both our patients had a past history of allergic reactions to shellfish. Iodine allergy has been anecdotally associated with allergy to shellfish although the link is tenuous and not supported by convincing clinical studies. None of the patients developed a clinically detectable allergic reaction during or following the treatment. It is possible, however, that a subclinical release of histamine followed by release of neuropeptides may have contributed to the hair growth.

Interestingly, both patients had never shaved or used any forms of depilatory procedures. The three cases reported by Marks also involved women who did not shave or use

hair removers⁷. Clearly the pre-requisite for detection of hypertrichosis is for sufficient time to elapse for the hair follicle to grow and convert vellus hair into coarser and longer terminal hair. Should this process be interrupted by



Figures 1 - 4: Localised hypertrichosis accompanied by hemosiderin pigmentation 3 months post-sclerotherapy

hair removal procedures, then the hypertrichotic condition, being self-limiting, would go undetected. Hence it can be expected that the practice of regular hair removal by patients would lead to under-detection. We therefore contend that post-sclerotherapy hypertrichosis is likely to be more common than is generally recognised.

SUMMARY

We report two cases of post-sclerotherapy hypertrichosis. This condition appears to be a rare but possibly under-detected phenomenon. The exact pathogenesis of this phenomenon remains a matter of conjecture. It seems plausible that the release of inflammatory mediators such as histamine, angiogenic factors and neuropeptides may all contribute to the development of transient hypertrichosis. Further studies are needed to establish more precisely, the role of inflammatory mediators in the pathogenesis of this condition.

PROPOSED MECHANISM FOR POST-SCLEROTHERAPY HYPERTRICHOSIS

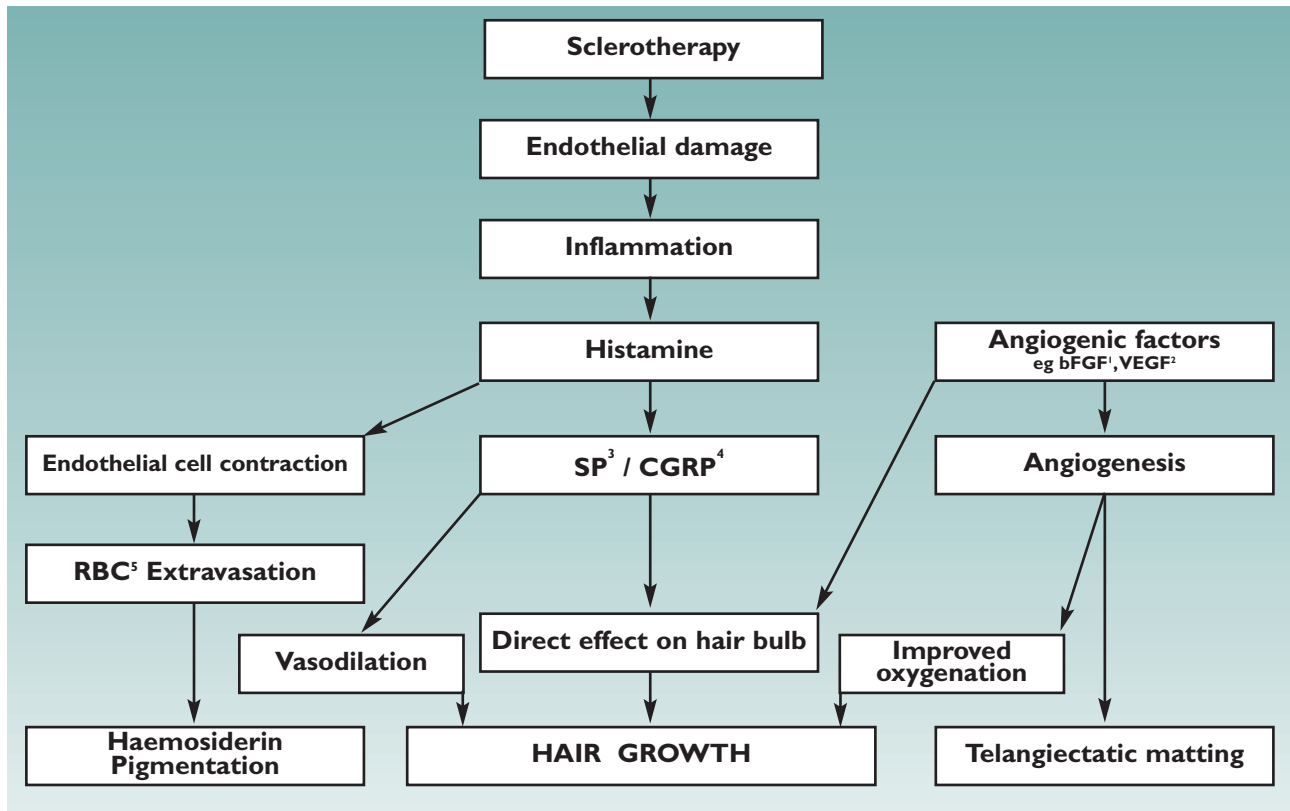


Figure A: Hypothetical pathway demonstrating the pathogenesis of post-sclerotherapy hypertrichosis. Well recognised post-sclerotherapy complications such as telangiectatic matting and haemosiderin staining are also represented.

