Nail matrix melanoma: consecutive cases in a general practice

"Melanoma writes its message on the skin with its own ink, and it is there for all to see. "

Dr Neville Davis. Modern concepts of melanoma and its management. Annals of Plastic Surgery 1978:1:page 628

Introduction

Nail matrix melanoma, otherwise known as subungual melanoma, is unique in that the actual primary cutaneous melanoma is occult, being covered by the nail-plate and the proximal nail fold. Fortunately the concealed melanoma may produce melanin which then appears as longitudinal pigmentation in the nail-plate. Thus melanin-producing nail matrix melanoma has a distinctive 'signature' to the informed observer.

Acral lentiginous melanoma was first described as a sub-group in 1976 by Reed (1). Prior to that Clark had proposed three histologic sub-types: Superficial spreading melanoma, lentigo maligna melanoma and nodular melanoma (2). About half of all hand and foot melanomas are of the acral lentiginous subtype. A Scottish study restricted to subungual melanoma showed that 45% were acral lentiginous, 27% nodular and 20% superficial spreading(3).

We present 2 consecutive cases of nail matrix melanoma from a general practice. The first patient was referred to the practice and the second patient was recommended to the practice by the first.

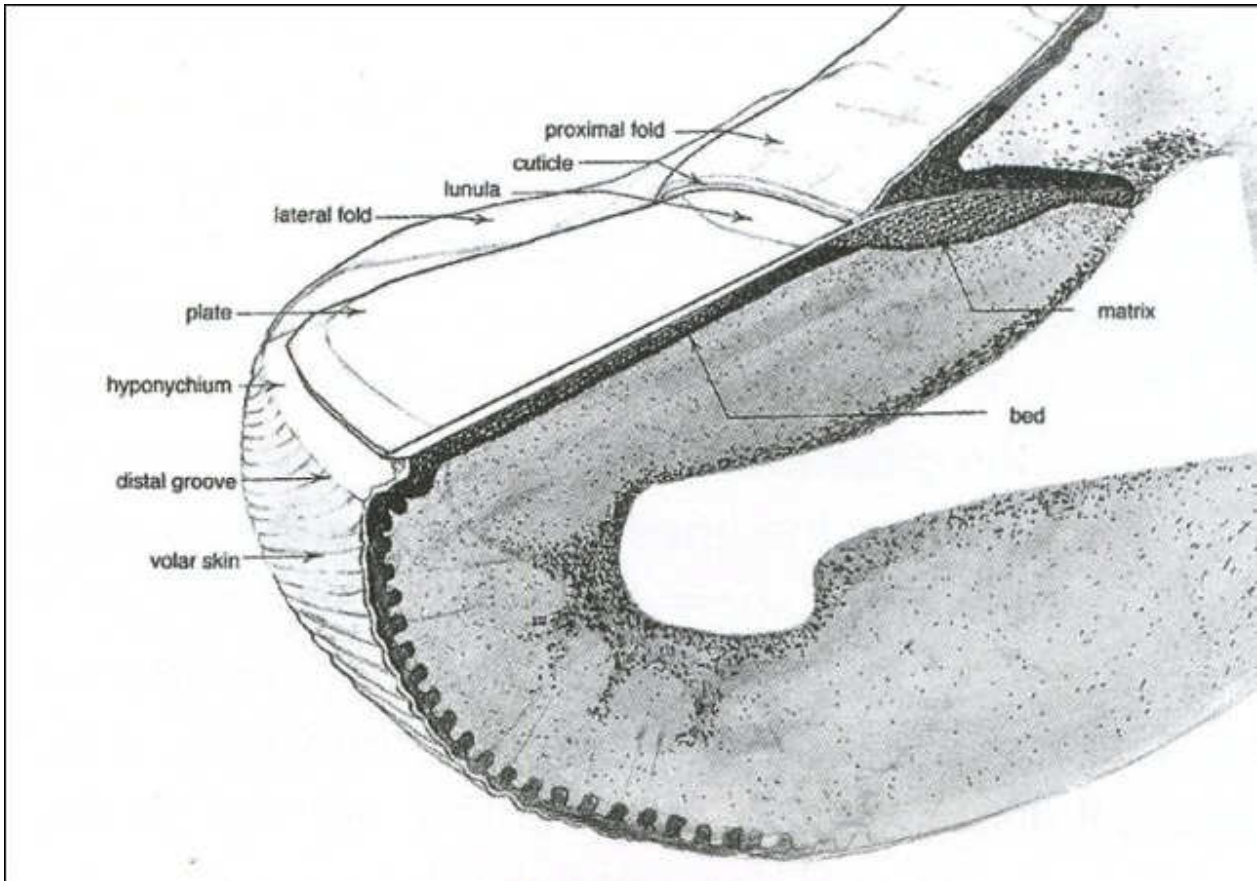

Figure 1: Anatomy of the nail plate. (Adapted from Ackerman and Boer, Histologic diagnosis of inflammatory skin diseases. An algorithmic method based on pattern analysis, 3rd edition)

Case report 1

A twenty-five year old high school science teacher was referred with a lesion on his right thumb nail (figure 2), arriving by a circuitous route. One of his teenage students had seen a photograph of a nail melanoma on a patient-education poster in the waiting room of a doctor's surgery and thought the photo looked like her teacher's thumb.

At first he was somewhat sceptical, but she persisted until he saw his GP, who referred him to a specialized melanoma centre. They in turn referred him to the general practice of author CR for a nail matrix biopsy because their preferred plastic surgeon had been temporarily incapacitated by an injury.

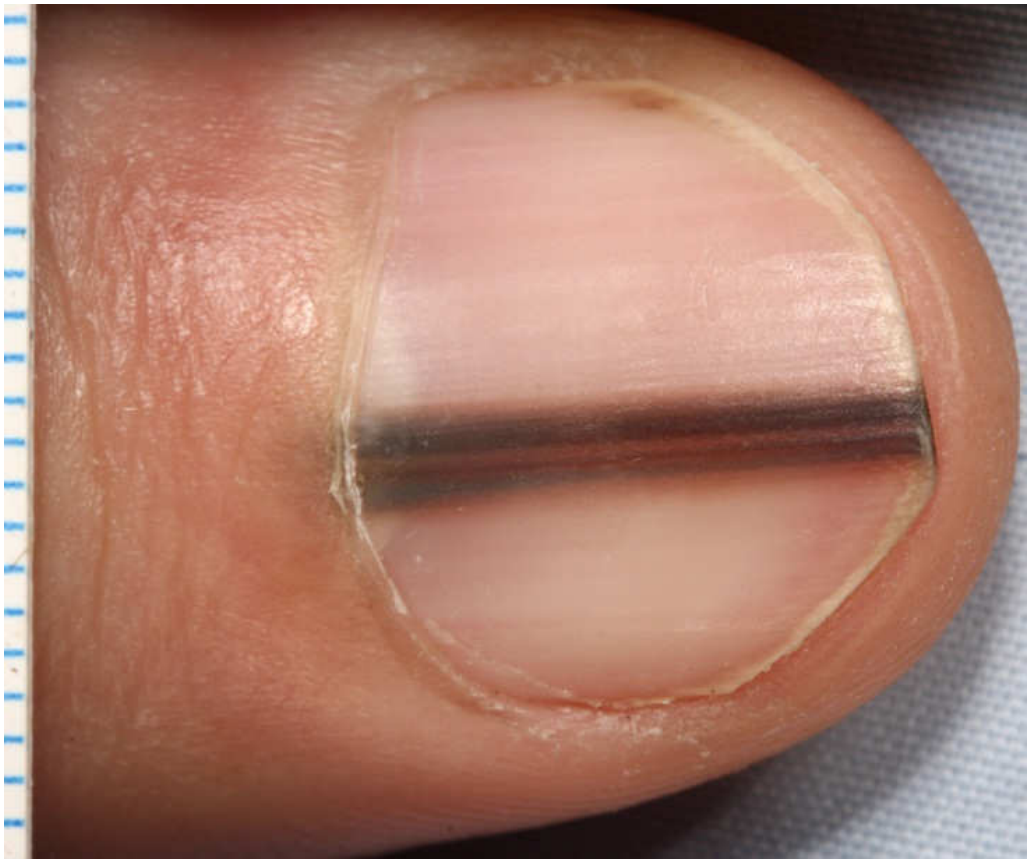

Figure 2: Close up image of longitudinal melanonychia, on the right thumbnail of a 25 year old man. This pigment band on the nail plate appeared and widened over the preceding ten months. Pigment is visible through the translucent cuticle and proximal nail fold (false Hutchison's sign) but there is no apparent pigmentation of these structures. The pigment band tapers from 3mm wide proximally to 2mm distally.

The patient had first noticed a fine band of pigment extending the full length of the nail 10 months earlier and it had become progressively wider since then.

Dermatoscopy of the surface of the nail plate (figure 3) revealed longitudinal melanonychia (also known as melanonychia striata) with lines parallel stretching from the proximal nail fold to the free edge of the nail. The parallel lines varied in width, colour (black, dark brown, light brown and gray) and interval. The pigmented band was wider proximally than distally, consistent with a growing lesion in the nail matrix.

Figure 3: Dermatoscopic image of the surface of the nail plate. Lines parallel vary in width, interval and colour. Colours present- black, brown and gray- are the colours of melanin. The overall band of pigment is broader proximally, consistent with origin from a growing lesion in the nail matrix.

Braun et al (4) have demonstrated how dermatoscopy of the free edge of the nail plate can be used to precisely predict tumor location in the nail matrix. Pigment located deeply in the nail plate (figure 4) corresponds to a tumor located in the distal nail matrix. (figure 5)

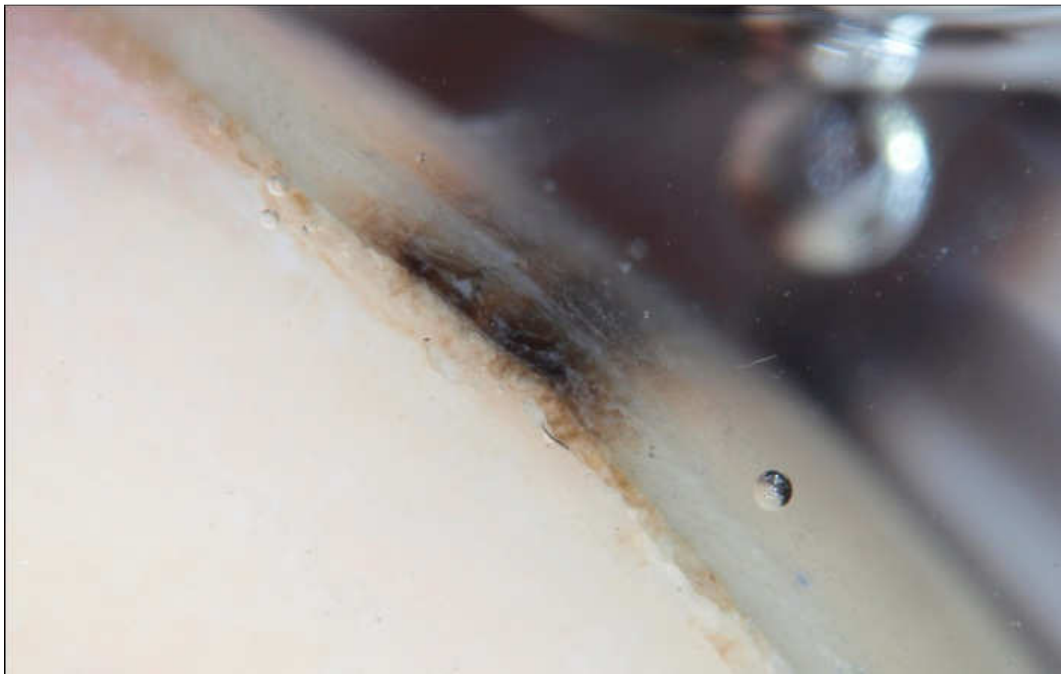

Figure 4: Dermatoscopy of the free edge of the nail plate shows that melanin has been preferentially incorporated into the deeper portion of the nail plate. This indicates that it is originating from a lesion in the distal portion of the nail matrix.

