



The clinical characteristics and outcomes of the patients with pyogenic granuloma: A retrospective study of 144 patients

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Abstract

Aim: Pyogenic granuloma (PG), also known as lobular capillary hemangioma, is a benign, reactive vascular tumor. We aimed to evaluate the demographic and clinical characteristics, treatments received, and outcomes of patients followed up at our clinic with PG.

Materials and Methods: We retrospectively evaluated all patients followed up at our clinic with PG in the last 4 years.

Results: A total of 144 patients were included in our study. 73 (51%) of the patients were female and 71 (49%) were male. The mean age of the patients was 31.3 ± 8.3 years. When we examined the PG locations in our patients, we observed that it was most commonly found in the arm/hand area (40%), on the face (29%), foot/leg area (19%), and on the trunk (8.3%). The highest numbers of lesions were respectively in the hand, foot nail edge, and lip locations. Out of the patients where the lesion side was specified, 63 had the lesion on the left while 20 had it on the right ($p=0.001$). 51% of our patients underwent excisional surgery. Other treatments applied to our patients, in order, were cryotherapy (15.3%), electrocauterization (8.3%), and cauterization with silver nitrate, cryotherapy + electrocauterization, topical antibiotic and cryotherapy + timolol drop. When evaluating the outcomes of the patients, we learned from the notes dropped into the system at later controls that 73% had recovered. The remaining patients were lost to follow-up. When comparing the features of patients who were treated with non-excisional methods to those who underwent excision, we observed that there was a higher rate of patients younger than 12 years ($p=0.023$), a higher incidence of foot nail edge ($p=0.016$) and lip location ($p=0.048$), and a higher frequency of pregnancy in this group.

Conclusion: PG is a vascular tumor of importance due to its potential for bleeding and ulceration and its chronic course if left untreated. Since there are malignant lesions in its differential diagnosis, we believe that surgical excision is a more appropriate treatment option in our clinical practice when feasible. We think that the data we have obtained needs to be supported by more comprehensive, broader, and prospective studies.



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Introduction

First identified in 1897, pyogenic granuloma (PG) was initially believed to be due to a Botryomycosis infection. It was named by Hartzell in 1904 [1]. Although its etiology is not fully understood, it is considered a reactive, tumor-like lesion caused by various stimuli such as chronic low-grade irritation, trauma, hormonal effects, and drug-induced reactions [2,3]. Currently, the term "pyogenic granuloma" is a misnomer. No evidence of an infectious agent has been found, furthermore there is no granulomatous appearance histologically. Referring it as "lobular capillary hemangioma" based on its histopathological appearance would be more accurate [4].

PGs can occur at any age but are more common in children and young adults. While gender distribution is equal, there is no racial or familial predisposition. Gingival lesions are relatively more common during pregnancy and are referred to as granuloma gravidarum [5,6].

Lesions appear as a single red papule or polyp that grows rapidly over a few weeks or months and then stabilizes; they rarely exceed 1 cm in size and can be permanent if not removed. Approximately one-third develop following minor trauma. The most common complications are profuse bleeding and ulceration [5-7].

A PG diagnosis can be made based on its characteristic location and history, along with clinical findings of a red papule that bleeds easily. On the other hand, it can be confused with amelanotic melanoma; bacillary angiomato-

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sis and Kaposi's sarcoma in immunosuppressed individuals. Glomus tumor, spitz nevus, irritated melanocytic nevi, and warts should also be considered in the differential diagnosis. Histological examination aids in distinguishing these conditions [3,4].

When we examine the pathology of PG, the lesion is well-defined, exophytic, sometimes pedunculated, and often consists of lobular capillary proliferation. Capillary vessel lumens can be small, branching, and sometimes dilated. The lobular appearance surrounded by dense fibrous tissue bands helps differentiate it from other lobular capillary proliferations. The lesion's lateral boundaries have been determined by adnexal hyperplasia or elongated rete ridges in a collar-like epithelium [6].

In our study, we aimed to evaluate the demographic and clinical characteristics, treatments received, and outcomes of patients followed up at our clinic due to PG.