¹ Basic Fibroblast Growth Factor ² Vascular Endothelial Growth Factor ³ Substance P ⁴ Calcitonin Gene Related Peptide ⁵ Red Blood Cell

REFERENCES

- Gloviczki P, Yao JST. Handbook of venous disorders. London: Chapman & Hall, 1996.
- Thibault P and Wlodarczyk J. Postsclerotherapy hyperpigmentation: the role of serum iron levels and the effectiveness of treatment with the copper vapor laser. *J Dermatol Surg Oncol* 1992;18:47.
- Weiss R and Weiss M. Resolution of pain associated with varicose and telangiectatic leg veins after compression sclerotherapy. *J Dermatol surg Oncol* 1990;16:333.
- Tretbar L L. Spider angioma: treatment with sclerosant injections. *J Kans Med Soc* 1978;79:198.
- Davis L T and Duffy D M. Determination of incidence and risk factors for post-sclerotherapy telangiectatic matting of the lower extremity: a retrospective analysis. *J Dermatol Surg Oncol*. 1990;16:327.
- Weissberg D. Treatment of varicose veins by compression sclerotherapy. *Surgery, Gynaecology and Obstetrics* 1980;151:353-356.
- Marks C G. Localized hirsuties following compression sclerotherapy with sodium tetradecyl sulphate. *Br J Surg* 1974;61:127-128.
- Dawber P P R, Ebling F J G, Wojnarowska F T. Disorders of hair: circumscribed acquired hypertrichosis. In: Champion R H, Burton J L, Ebling F J G, eds. *Textbook of Dermatology*. United Kingdom: Blackwell Science, 1998:2869-2953.
- Behrman H T. Diagnosis & management of hirsutism. *JAMA* 1960;172:1924-1931.
- Chang C H, Phillip R C. Ipsilateral post-cast hypertrichosis and dyshidrotic dermatitis. *Arch Phys Med Rehabil* 1995;76:97-100.
- Naveh Y, Friedman A. Transient circumscribed hypertrichosis following chickenpox. *Pediatrics* 1972;50(3):487-8.
- Kumar LR, Goyal BG. Pigmented hairy scar following smallpox vaccination. *Indian Journal of Pediatrics* 1968 35(245):283-4.
- Kobayshi S, Okuyama F, Tagaki K. Experimental studies on the hemitrichosis and the nervous influences of hair growth. *Acta Neurovegetativa* 1958;18:169-190.
- Schraibman I G. Localised hirsuties. *Postgrad Med J* 1967;43:545-547.
- Soyuer U, Aktas E, Ozesmi M. Postphlebotic localized hypertrichosis [letter]. *Archives of Dermatology* 1988;124(1):30.
- Epstein E. *Dermatologic Disorders*. In: Berkow R, Fletcher AJ, eds. *The Merck Manual*. NJ USA: Merck Research Laboratories page, 1992:2432.
- Folkman J and Klagsbrun M. Angiogenic factors. *Science* 1987;235:442.
- Arbiser J. Angiogenesis & the skin: A primer. *J Am Acad Dermatol* 1996;34: 486-497.
- Lachgar S, Moukadir H, Jonca F, Chaveron M, Bouhaddiou N, Gall Y, Bonafe JL and Plouet J. Vascular endothelial growth factor is an autocrine growth factor for hair dermal papilla cells. *J Invest Dermatol* 1996;106:17-23.
- Botchkarev VA, Paus R, Czarnetzki BM, Kupriyanov VS, Gordon DS, Johansson O. Hair cycle-dependent changes in mast cell histochemistry in murine skin. *Arch Dermatol Res* 1995;287:683-686.
- Goldman MP et al. Sclerosing agents in the treatment of telangiectasia: comparison of the clinical and histological effects of intravascular polidocanol, sodium tetradecyl sulfate, and hypertonic saline in the dorsal rabbit ear vein model. *Arch Dermatol* 1987;123:1196.
- Paus R, Peters EMJ, Eichmuller S and botchkarev V. Neural mechanism of hair growth control. *J Invest Dermatol Symp* 1997;2:61-68.
- Paus R, Heinzelmann T, Schultz KD, Furkert J, Fechner K, Czarnetki BM: Hair growth induction by Substance P. *Lab Invest* 1994;71:134-140.
- Paus R, Heinzelmann T, Robicsek S, Czarnetzki BM, Maurer M: Substance P stimulates murine epidermal keratinocytes proliferation and dermal mast cells degranulation in situ. *Arch Dermatol Res* 1995;287:500-502. ■