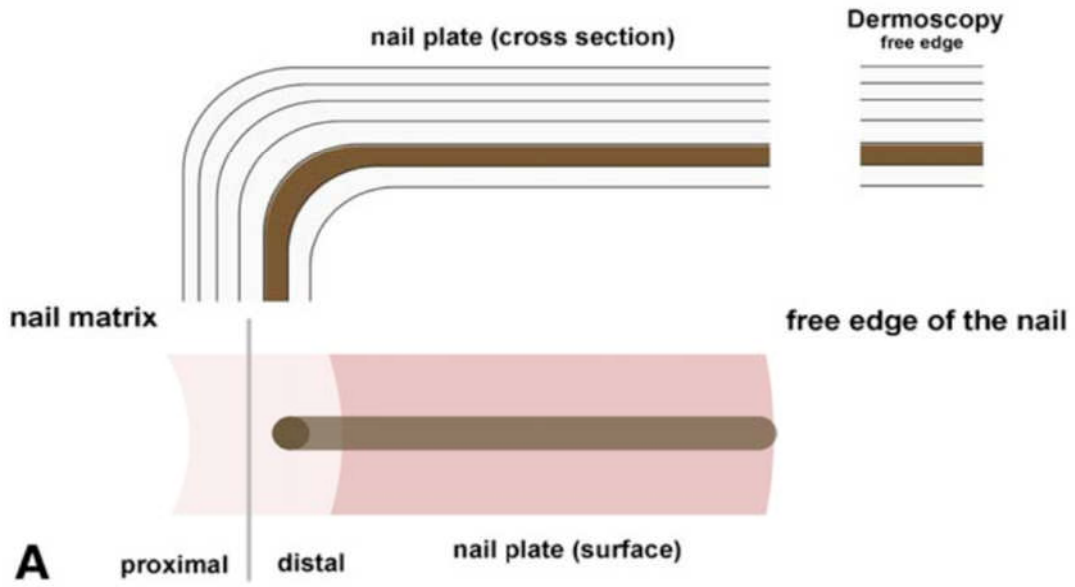

Figure 5: Melanin incorporated into the deep layers of the nail plate is produced by tumors of the distal nail matrix. (Adapted from Braun RP, Baran R, Saurat JH, Thomas L. Surgical Pearl: Dermoscopy of the free edge of the nail to determine the level of nail plate pigmentation and the location of its probable origin in the proximal or distal nail matrix. *J. Am. Acad. Dermatol.* 2006;55(3):512-513.)

A provisional diagnosis of nail matrix melanoma was supported by both the history of a new and progressively widening nail plate pigmentation and the dermatoscopy showing lines parallel of varying thickness interval and colour. The required diagnostic procedure of nail matrix biopsy was explained to the patient. He consented, understanding it was likely to result in permanent nail dystrophy.

The procedure was performed under sterile conditions in the operating room of the general practice. Anaesthesia was achieved using a digital block with 2% plain xylocaine, and a tourniquet was applied. An incision was made on each side of the proximal nail fold which was then separated from the nail plate by sweeping the scalpel blade over its surface. The proximal nail fold was retracted with two sutures, exposing that part of the nail plate overlying the nail matrix.

A 6mm biopsy punch was then used to fenestrate the nail plate overlying the predicted location of the tumor; the distal nail matrix in line with the longitudinal melanonychia (figure 6). The punch was rotated while applying gentle pressure. The circular incision was probed with the scalpel blade at

intervals until it was found to have penetrated at one point. The circular plug of nail was lifted away from the matrix with fine forceps used as an elevator. The incision through the remainder of the nail plate was completed using the scalpel, taking care not to incise the underlying mail matrix. The circular plug of nail plate was lifted out to reveal a densely pigmented lesion in the underlying nail matrix (figure 6). This was circumscribed with a 4mm biopsy punch and dissected from underlying periosteum with a scalpel blade. This achieved an excision biopsy of the entire visible pigmented lesion.

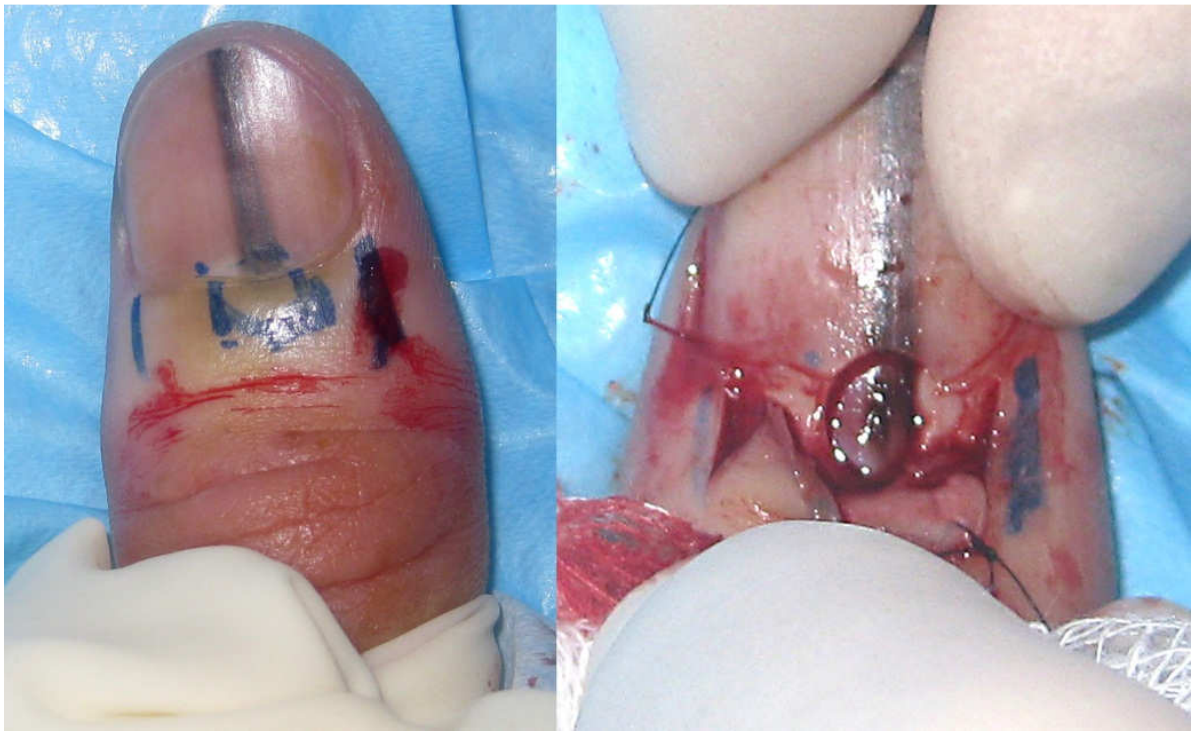

Figure 6: The image on the left shows the proposed incision lines on each side of the proximal nail fold. The marks in the centre are not for incision but indicate the anticipated location of the target lesion in the distal nail matrix. The image on the right shows the proximal nail fold retracted and a densely pigmented lesion in the nail matrix underlying a fenestration in the nail plate.

Both the excised nail matrix and the plug of nail plate were submitted in formalin. The laboratory was contacted to ensure the two different portions received the different processing they required. Histopathology (figures 7 and 8) revealed an increased number of atypical melanocytes in lentiginous array. There were prominent thick dendrites which were visible on H&E staining because of the amount of melanin they contained. Because it can be difficult to distinguish melanocytes from

keratinocytes, immunostaining was employed (figure 9) with the pan-melanoma antibody cocktail and, quoting from the pathology report, this showed "…both basal and suprabasal melanocytes with focal junctional confluence indicative of level 1 (in-situ) subungual melanoma."

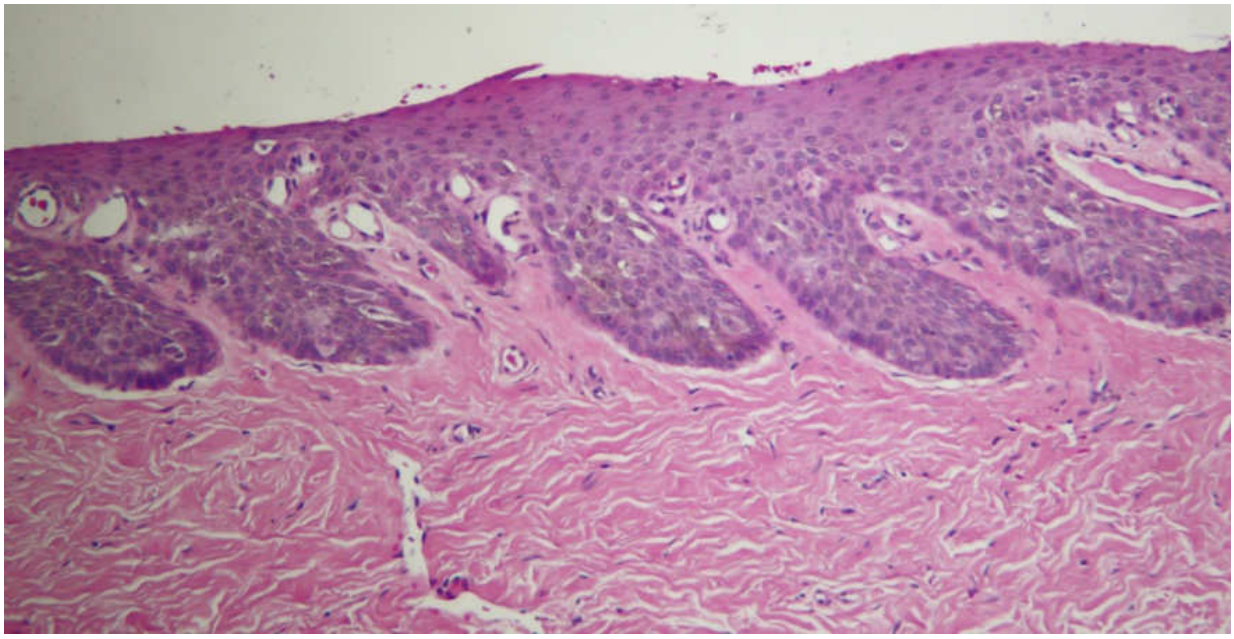

Figure 7: Low power micrograph of an H&E stained specimen of nail matrix from case 1. It is difficult to distinguish melanocytes from keratinocytes.

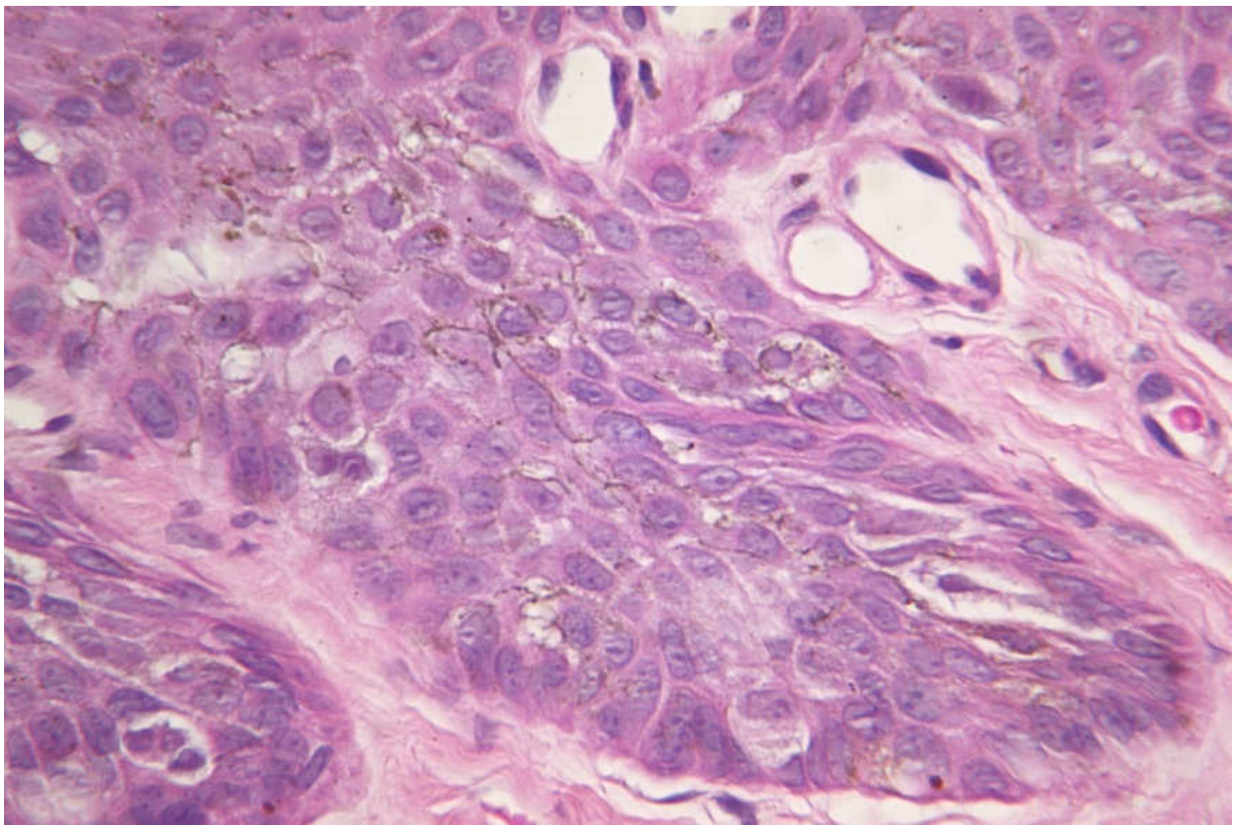

Figure 8: High power micrograph of the H&E stained section shown in figure 7 shows plump pale melanocytes at the dermo-epidermal junction with prominent heavily pigmented dendrites seen in the centre of the image.