Materials and Methods

Before to the study, ethics committee approval was obtained from Ankara Bilkent City Hospital Ethics Committee (E1-23-4144). Our study was conducted in accordance with the ethical principles in Helsinki Declaration.

We retrospectively evaluated the patients who were followed up at Ankara Bilkent City Hospital due to PG between the years 2019-2023. In order to minimize bias, we designed our study clearly outlining data collection. Initially, we formed a list of all the patients followed with the diagnosis of PG in the defined period. We included our patients in a randomized order only excluding the patients who had missing data. Demographic and clinical characteristics of the patients, the treatments received and outcomes of patients were recorded in our study.

Statistical analysis

Statistical analysis calculations were performed using the SPSS 24.0 program. Continuous variables are expressed as mean and standard deviation, and categorical variables are expressed as number and percentage. The Chi-Square test statistic was used to compare categorical measurements. The statistical significance level was accepted as 0.05 for all tests.

Results

Of the 233 patients diagnosed with PG, those without specified localization information and those with incomplete clinical findings were excluded, leaving 144 patients included in our study. Of these, 73 (51%) were female and 71 (49%) were male. The average age of the patients

Table 1. Demographic characteristics of our patients.

| Gender | N (%) |
|-----------------|--------------------------|
| Female | 73 |
| Male | 71 |
| Mean age (year) | 31.3±8.3 (min-max: 2-78) |

Table 2. Localizations of the pyogenic granuloma lesions.

| N (%) | N |
|--------------------------|--------------------------------------|
| Hand/arm region: 58 (40) | Hand: 42 |
| | Hand Finger: 8 |
| | Forearm: 4 |
| | Arm: 4 |
| Face region: 42 (29) | Nose: 3 |
| | Jaw: 4 |
| | Forehead: 4 |
| | Cheek: 6 |
| | Face (localization not specified): 6 |
| Foot/leg region: 27 (19) | Lip: 15 |
| | Ear/behind the ear: 4 |
| | Foot nail edge: 17 |
| | Foot sole: 2 |
| | Foot finger: 3 |
| Trunk: 12 (8.3) | Foot (localization not specified): 4 |
| | Leg: 1 |
| | Torso: 7 |
| | Periumblical: 4 |
| Neck: 3 (2) | Intergluteal: 1 |
| | Scalp: 2 (1.4) |

Table 3. The treatments applied to the patients.

| The treatments applied to patients | N |
|------------------------------------|----|
| Excisional surgery | 73 |
| Cryotherapy alone | 22 |
| Electrocauterization alone | 12 |
| Silver nitrate cauterization | 4 |
| Cryotherapy+electrocauterization | 4 |
| Topical antibiotics | 3 |
| Cryotherapy+timolol drops | 1 |

was 31.3±8.3 (ranging from 2 to 78) (Table 1.) 47 patients (33%) were under 18 years of age. Upon examination of PG localizations, 58 patients had lesions in the arm and hand region (hand:42, hand finger:8, forearm:4, arm:4), 42 had facial lesions (nose:3, jaw:4, cheek:6, forehead:4, face:6, lip:15, ear/behind the ear:4), 27 had lesions in the foot/leg region (foot nail edge:17, foot sole:2, foot finger:3, foot:4, leg:1), 12 had trunk localizations (torso:7, periumblical:4, intergluteal:1), 3 had neck lesions, and 2 had lesions on the scalp. Localizations of the lesions are shown in Table 2. Of the patients where the side of the lesion was specified, 63 had lesions on the left side, while 20 had lesions on the right side. Patients with lesions on the left side were statistically significantly more common than those on the right side (p=0.001). The side of the lesion (right or left) was not mentioned in the rest. In evaluating the treatments applied, 73 underwent excisional surgery. Eighteen patients were given an appointment for excision, 6 patients declined excision despite the recommendation. Twenty-two patients underwent cryotherapy alone, 12 underwent cauterization alone. Four patients were treated

with silver nitrate cauterization, while 4 underwent both cryotherapy and cauterization. Three patients received topical antibiotics. One patient underwent cryotherapy and was administered timolol drops. The treatments applied to the patients are shown in Table 3. Two patients were followed without treatment.

