## Multiple Eruptive Pyogenic Granulomas on the Proximal Nail Folds Following Cast Immobilization: A Case Report with Nail Unit Ultrasound Findings

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Pyogenic granuloma (PG), also designated lobular capillary haemangioma, is a common benign acquired vascular neoformation that typically appears as a solitary, rapidly growing, exophytic vascular papule or nodule, often located on the distal extremities, face and gingiva. PG usually arises spontaneously, but in some instances may be associated with chronic or acute trauma, pregnancy. infections and some drugs. PG often develops on areas frequently exposed to trauma and inflammation, such as the fingers and toes, including the nail folds and subungual regions. An increased expression of angiogenic growth factors in a highly vascularized area, such as the paronychium, has been postulated to explain the development of these lesions (1). In addition, the development of multiple eruptive PGs on the proximal or lateral nail folds has been reported, mainly associated with several drugs (retinoids, antineoplastic drugs, epidermal growth factor receptor inhibitors, imatinib (2), anti-retrovirals (mostly indinavir) and, rarely, rituximab, etanercept and levothyroxine). Systemic inflammatory diseases (sarcoidosis, psoriasis and spondyloarthritis) and peripheral nerve injuries of varying aetiology (trauma, reflex sympathetic dystrophy (3), hypoxemia (4), Guillain-Barre syndrome (5), hemiplegia (6)) have also been related occasionally to the development of multiple subungual and periungual PGs. In rare instances, multiple PGs may develop on the proximal nail fold after upper-limb immobilization (1, 7-12).

heterozygous prothrombin 20210G/A mutation and a traumatic fissure of the head of the radius 3 months before consultation. Prophylactic treatment with heparin was prescribed and a plaster cast was applied on the right arm from above the elbow up to the metatarsophalangeal joint for 6 weeks. Physical examination disclosed a proximal nail detachment associated with solitary erosive, moist erythematous nodules, 0.6-0.8 cm in diameter, located on the proximal nail fold of the 2<sup>nd</sup>, 3<sup>rd</sup> and 4<sup>th</sup> fingers of the right hand. A discrete periungual oedema of the involved fingers and onychomadesis (transversal depressions) of the second to fifth nail plates were also noted (Fig. 1a, b). The lesions were not painful, but bled easily after minimal trauma. No associated neurological symptoms, such as paraesthesia, loss of strength or sensitivity, pain or increased sweating, were present. The lesions had developed one month after plaster removal. A hand X-ray disclosed no underlying bone abnormalities. An 18-MHz ultrasound image revealed, on the longitudinal view, ill-defined hypoechoic nodules located between the proximal nail fold and the nail matrix, along with increased thickness of the periungual folds. On transverse views, a hypoechoic nodule located in the proximal third of the nail bed without erosion of the phalanx could be identified. Increased vascularity was observed by colour-Doppler. Separation of the nail plate into 2 portions with loss of the double hyperechoic band was also noted (Fig. 1c). A skin biopsy of one of the lesions revealed vascular proliferation of small capillaries within an oedematous dermis, accompanied by a mild inflammatory infiltrate composed of neutrophils and lymphocytes (Fig. 1d), consistent with PG. Initially, curettage excision of the nodules was performed and topical timolol 0.5% was applied during the first month with partial response. The lesions resolved spontaneously in 2 months with no residual nail deformity.

## CASE REPORT

An 18-year-old Caucasian male was referred to our department for evaluation of multiple fleshy red nodules that developed on the proximal nail folds of the right hand. Past medical history included

**Fig. 1.** (a) Unilateral pyogenic granulomas on the proximal nail fold of the  $2^{nd}$  to  $4^{th}$  fingers of the right hand. (b) Close-up view of the multiple periungual PGs. Onychomadesis can be observed on the  $2^{nd}$  to  $5^{th}$  fingernails. (c) Longitudinal 18-MHz ultrasound view with identification of an ill-defined hypoechoic nodule (*red asterisks*) between the proximal nail fold and the nail matrix of the  $4^{th}$ finger and separation of the nail plate into 2 portions. (d) Lobular small capillary proliferation within lax and oedematous stroma with mild inflammatory infiltrate (haematoxylin-eosin ×40) and close-up view of the vascular proliferation (*lower inset*) (haematoxylin-eosin ×200).



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## DISCUSSION

Eruptive PGs in the proximal nail fold secondary to plaster cast immobilization were first described by Price et al. in 1994 (7) and, as far as we know, fewer than 20 additional cases have been reported since, consisting of young male individuals with exclusive involvement of the upper limbs. During cast immobilization, patients often reported different neurological local symptoms, such as pain, paraesthesia or periungual hyperhidrosis (7, 8, 11). Clinically, the lesions are manifested by the sudden onset of a proximal nail detachment and the protrusion of red vascular nodules on the proximal nail fold involving one or several fingers. Histologically, characteristic features of pyogenic granuloma are observed. PGs tend to develop from 7 to 30 days after cast removal and secondary onychomadesis is a commonly associated symptom. The lesions tend to resolve spontaneously in a variable period of time (1-3 months) and a wait and see conduct has been recommended. Other possible therapeutic options include oral and topical antibiotics and corticosteroids, silver nitrate, laser treatment and curettage (1, 7-12).

Ultrasound imaging provides both morphological and vascular information, and has been proposed as a non-invasive, cost-effective technique for real-time evaluation of lesions of the nail unit. A high-resolution compact linear transducer of 15 MHz or higher is required to achieve good definition of the nail unit structures. Ultrasound examination of PGs usually shows ill-defined nodules, hypoechoic compared with the subcutaneous fat, with slightly increased vascularization by colour-Doppler (13). The sonographic differential diagnosis should include other hypervascular tumours, such as true haemangioma and glomus tumour. Due to the higher echogenicity of PGs, ultrasound has been proposed as helpful in distinguishing PG from other hypervascular periungual or subungual tumours, which are usually more hypoechoic (14). The 2 parallel hyperechoic bands of the nail plate (bi-laminar structure) merge into a single hyperechoic band and the nail plate is disrupted in 2 portions with thickening of the nail bed. This latter finding corresponds clinically to the onychomadesis (15). These sonographic features were easily identified in our patient. Due to the characteristically similar presentation features of the current case and the previously reported ones, the practice of skin biopsies may be avoided in a patient with eruptive multiple periungual fleshy red nodules after cast immobilization. On the other hand, performing a biopsy is recommended to rule out malignancy if the case presented as an eruptive single isolated periungual nodule. Ultrasound examination is an additional non-invasive diagnostic technique that can be used in clinically nontypical cases.

The pathogenic mechanisms implicated in the development of eruptive PGs after cast immobilization are unknown. A possible peripheral autonomic nerve injury leading to acute inhibition of the nail matrix proliferation has been hypothesized (11). The observation of cases of reflex sympathetic dystrophy, Guillain-Barré syndrome and hemiplegia associated with eruptive PGs would support this theory (3–6). However, neurological associated symptoms, as in the current case, are absent in most of the reported cases (12). A possible vascular imbalanced regulation of angiogenesis secondary to trauma has also been suggested.

In summary, eruptive PGs of the proximal nail fold with secondary onychomadesis after cast immobilization is a rare phenomenon of unknown aetiology. The diagnosis could be easily established on the basis of a detailed clinical history and unique clinical features. The observed ultrasound features in subungual PG appear to be characteristic and may support the diagnosis, and thus avoid the use of more aggressive diagnostic procedures, in non-typical cases.

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