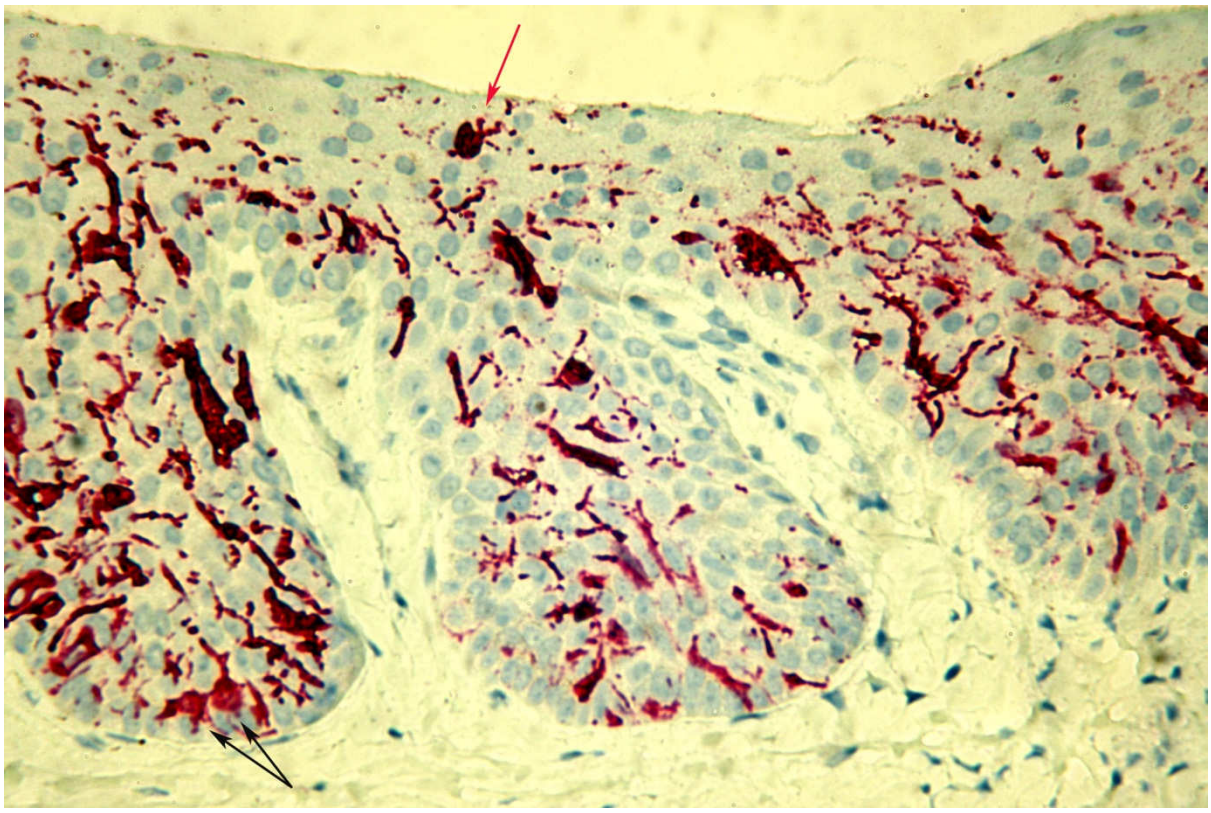

Figure 9: A micrograph of the lesion shown in figure 6 stained with pan-melanoma immunoperoxidase stain shows prominent dendrites with focally confluent plump junctional melanocytes (black arrows) and a Pagetoid melanocyte (red arrow).

The patient was referred to a plastic surgeon for definitive treatment. After discussion with the patient a decision was made not to amputate the digit, but to perform a conservative excision with 5mm lateral margins and to periosteum in depth. The procedure was performed under sterile conditions in the operating theatre of a day-centre under local anaesthetic. The nail plate was removed before the excision was performed, allowing an intact specimen to be submitted in formalin, along with an intact nail plate. The surgical defect was covered with a full-thickness skin graft harvested from the contralateral forearm. The pathologist found no residual tumour in the re-excision specimens.

Case report 2

A 30 year old female patient presented with a pigmented lesion on the nail of her right hallux (figure 10) at the urging of a friend, the patient presented in case 1. The lesion had appeared approximately 5 years earlier but had not concerned her until she learned that the rather similar lesion on her friend's thumb was an early melanoma. She was not aware of recent change but readily conceded that she had not paid particular attention to it.

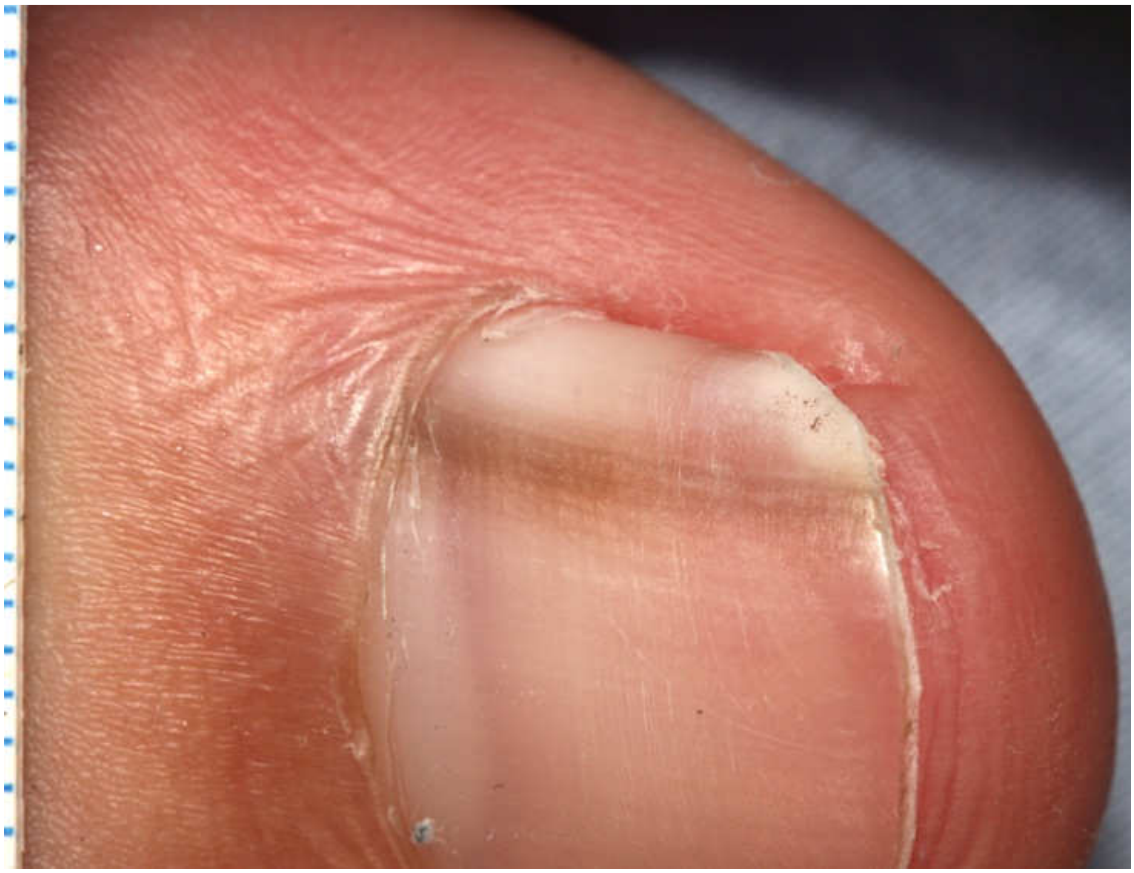

Figure 10: Close up image of longitudinal melanonychia on the right hallux of a 30 year old woman. This pigment band on the nail plate had been present for approximately five years with no reported recent change. The pigment band tapers only slightly from 2mm wide proximally to a little less than 2 mm distally.

Dermatoscopy of the surface of the nail plate (figure 11) revealed longitudinal melanonychia with lines parallel stretching from the proximal nail fold to the free edge of the nail. There was some variation in the width and interval of the lines but it was not marked. Colours included brown and a

suggestion of gray. The pigment was visible through the translucent nail cuticle (false Hutchison's sign) although that structure did not appear to be pigmented.

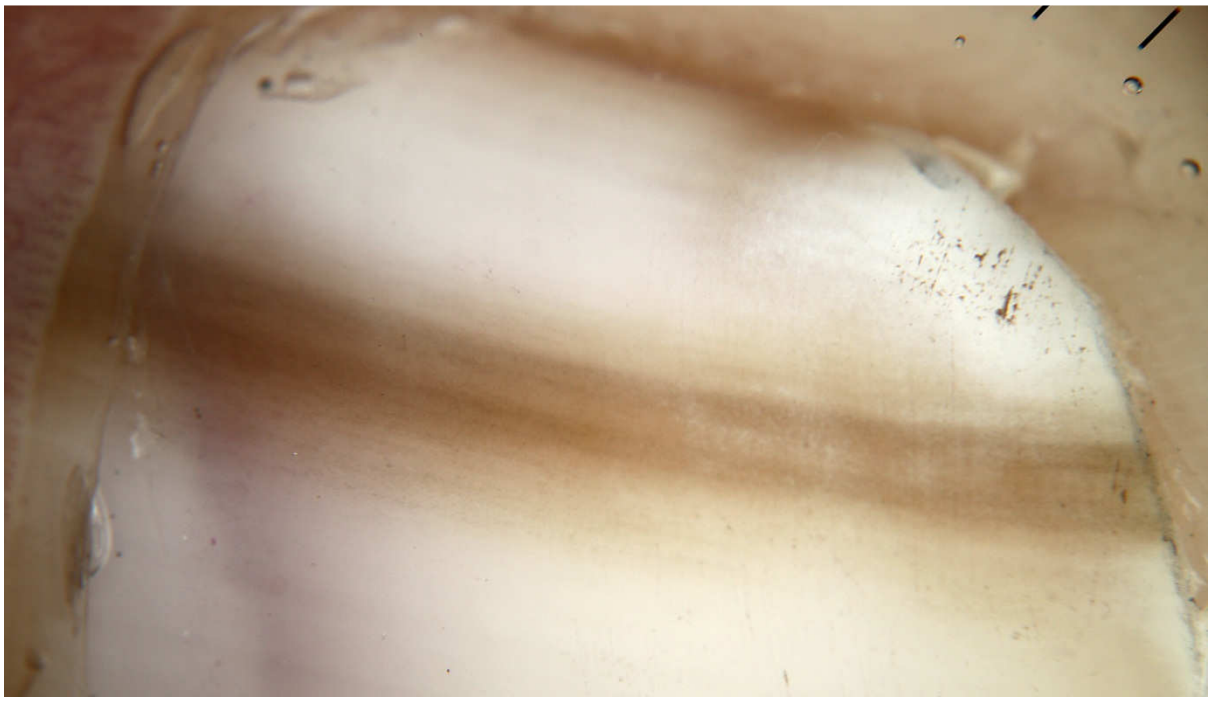

Figure 11: Dermatoscopy of the lesion shown in figure 10. Lines parallel show only slight variation in width interval and colour. Colours present- brown and gray- are the colours of melanin. The pigment band is wider proximally than distally.