Upon reviewing the patients' outcomes, we learned from the hospital system notes that 105 patients had recovered at the control examination. Seven patients did not attend their appointment for excision. Thirty-two patients who either did not undergo excision or did not receive an excision appointment did not attend the follow-up. Upon examining the additional diseases and conditions of the patients, we determined that 5 patients were pregnant, and in 3 patients, the chemotherapeutic drugs taken due to malignancy triggered periungual PG. Of the patients followed with a preliminary PG diagnosis and underwent excision, 3 had a different pathological diagnosis, while the rest were consistent with PG. In one patient, the lesion on the jaw was consistent with Kaposi's sarcoma, one patient with a foot lesion had pathology results consistent with malignant melanoma, and one patient with a lip lesion had pathology results consistent with mucocele. These 3 patients were not included in our patient group for the study and were in the excluded group. When comparing the characteristics of patients treated with non-excision methods with the characteristics of patients who underwent excision, we observed that the proportion of patients under 12 years of age was higher ($p=0.023$), the incidence of foot nail edge ($p=0.016$) and lip localization ($p=0.048$) was higher among these patients, and the frequency of pregnancy was higher in this group.

Discussion

In our study, the gender distribution of the patients was similar, with an average age of 31.3 ± 8.3 . Thirty-three percent of our patients were under 18 years of age. In Koo et al.'s study, data from 155 patients with PG were retrospectively evaluated. That study included 70 males (45%) and 85 females (55%). The average age was 35.3 (0-82) years [2]. There are studies reporting the average age to be in the range of 30-40 [3,5].

When examining PG localizations in our patients, we observed that it most frequently occurred in the arm and hand region (40%), face (29%), foot/leg region (19%), and trunk (8.3%) respectively. If we consider PG lesions without grouping, the lesions were located in the hand, nail edge of the foot, and lip most frequently. Although literature indicates that PG most commonly occurs in the neck, face, arms, and hands, PG can settle anywhere in the skin and mucosa [3,5,6]. Rarely, intravascular and subcutaneous locations have also been reported [8]. In one series, the most common sites were the gingiva, fingers, lips, and tongue [6]. In Koo et al.'s study, 47 patients (30%) had facial involvement, and 35 (23%) had finger involvement. The scalp was the third most common site of involvement; they identified scalp involvement in 19 patients and reported that scalp involvement might have a significant place among PG cases [2]. In our study, only 2 patients had scalp involvement. While the face was the most common site of involvement in the first decade, fin-

gers were the most common in the fifth decade in Koo et al.'s study. The most common site of involvement in the face was the cheek [2]. In the study conducted by Akamatsu et al. with 82 patients, the head-neck was the most frequently involved areas (56%), followed by the upper extremity (22%), trunk (16%), and lower extremities (6%), respectively [5]. Mucosal pyogenic granuloma is seen 2 times more frequently in women than in men [3]. Interestingly, in our study, there was no mucosal PG. This situation might be related to patients with lesions in the oral mucosa preferring to consult Ear, Nose, and Throat Clinics. In our study, the number of patients with periungual PG lesions was high. Piraccini et al. divided nail pyogenic granulomas into 4 groups according to their mechanism of formation: drug-induced (such as retinoids like acitretin, isotretinoin, antiretrovirals like indinavir, EGFR inhibitors) PG; those developed due to mechanical trauma; those formed due to peripheral nerve damage and those associated with systemic inflammatory diseases (sarcoidosis, psoriasis, seronegative spondyloarthritis) [9]. Of our patients with PG developed on the nail edge, 3 were taking EGFR inhibitors due to malignancy, and 2 were using systemic retinoids.

In our study, we observed a situation that we could not find a counterpart in the literature; the patients with lesions on the left side were statistically significantly more frequent than those with lesions on the right side. Of the 83 patients whose side was specified, 63 had their lesions on the left side. We speculate that this situation might be related to circulatory dynamics. In addition, the left side of the body may be more prone to be exposed to trauma.

