Annals of Hematology (2019) 98:2247–2248
https://doi.org/10.1007/s00277-019-03732-9

LETTER TO THE EDITOR

Pyoderma gangrenosum: a too often overlooked facultative paraneoplastic disease

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Received: 9 February 2019 / Accepted: 10 June 2019 / Published online: 22 June 2019

Dear Editor,

Pyoderma gangrenosum (PG) is an ulcerative and neutrophilic dermatosis with poorly understood pathogenesis. Almost half of patients with PG have an underlying inflammatory disease [1]. The frequency of concomitant malignant disease in PG patients has been estimated at 4.5–9% [1, 2], and there have been increasing reports of PG in patients with an underlying solid malignancy [2] leading us to further characterize this association.

A systematic review of PubMed, Web of Science, and the Cochrane database with the search terms "Pyoderma gangrenosum" AND "cancer" OR "malignancy" OR "tumor" OR "leukemia" OR "lymphoma" led to a total of 876 publications retrieved. Cases of PG in cancer patients that were pathergy induced (i.e., after surgical excision of the tumor), large-scale studies that did not provide patient details, and cases with concurrent solid and hematologic malignancy were excluded. A total of 186 patient cases were identified from the literature search. Eighty-two percent of patients had an underlying hematologic malignancy and 18% a solid malignancy (Table 1).

In 71% of cases with solid tumors, PG presented after the diagnosis of malignancy. This was slightly decreased in patients with hematologic malignancy (54%); however, this difference was not statistically significant (Table 2). As expected, reported mortality was significantly higher in patients with hematologic malignancy versus solid malignancy (16% versus 41%, chi square test $p < 0.05$). Mortality was further analyzed using a univariate logistic regression model which determined that patients with leukemia and PG have a higher likelihood of death compared with PG patients with non-leukemia hematologic malignancies ($p < 0.05$, 95% CI = 1.01–3.34). A multivariate logistic regression did not identify any increase in mortality when adjusting for gender, size of lesion, or age.

Lower extremity was the most common site of PG in both types of malignancy. Interestingly, there was a higher number of reported cases of PG of the head and neck in patients with hematologic malignancy ($n = 16$) compared with patients with solid malignancy ($n = 1$). PG was mostly treated with oral and topical corticosteroids. Most studies did not report the effect of removal of the underlying malignancy on PG; however, numerous cases resolved with active malignancy.

Our systematic review has many limitations including reporting bias and differing reporting periods. However, this report still highlights the necessity of future research into the association between PG and solid malignancies. A recent meta-analysis has noted that the pooled prevalence of solid malignancies is surprisingly high at 7.4%, and our study provides more insight into the specific clinical characteristics of these patients [3].

Many patients with advanced cancer show high levels of blood neutrophilia [4, 5]. This underlying neutrophilic state may predispose these individuals to neutrophilic dermatoses such as PG. IL-1 is also highly produced by several solid tumors [6], which is a cytokine that is overexpressed in PG skin lesions [7].

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Table 1 Frequency of hematologic and solid malignancies in patients with PG

Hematologic malignancy	
Leukemia	
AML	30
CML	18
CLL	4
ALL	2
Hairy cell leukemia	4
JMML	1
Leukemia (unspecified)	16
Lymphoma	
Hodgkins lymphoma	6
Non-Hodgkins lymphoma	1
Lymphoma (unspecified)	11
Myelodysplastic syndrome	26
Multiple myeloma	10
Polycythemia vera	9
Myelofibrosis	5
IgA myeloma	3
Myeloproliferative disorder (unspecified)	7
Solid malignancy	
Breast	5
Colorectal	8
Lung	1
Renal cell carcinoma	3
Hepatocellular carcinoma	1
Acinar cell carcinoma of the parotid	1
Prostate	4
Stomach adenocarcinoma	3
Neurofibromatosis	1
Carcinoid tumor	1
Vulvar	1
Ovarian	1
GIST	2
Rectal	1

Table 2 PG most commonly present after malignancy is diagnosed

	PG diagnosed before (%)	PG diagnosed after (%)	PG diagnosed at the same time (%)
Hematologic malignancy	25	54	21
Solid malignancy	17	71	12

In conclusion, PG is a dermatologic entity that is becoming increasingly recognized in patients with underlying malignancy. The neutrophilic and IL-1-driven nature of PG correlates to the pro-inflammatory phenotype of many solid tumors reinforcing the concept of PG as a paraneoplastic entity. Future investigation on the correlation of PG and cancer is needed to verify and elucidate the underlying pathogenesis of this association as well as its impact on treatment and outcomes.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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