Dermatoscopy of the free edge of the nail plate (figure 12) revealed the presence of pigment preferentially in the superficial layers, suggesting that the tumor would be located in the proximal nail matrix (figure 13).

Figure 12: Dermatoscopy of the free edge of the nail plate shows that melanin has been preferentially incorporated into the superficial portion of the nail plate. This indicates that it is originating from a lesion in the proximal portion of the nail matrix.

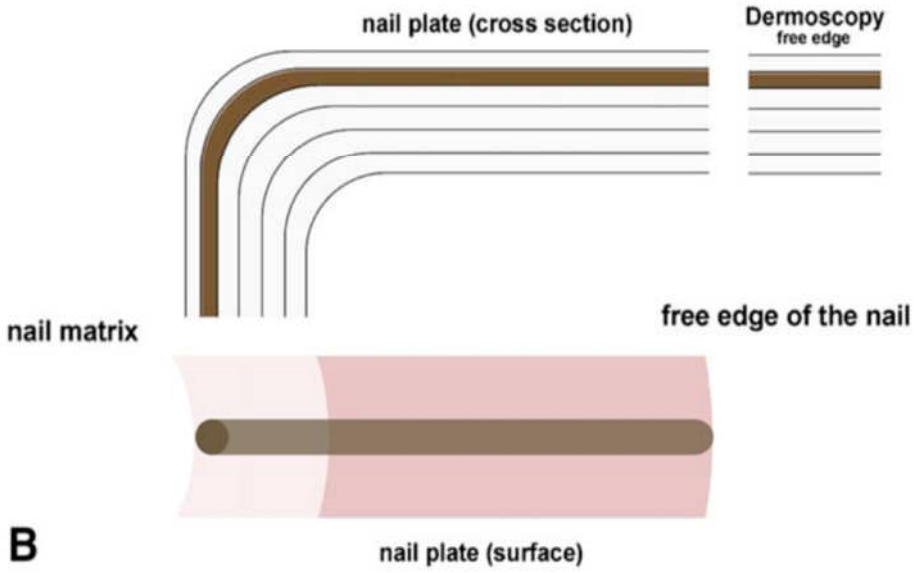

Figure 13: Tumors of the proximal nail matrix produce melanin incorporated into the superficial layers of the nail plate. (Adapted from Braun RP, Baran R, Saurat JH, Thomas L. Surgical Pearl: Dermoscopy of the free edge of the nail to determine the level of nail plate pigmentation and the location of its probable origin in the proximal or distal nail matrix. *J. Am. Acad. Dermatol.* 2006;55(3):512-513.)

On the basis of longitudinal melanonychia present for approximately 5 years with no reported recent change, combined with dermatoscopic findings of only slight variability of line width, interval and colour, a provisional diagnosis was made of nail matrix nevus. However, nail matrix melanoma could not be excluded with any degree of certainty so a nail matrix biopsy was proposed to the patient, including an explanation that it would cause a degree of permanent nail dystrophy.

The patient agreed and the procedure was performed 2 weeks later under sterile conditions in the operating room of the general practice using a similar method to the one described in the case 1. Author AC attended and photo-documented the procedure which is presented in figures 14-23.

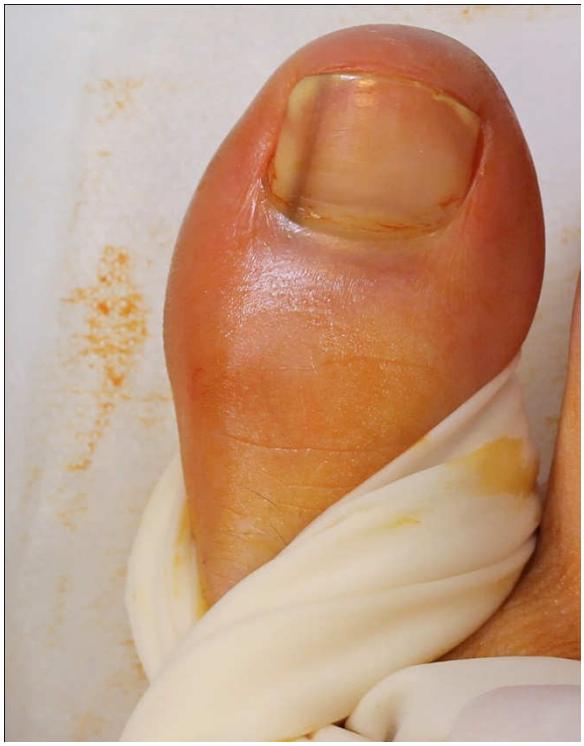

Figure 14: Following skin preparation with betadine and a local anaesthetic digital block with 2% plain xylocaine a tourniquet (sterile glove) is applied and secured with artery forceps.

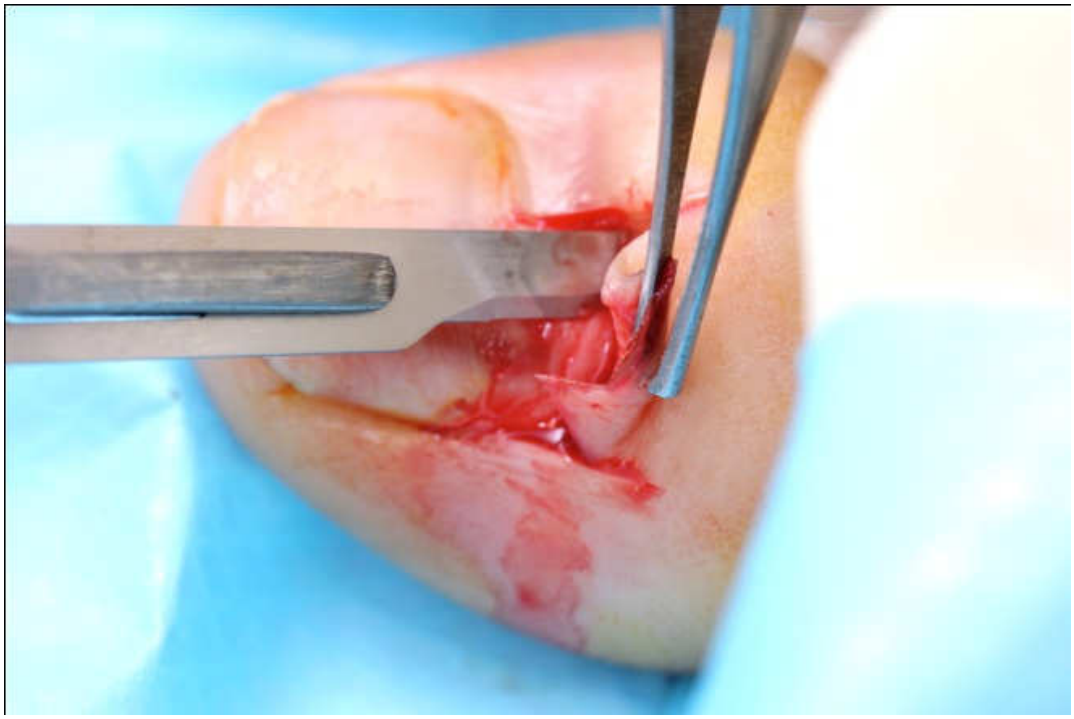

Figure 15: The proximal nail fold is incised on each side and separated from the nail plate with a scalpel