Upon evaluating the treatments administered to our patients, we found that 51% underwent excisional surgery. 18 patients were given excision appointments, whereas 6 patients declined the treatment despite the recommendation for excision. Other treatments provided to our patients, in order, included cryotherapy (15.3%), electrocautery (8.3%), cauterization with silver nitrate, cryotherapy + electrocautery, topical antibiotics, and cryotherapy + timolol drops. As per the notes entered into the hospital system during subsequent visits, 73% of the patients were found to have recovered from PG. The remaining patients were lost to follow-up.

PGs sometimes undergo spontaneous resolution. However, in many cases, treatment is necessary to control ulceration and bleeding. Even after effective treatment, relapses or satellite lesions surrounding the original PG can occur. Treatment options include surgical excision, laser surgery (carbon dioxide or pulsed-dye laser), electrocautery, electrodesiccation, cryotherapy, and topically applied imiquimod and timolol, microembolization, and sclerotherapy [10-16]. Surgical excision is the most frequently employed modality [10]. In a study conducted by Giblin et al., which evaluated the treatments of 408 patients with PG, it was reported that 80% underwent surgical excision. A review reported that 64.8% of 1196 patients with PG underwent surgical excision [17]. Post-surgical excision recurrence rate has been reported as 3-4% [10]. Curettage/shave excision/electrocautery has a recurrence rate of 10% [4]. In the study by Koo et al., 48% of patients underwent surgical excision, 38% laser ablation, 5% elec-

trodesiccation, and 10% were observed and followed-up. Patients were monitored for an average of 39.1 months, with 7.7% experiencing a recurrence [2]. There are a few cases suggesting the efficacy of intralesional triamcinolone acetonide [18]. Recently, Çelik et al. in their prospective clinical study reported that the application of silver nitrate in PG could be an effective, safe, and low-cost treatment alternative to surgical excision [16]. In our study, 4 patients who were treated with silver nitrate benefited from the treatment.

We assume that some of the patients (27%) who did not return for follow-up might have undergone spontaneous regression. In their study evaluating 21 cases with PG, Yenidünya et al. observed the formation of a whitish membranous layer on the surface of lesions that had persisted for a long time (several months or longer) following recurrent traumas [7]. In this context, some of our patients might not have returned for follow-up due to a reduction in bleeding associated with the formation of this membranous layer. It is known that granuloma gravidarum can disappear after pregnancy [19]. Our three pregnant patients might not have returned for follow-up as their lesions regressed post-pregnancy.

The fact that two patients, initially followed up with a preliminary diagnosis of PG and later excised, were diagnosed with malignancies (Kaposi sarcoma and malignant melanoma) underscores for us that excisional surgery should be the primary treatment option for PG to stay on the safe side. When we compared the characteristics of patients who received non-excision treatments with those who underwent excision, we observed a higher rate of patients under 12 years of age ($p=0.023$), a higher incidence of lesions at the side of toenails ($p=0.016$) and on the lip ($p=0.048$), and a higher pregnancy frequency in this group. Considering these groups individually: surgical procedures can be challenging in children; successful outcomes with partial matrixectomy and other options to prevent trauma at the toenail side; the lip being a difficult region for surgical excision and cosmetic concerns arising from excision; and the possibility of PG regression after pregnancy in pregnant patients might be the reasons why alternative treatments were preferred over excisional surgery in these patients.

The most significant limitation of our study is the infeasibility to obtain some of data due to its retrospective nature. Although we intended to include all the patients with the diagnosis of PG, we had to remove 89 patients from our study due to the deficiency of recorded data. For this reason we could not exclude the potential biases.

Conclusion

PG is a vascular tumor of significance due to its potential for bleeding and ulceration and its tendency to persist if left untreated. Given the possibility of malignant lesions in its differential diagnosis, we believe that surgical excision is a more suitable treatment option when feasible. In our study, we observed that PG predominantly localized on the left side, yet we found no data explaining this disposition. Studies on PG in the literature are limited, and we believe our findings should be reinforced with more comprehensive, extensive and prospective studies.

Conflict of interest

The authors declare no conflict of interest regarding this article.

Ethical approval

The study protocol was approved by Ankara Bilkent City Hospital Ethics Committee, decision number: E1-23-4144, date: 18.10.2023.

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