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Geriatrics and Gerontology International (2016.10) 16(10):1173–1174.

Bullous pemphigoid and percutaneous endoscopic gastrostomy

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1 **Bullous pemphigoid and percutaneous endoscopic gastrostomy**

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9 **Author contribution:**

10 Tsukasa Nozu drafted the manuscript, revised the article, and approved the  
11 final version of the manuscript. Toshikatsu Okumura critically revised the  
12 manuscript, and approved the final version of the manuscript.

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14 **Running title:** Bullous pemphigoid and PEG

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16 **Key words:** Bullous pemphigoid, Institutionalized patients, Percutaneous  
17 endoscopic gastrostomy, Risk factor, Tube feeding

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25 Dear Editor

26 Bullous pemphigoid (BP) is an autoimmune subepidermal blistering  
27 disorder with autoantibodies directed against BP180 and BP230, mainly  
28 occurring in the elderly population.<sup>1</sup> It is a rare disease among the general  
29 population and the incidences vary between 12.1 and 66 per 1 million people  
30 per year in European countries. However, it rises to 150 – 330 in people older  
31 than 80 years,<sup>1</sup> and moreover, it was reported to be much higher among  
32 elderly in nursing homes, i.e. 4.8 per 100 person per year.<sup>2</sup> The risk of death  
33 for BP patients was two to six times greater than that of age and  
34 sex-matched general population.<sup>1, 3</sup> Since management of the  
35 institutionalized elders is principally performed by physicians, the diagnosis  
36 and treatment of BP are thought to be an important mission for not only  
37 dermatologists but also physicians.

38 Several risk factors for BP such as skin trauma, surgical procedures,  
39 neurological disorders, etc. have been reported.<sup>3-5</sup> Regarding surgical  
40 procedures, ostomy surgery such as colostomy or urostomy is known to  
41 induce localized BP around stoma.<sup>6</sup> Since disabled elderly patients undergo  
42 percutaneous endoscopic gastrostomy (PEG) frequently, PEG is also  
43 presumed to be a risk factor for BP. In this context, we previously performed  
44 the retrospective survey with 36 hospitalized elderly patients, aged 64 to 101  
45 years, (5 BP and 31 non BP cases) staying more than 2 years in order to  
46 clarify this issue and published the paper in 2010.<sup>7</sup> In that survey, all the BP  
47 cases developed generalized BP and underwent enteral feeding by PEG or  
48 nasogastric (NG) tube. In the univariate analysis, PEG and tube feeding (by

49 PEG or NG tube) were associated with BP. The multivariate logistic and Cox  
50 proportional hazard regression analysis were performed with age, sex and  
51 PEG or tube feeding, demonstrating PEG was independently associated with  
52 BP.

53 As mentioned before, neurological diseases such as Parkinson's  
54 disease, dementia, etc. were known to be significant risk for BP.<sup>4</sup> Besides,  
55 bedridden condition was also reported to be an independent risk factor.<sup>4</sup> In  
56 this context, it is reasonable to think that the one of the possible reasons for  
57 the link between BP and neurological disorders can be due to the increased  
58 frequency of undergoing PEG in the disabled patients. However, none of the  
59 studies have been performed to evaluate a risk factor for BP among the  
60 patients with neurological disorders with focusing on PEG.

61 BP associated with ostomy surgery is known to be localized but not  
62 generalized BP, suggesting that the lesions may be directly related to the  
63 skin damage by surgery. The damage to dermo-epidermal junction with  
64 subsequent antigen exposure and activation of the immune system leading  
65 to the production of autoantibodies might be involved with this association.<sup>8</sup>  
66 However, in our study, all BP cases with PEG were generalized type,  
67 suggesting that other factors may contribute to develop the lesions in  
68 addition to local skin damage associated with PEG surgery. The skin around  
69 PEG tube is frequently inflamed by gastric juice and chronically irritating  
70 skin might induce systemic activation of the immune system, thereby  
71 inducing generalized lesions, which might be one of the possible  
72 mechanisms.

73 PEG is one of the most common endoscopic procedures performed  
74 worldwide nowadays, and clinical importance of this procedure has been  
75 increased. Therefore, knowing the complications of PEG is very important  
76 but none of the studies have demonstrated the relationship between PEG  
77 and BP other than ours. Since our study is the retrospective survey  
78 conducted at the single institution with small sample size, which does not  
79 have strong power. It should be still premature to generalize this finding to  
80 other populations. Large-scale clinical prospective studies in multiple  
81 medical institutions would be warranted. Since the incidence is much higher  
82 among elderly in nursing homes,<sup>2</sup> and PEG is thought to be performed  
83 frequently among these institutionalized elders, the survey should be mainly  
84 conducted in nursing homes.

85 In conclusions, PEG may be a significant risk factor for BP in some  
86 populations. PEG has become the primary choice to establish enteral access  
87 for disabled elders unable to take oral feedings lately, the frequency of BP  
88 may be increased more in the near future. Since physicians manage these  
89 patients with PEG, a greater awareness of this disease is needed for not only  
90 dermatologists but also physicians, and they should take leadership in  
91 conducting the survey to further confirm the link between BP and PEG, and  
92 explore the mechanism.

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94 **Disclosure Statement:**

95 The authors declare that they have no conflicts of interest to disclose.

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