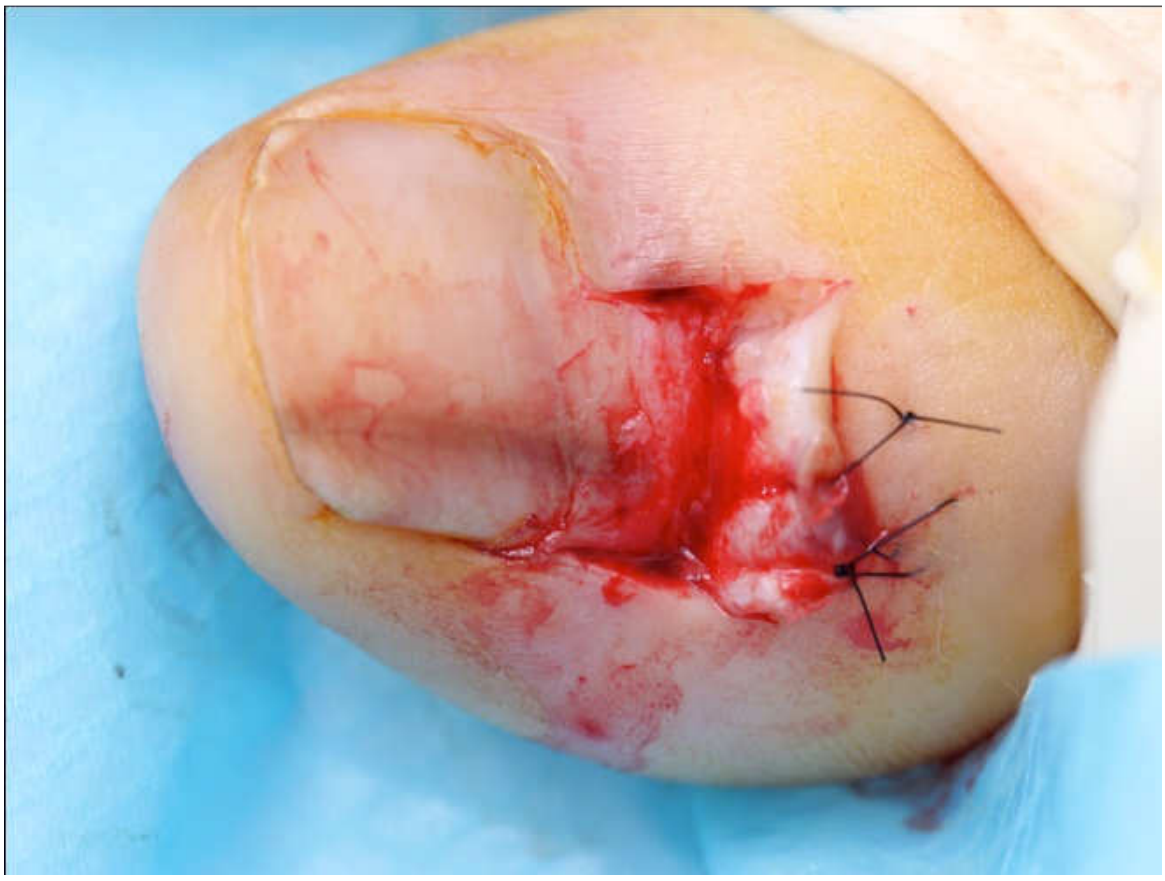

Figure 16: The mobilised proximal nail fold is retracted with two sutures

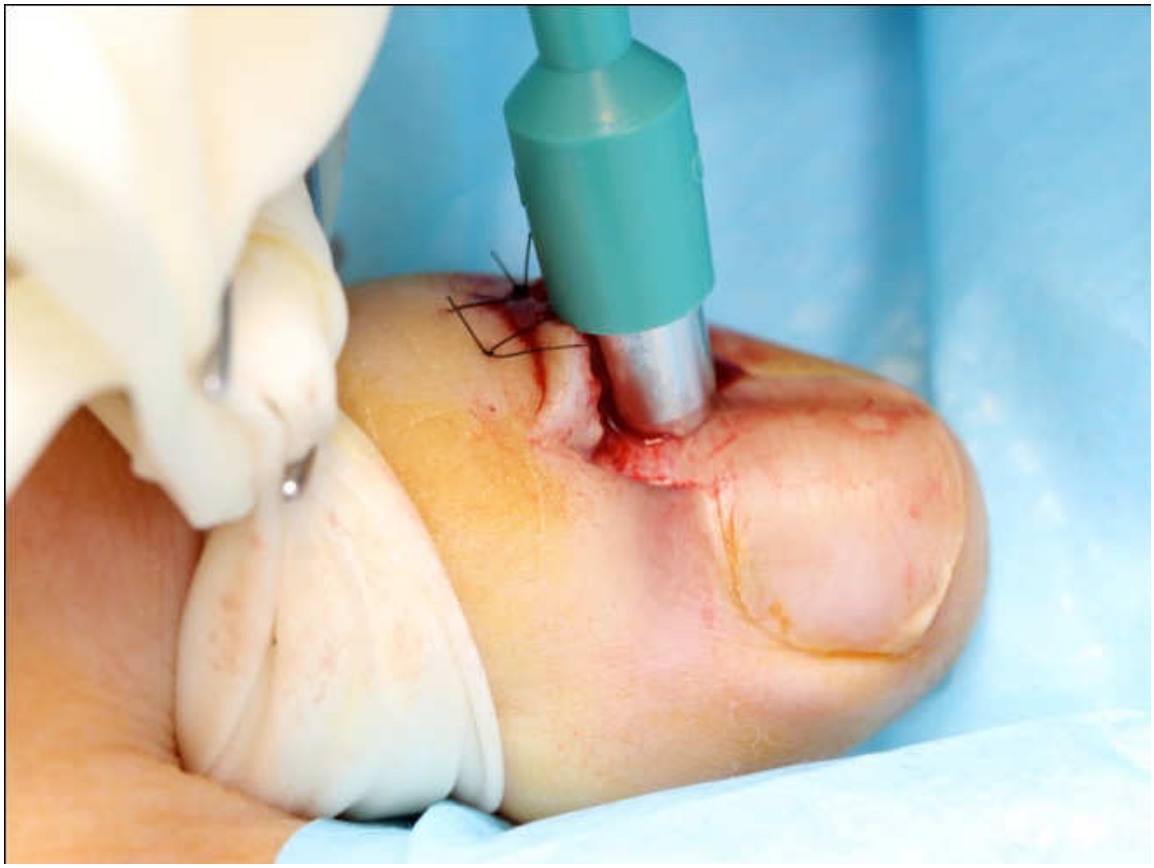

Figure 17: A 6mm biopsy punch is rotated with gentle pressure applied in the first step in nail plate fenestration

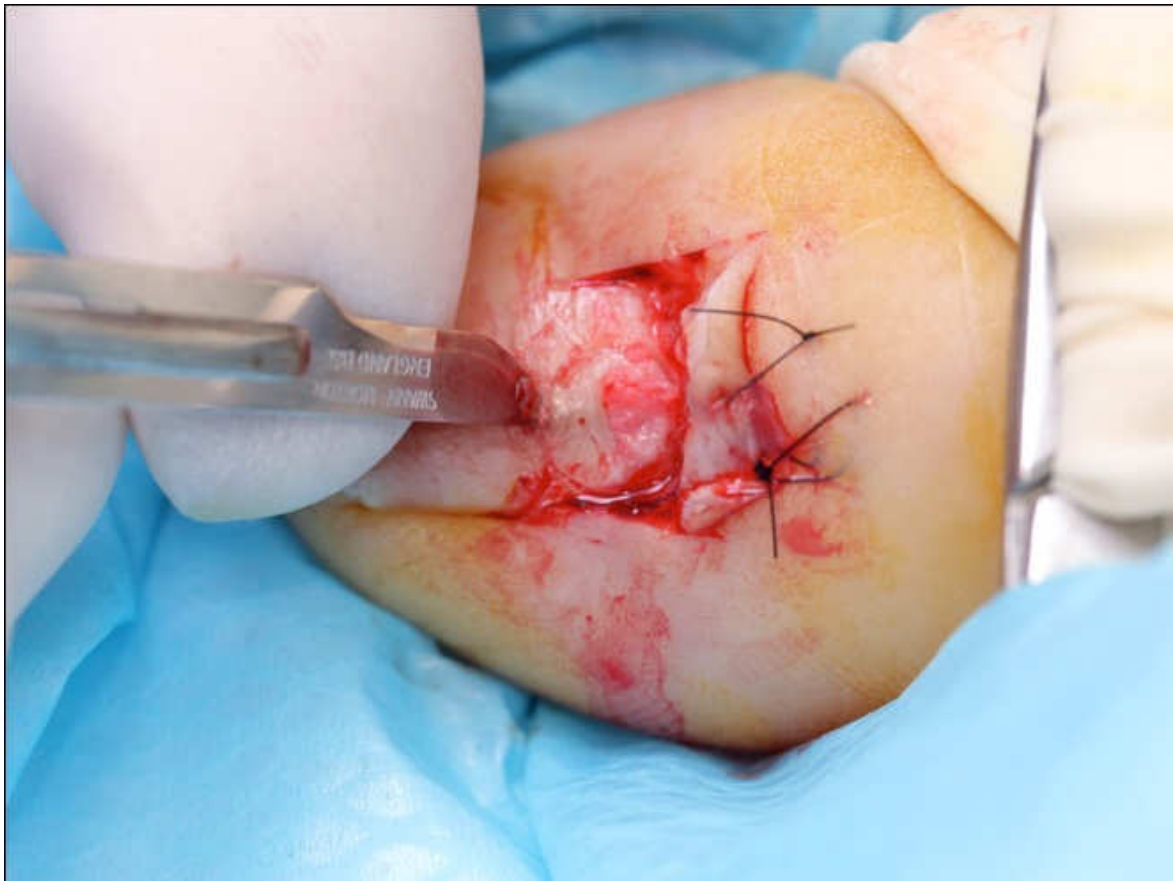

Figure 18: The fenestration incision is tested with a scalpel blade until full thickness penetration is confirmed at this point.

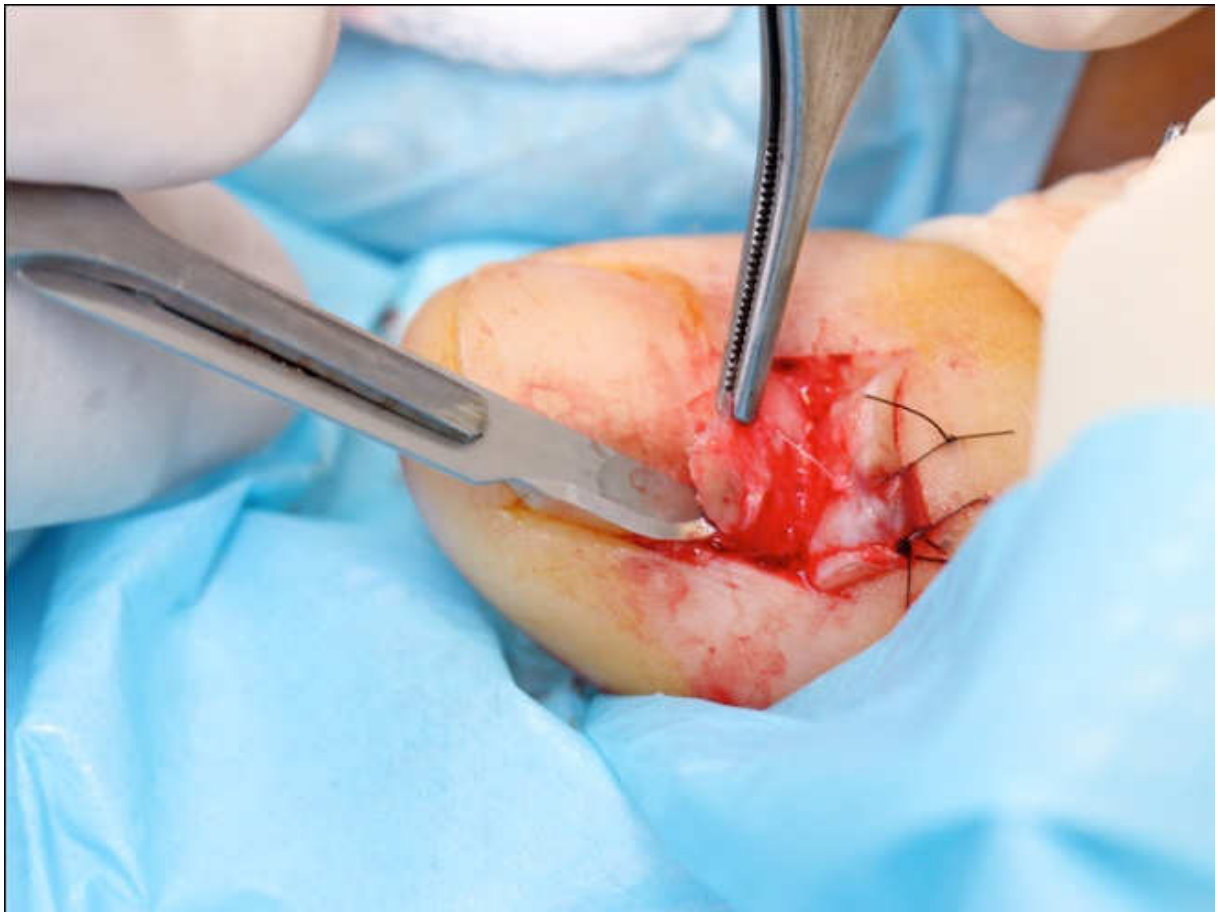

Figure 19: Forceps are used as an elevator to lift the fenestrated nail plate away from the underlying nail matrix while fenestration is completed with a scalpel. The cutting edge of the scalpel blade is directed outwards away from the nail matrix.

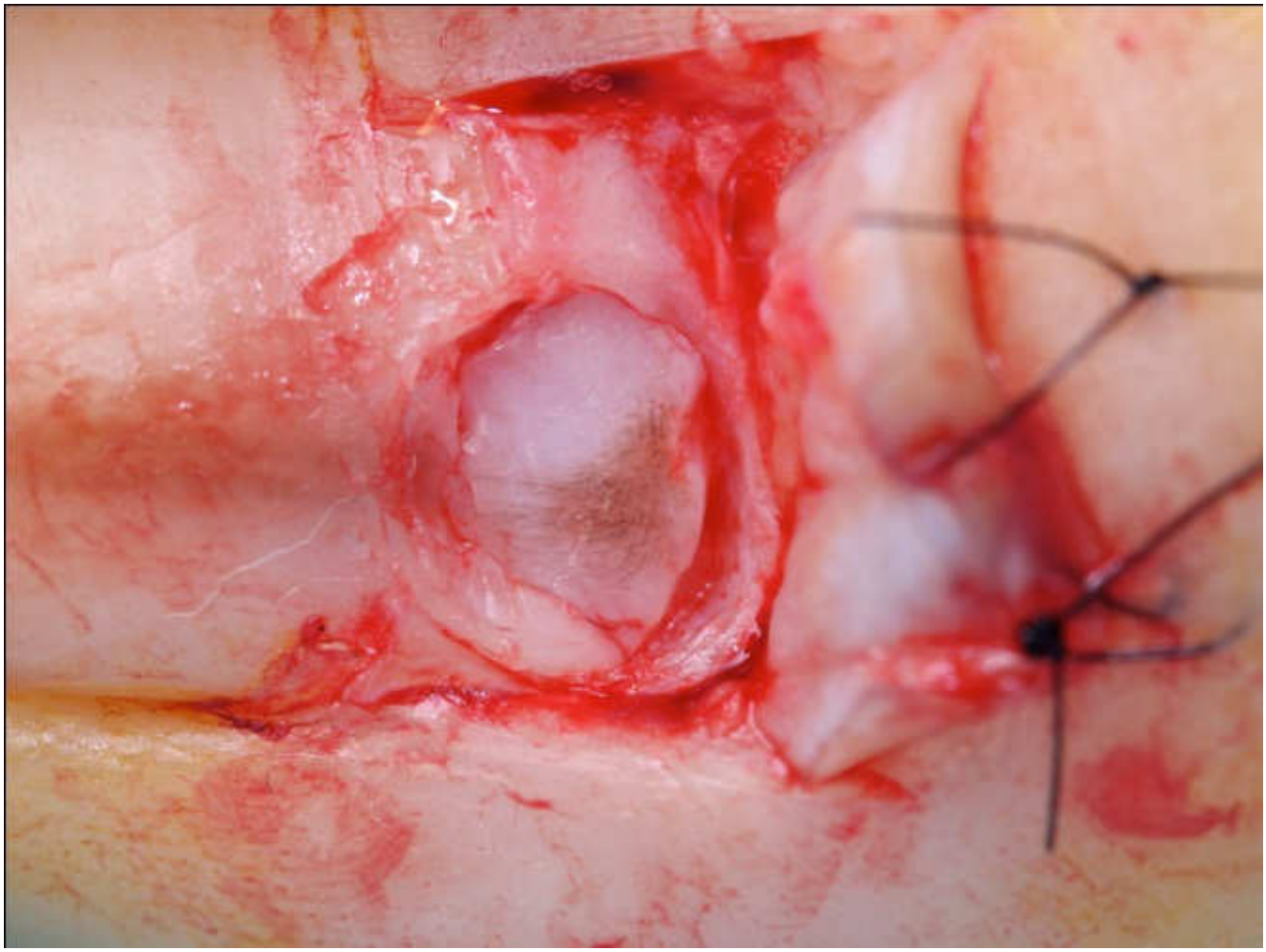

Figure 20: After removal of the nail plate plug a pigmented lesion is clearly seen on the nail matrix. Lines parallel extend distally from the central lesion which appears to have a structure of reticular lines although this is a macroscopic, not a dermatoscopic image. The posterior margin has already been (inadvertently) incised with the biopsy punch and appears just clear of the pigmented lesion.

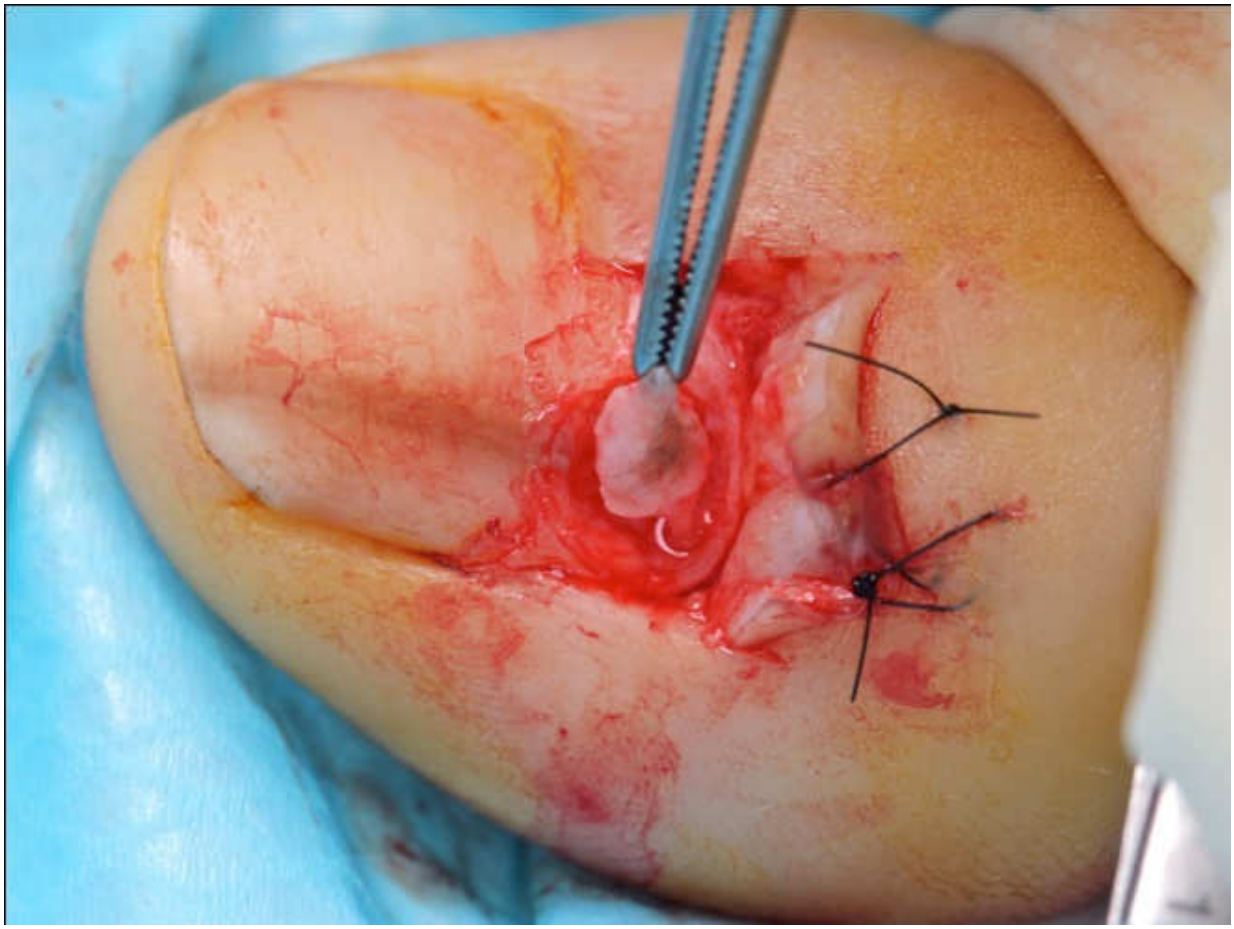

Figure 21: The nail matrix containing the pigmented lesion is removed as an excision biopsy. The only portion to have a visible positive margin is where the parallel lines of pigment extend to the distal margin where they are continuous with lines in the developing nail plate which in turn appear to be continuous with the lines on the exposed nail plate. The specimen is gripped at one edge, as remote as possible from the pigmented lesion, to avoid crush artefact of the tumor.

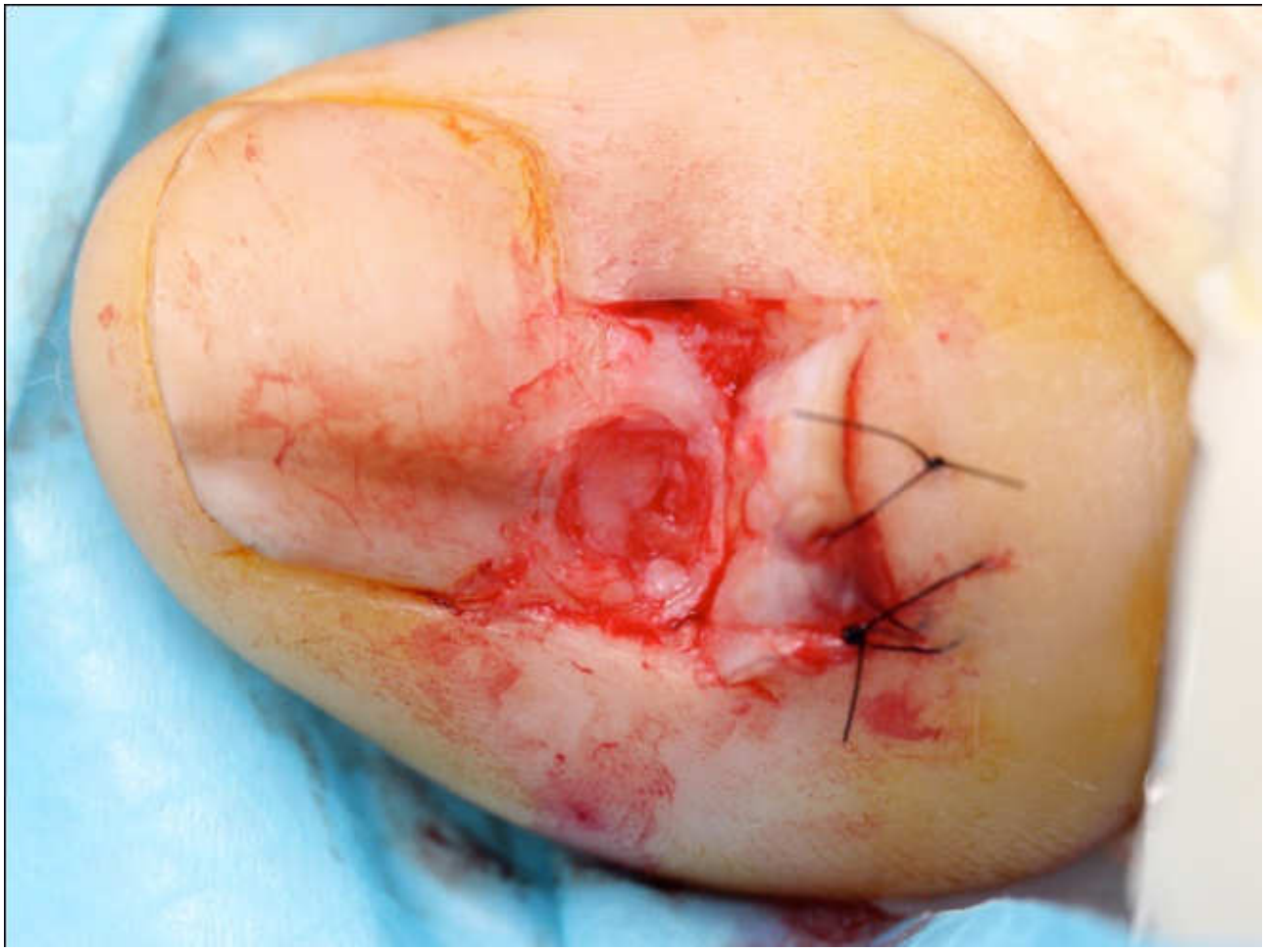

Figure 22: The excision biopsy has been dissected at the level of the periosteum. Careful inspection of the base reveals no evidence of residual melanin pigment.

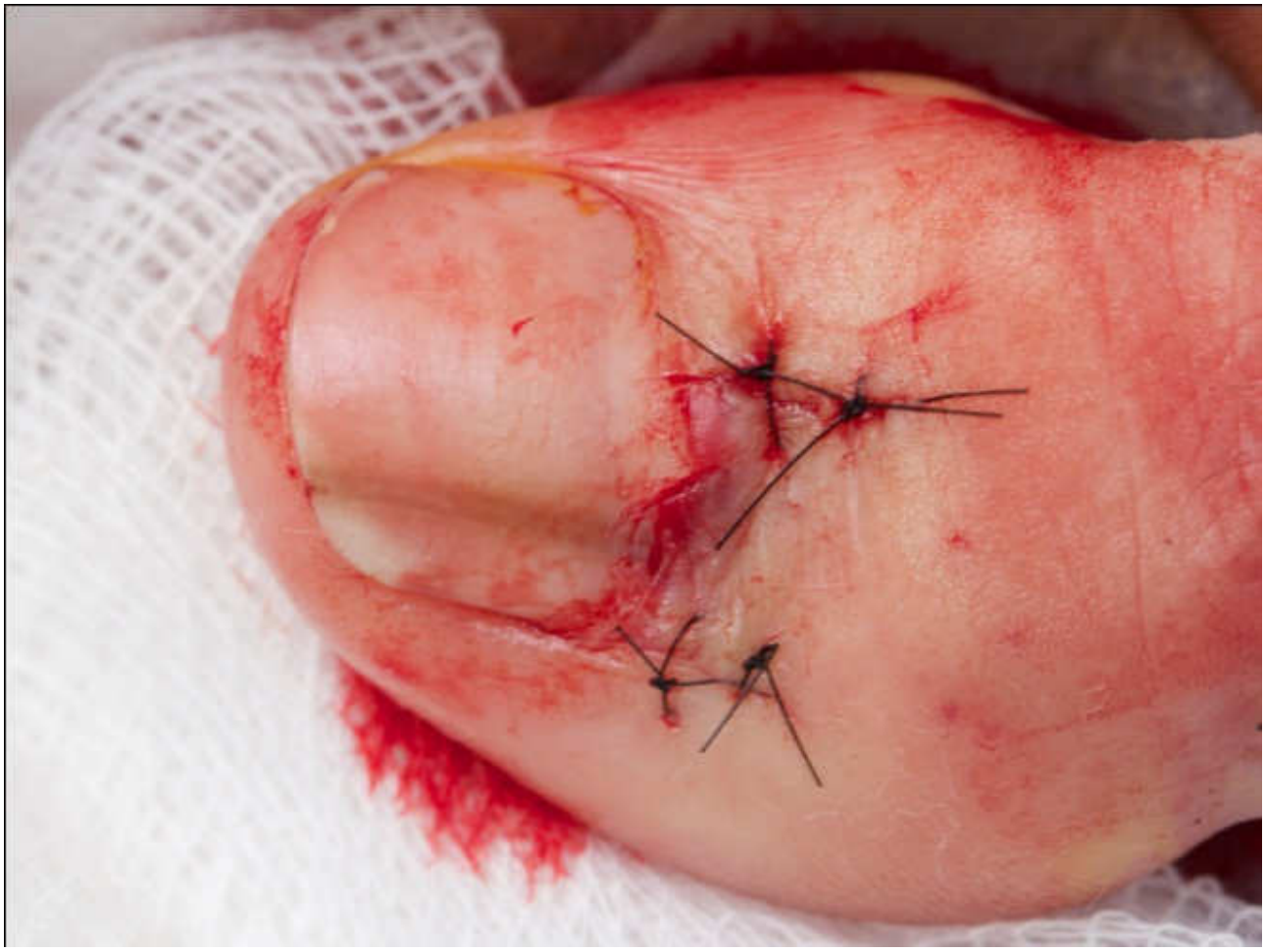

Figure 23: The proximal nail fold is laid back over the defect and secured with two 5-0 nylon sutures on each side. The tourniquet is released with consequent brisk bleeding and dressing is delayed until haemostasis has been achieved with the assistance of direct pressure and the passage of time. With the dressing, care is taken not to apply any constriction and the skin of the distal end of the toe is left uncovered. The patient is instructed about checking this for colour and capillary return in the event of undue pain or discomfort.

Histopathology revealed (quoting from the pathology report) “a mild increase in basal melanocytes.”

The pathologist went on to state “As usual in matrix preparations it is almost impossible to detect any atypia... I am performing a battery of four melanocytic markers in an attempt to clarify the pathology.”

The follow-up report stated “Three of the immunoperoxidase stains (S100, panmelanoma and HMB45) show an increase in melanocytes with Pagetoid spread and some plump cells. These changes are those of an evolving level 1 (in situ) acral melanoma. The Melan A stain shows less

Pagetoid spread but still some plump melanocytes. ... There is no regression, ulceration, significant lymphocytic infiltrate or dermal invasion."

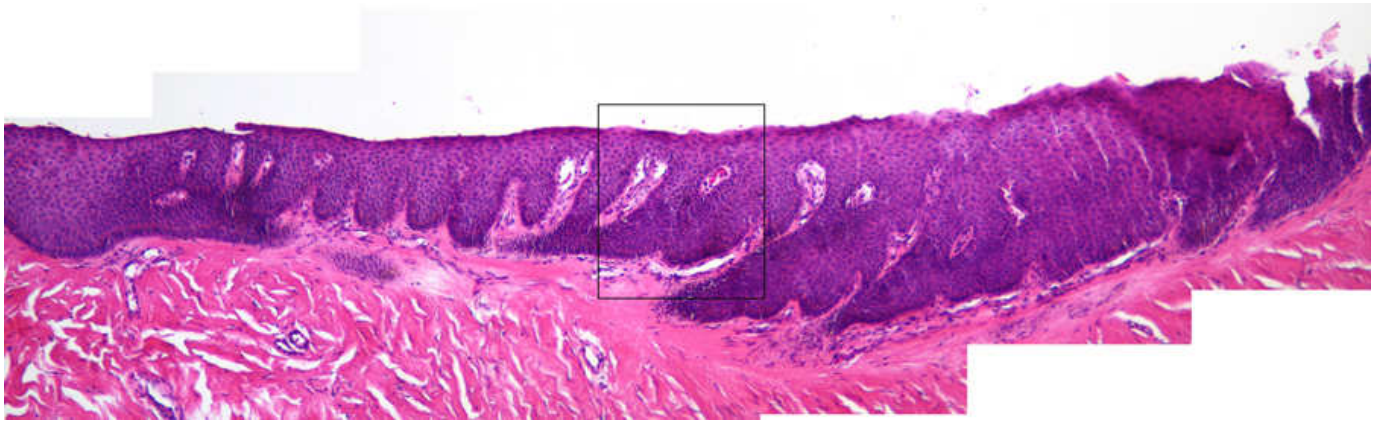

Figure 24: Low power micrograph of the nail matrix specimen from case 2.

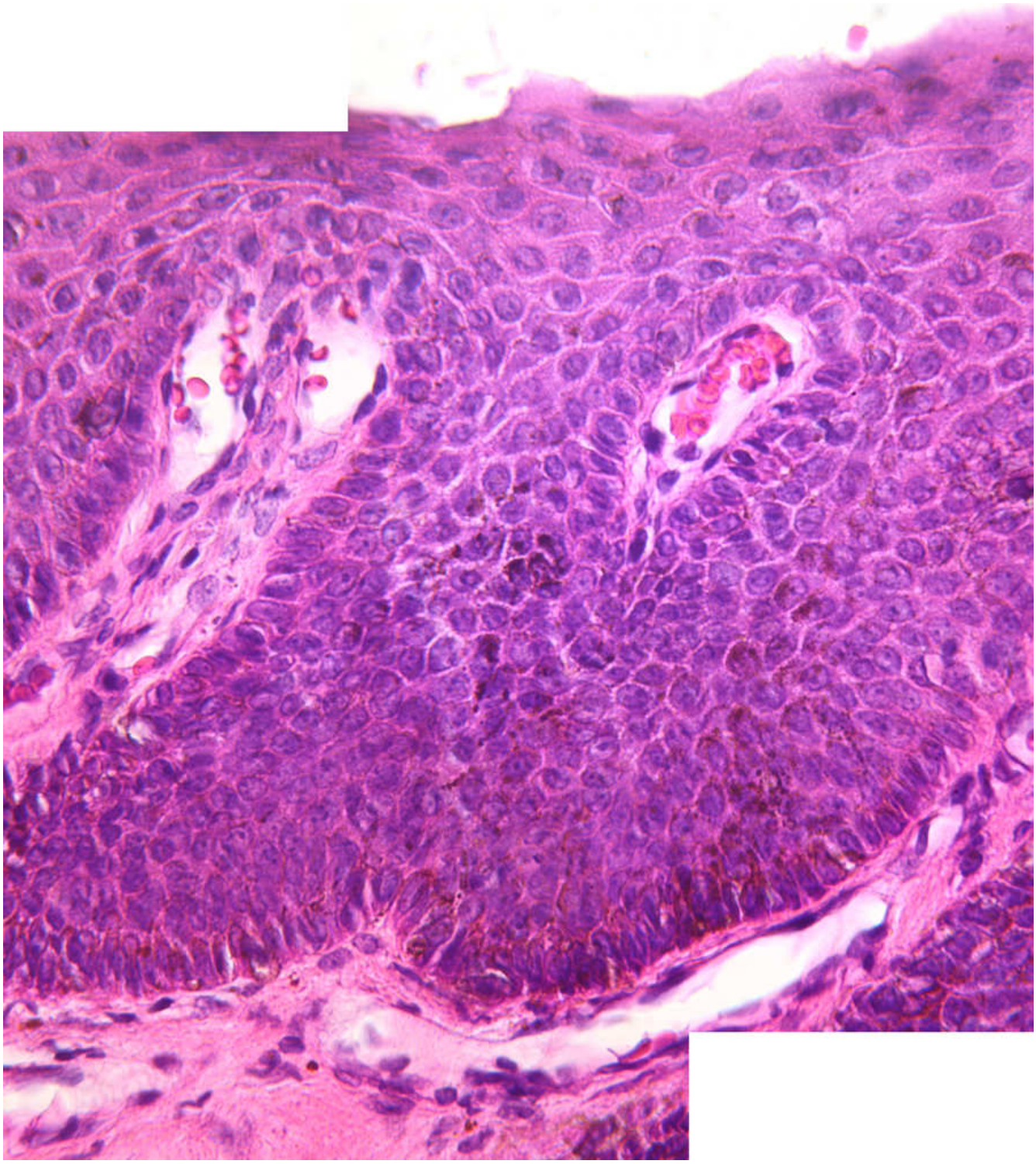

Figure 25: High power micrograph of the boxed area in fig. 24. Prominent heavily pigmented dendrites raise suspicion of a malignant neoplastic process but a diagnosis of nail-matrix melanoma is not rendered on this H&E stained tissue.

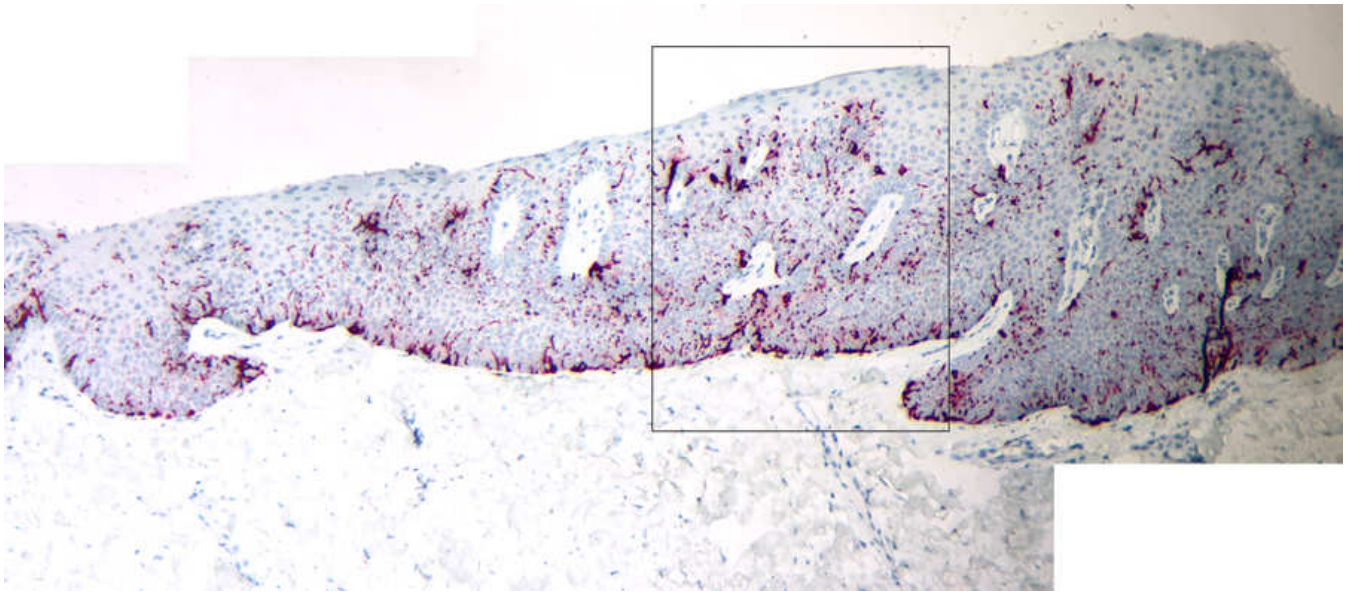

Figure 26: A Low power micrograph of nail matrix from case 2 stained with pan melanoma stain.

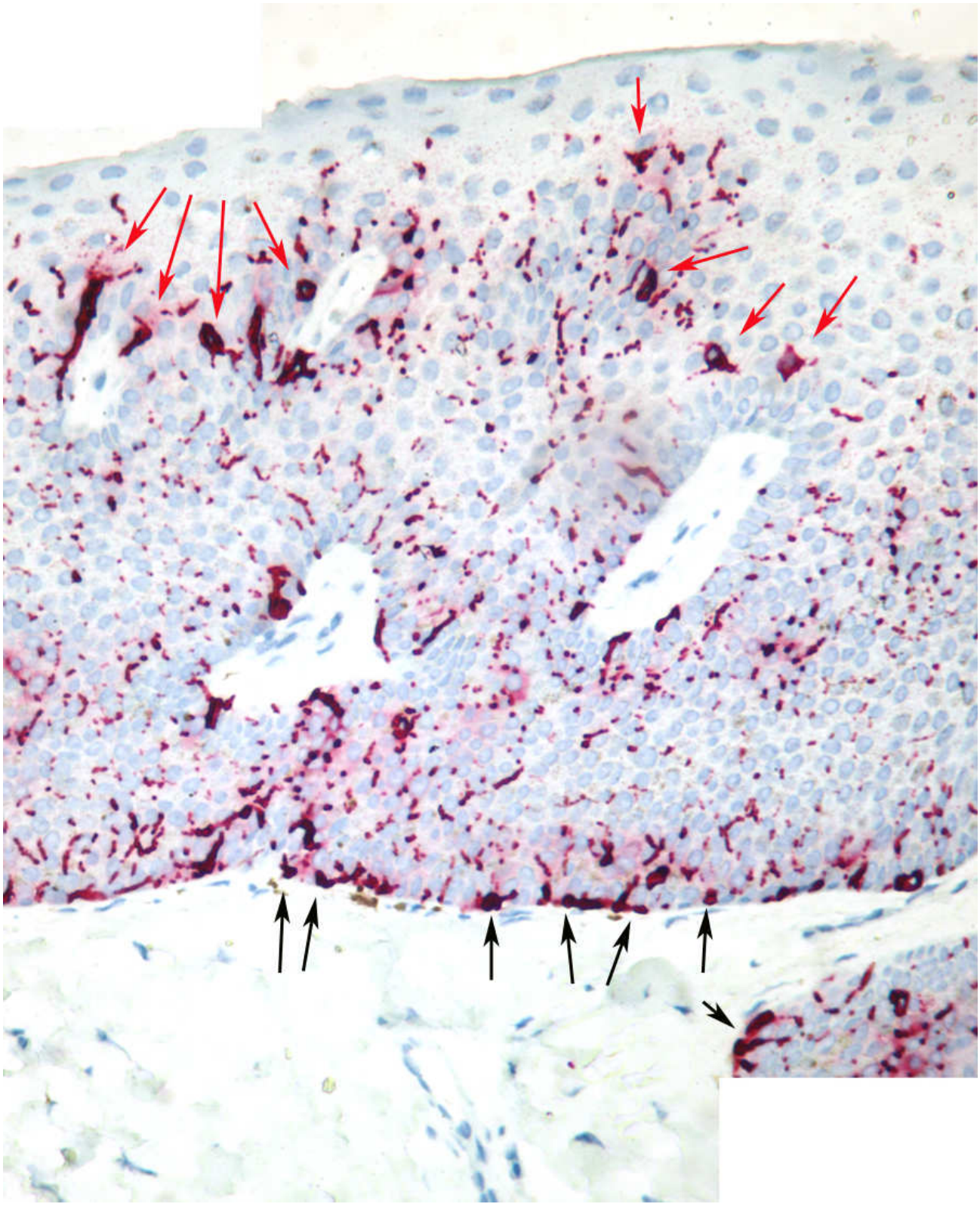

Figure 27: High power micrograph of the boxed area in fig. 26 with pan-melanoma stain. Plump atypical melanocytes are seen in lentiginous array (black arrows), in some parts confluent. Pagetoid spread of melanocytes is also seen (red arrows).

The patient was referred to a plastic surgeon for definitive treatment of a level 1 nail matrix melanoma.

Discussion

Durbec et al performed a comprehensive literature review of the epidemiology of hand and foot melanoma (HFM) (5). They conclude that HFM are rare in all populations, with estimates of incidence of HFM ranging from 0.04 to 0.25 per 100,000 per year. They found one study which specifically addressed the incidence of (invasive) subungual melanoma, with a finding of 0.1 per 100,000 per year (1 in a million per year) (7). For HFM in general, ultraviolet radiation appears to have at most a very limited causative role, with previous trauma and nevi on the soles or toes being the most consistent risk factors across the few relevant studies. In one study nail trauma was recalled by 50% of patients with subungual melanoma (6). Subungual melanomas were evenly distributed between hand and foot, but hallux and thumb nails were disproportionately affected compared to other digits and there was equal incidence of nail subungual melanoma across all races.

HFM appears to have a worse prognosis than cutaneous melanoma in general. This is thought to be mainly due to delay in diagnosis, with possible contributions from more aggressive tumour behaviour at acral sites or of the acral lentiginous melanoma subtype. While Breslow thickness and tumour ulceration remain the main prognostic factors, Durbec et al found them less reliable for HFM than melanoma in general. No recent population based studies of subungual melanoma mortality were discovered but in a cancer registry-based English study on cases from 1984-93, the 5 year survival for invasive subungual melanoma was only 51%(7).

Although nail apparatus melanoma is not common, the cardinal clinical sign of longitudinal melanonychia is a distinctive one. Furthermore, the dermatoscopic feature of longitudinal pigmented lines running the full length of the nail plate and varying in width, interval and colour has

been shown to assist in differentiating early nail matrix melanoma from other causes of nail pigmentation.(8) In case 1 these features were clearly present but in case 2 they were equivocal. Another described clue to subungual melanoma is onset of longitudinal melanonychia during adulthood (8) and taking this into account, along with equivocal dermatoscopic features, a nail matrix biopsy was appropriate in case 2.

An inadequate biopsy can impair the pathologist's ability to provide an accurate diagnosis (6) and for this reason the quality of biopsy material is important. Nail plate tissue is routinely placed in a softening agent. If an inexperienced laboratory assistant placed nail matrix in softener, even a carefully collected specimen could be compromised.

As with other melanomas there is overlap between normal findings and criteria for a diagnosis of melanoma. Both architectural criteria (including with nail-matrix melanomas, confluent junctional proliferation of melanocytes and a degree of partial or full-thickness Pagetoid spread) as well as cytological features (including in nail-matrix melanomas, plump atypical melanocytes and dendrites packed with melanin) are needed for the diagnosis of melanoma to be made. Furthermore the differentiation between melanocytes and keratinocytes can be difficult with H&E stained specimens. In both of the cases reported here immunoperoxidase stains were performed to facilitate a confident diagnosis.

Braun et al. (6) describe a full range of biopsy techniques suitable for longitudinal melanonychia of varying sizes and locations. The biopsy technique used for these two cases is a modification of the punch method, with the fenestrated portion of nail plate being submitted for histology rather than being placed back into the defect as a "biological dressing". In both these cases healing proceeded rapidly without replacing the nail plug.

While invasive nail-matrix melanomas are inevitably treated by partial or complete amputation of the affected digit according to tumour thickness, in-situ nail matrix melanomas can be treated by conservative excision of the entire nail apparatus (nail plate, bed and matrix) with graft reconstruction. (6,9) As even partial loss of thumb or big toe causes significant disability, diagnosis at

the in situ stage has led to a better functional outcome as well as a better prognosis for these two patients.

Conclusion

An uncommon, occult form of melanoma was diagnosed at an early stage in two young adults, because an informed teenager recognised its signature. Her discovery also made this presentation possible. A simple image-based patient education initiative paid a huge dividend.

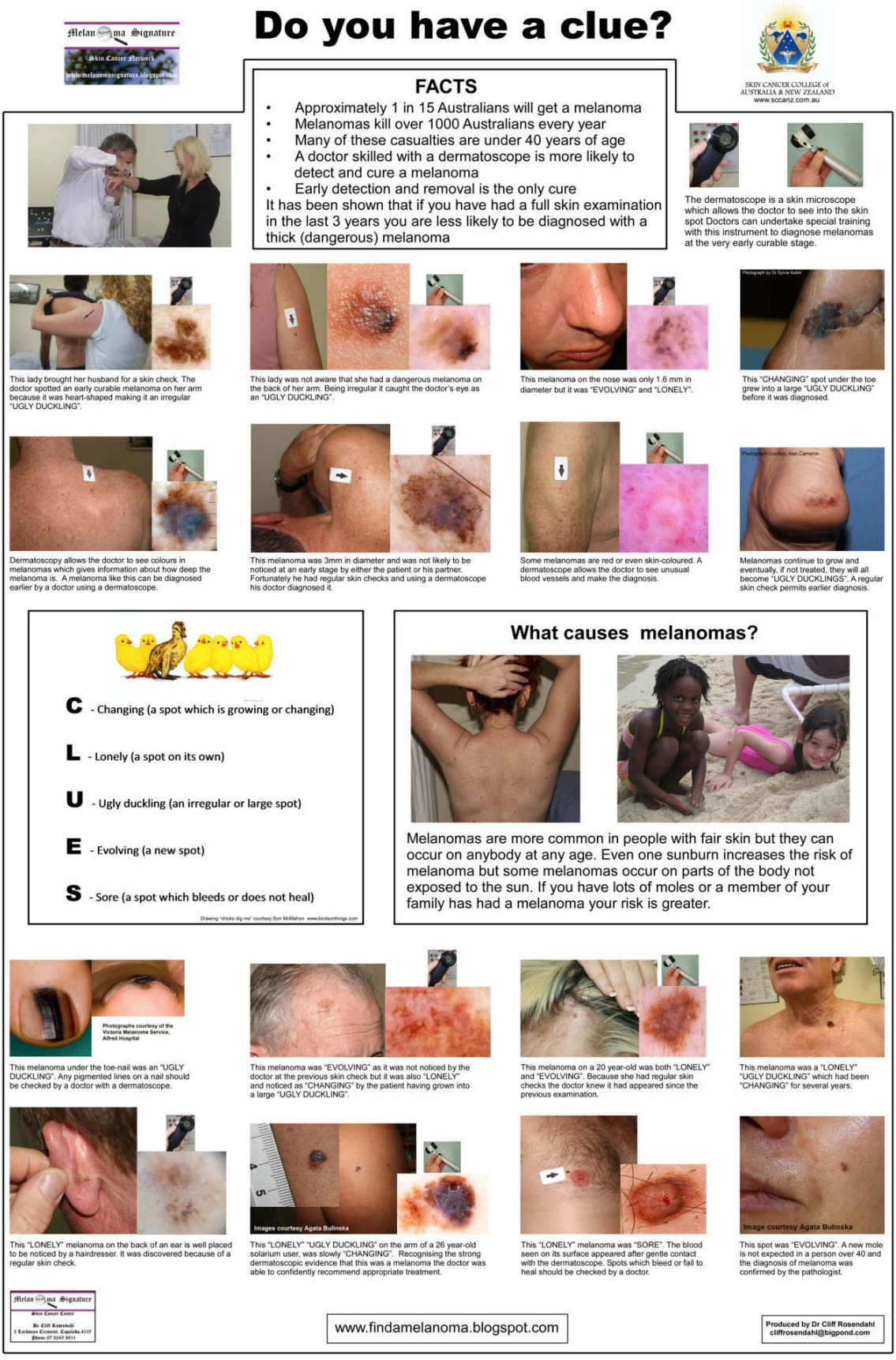

Figure 28: The patient education poster which prompted a teenager to suggest that her teacher consult his general practitioner about a discoloured thumb-nail

Images

Equipment used for images

Macro	Canon EOS 50D or 60D with Canon EF-S 60mm ƒ2.8 macro lens
Dermatoscopy	Dermlite Fluid/Canon EOS 50D for nail plate surface
	Dermlite DL3/Olympus E-450 for free nail edge
	Ultrasound gel used as coupling fluid
Micrographs	Olympus BH2 microscope/Canon EOS 50D

Where necessary multiple images have been merged using Adobe Photoshop to achieve the required field of view.

Canon EOS 50D, 60D cameras: Canon, Tokyo, Japan

Dermlite Fluid and Dermlite DL3 dermatoscopes: 3 Gen LLC, San Juan Capistrano, CA

Olympus E-450 camera: Olympus Corporation, Tokyo, Japan

Adobe Photoshop: Adobe Systems, San Jose CA

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