

## Case Report: Bullous Scabies

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**Abstract.** Scabies is a common contagious cutaneous disease and usually affects the young, characterized by polymorphous lesions that may present as burrows, pruritic papules, and inflammatory nodules. Bullous scabies (BS) is its rather rare subtype, mimicking bullous pemphigoid. We report a 15-year-old Chinese boy presenting with 1-month history of pruritic bullae on his penile skin, showing poor response to both topical steroids and systemic antihistamines, but cured by sulfur ointment alone. No recurrence occurred in the 5 years of follow-up. We also reviewed the published cases. Up to date, 44 cases, including the present, have been reported. Of them, 30 were male and 14 were female. The age range was from 1 to 89 years old, with a median age of 70.6 years. The bullous lesions may involve the arms, legs, trunk, genitals, feet, buttocks, thighs, neck, inguinal folds, and may even be generalized. Trunk and extremities are the most common involved locations. Facial or mucosa involvement had never been reported. The histological findings present as a subepidermal split with variable inflammatory infiltrate predominantly neutrophils, and eosinophilic spongiosis, or both. Eighteen of 32 patients showed positive deposition of linear-granular IgG or complement 3 alone or in various combinations, and five of 24 patients revealed circulating IgG. All the 40 cases with therapeutic details were cured by antiscabietic remedy. BS always involves the trunk and extremities. It has a predilection for elderlies and males. The treatments for BS are similar to those of classical scabies.

### INTRODUCTION

Scabies is a common, worldwide, contagious cutaneous disease, which is caused by *Sarcoptes scabiei* and affects the individuals of all ages, races, and social classes in any climate.<sup>1</sup> It has a preference for the young,<sup>2–4</sup> but no gender difference and racial predominance have been described.<sup>3</sup> The common risk factors for scabies include overcrowding, immigration, poor hygiene, poor nutritional status, homelessness, dementia, sexual or close contact,<sup>3–6</sup> and immunocompromised individuals.<sup>7</sup> The typical symptom is an intense, intractable, generalized pruritus that is worse at night<sup>3–6</sup>; but occasionally, patients may be asymptomatic.<sup>8</sup> The most common presentations of scabies include classic burrows, pruritic papules, and inflammatory nodules.<sup>3–6</sup> Occasionally, the lesions may resemble impetigo,<sup>9</sup> psoriasis,<sup>9</sup> contact dermatitis,<sup>9</sup> urticaria,<sup>10</sup> Darier's disease,<sup>11</sup> or dermatitis herpetiformis.<sup>12</sup> In 1974, Bean<sup>13</sup> first described bullous scabies (BS): a rare subtype of scabies. To our knowledge, 43 cases<sup>13–50</sup> have been reported up to date. Herein, we report a Chinese boy with BS and review the literature including the clinical and pathological features.

### CASE PRESENTATION

A 15-year-old Chinese boy presented with 1-month history of pruritic bullae on his penile skin, which had poor response to both topical steroids and systemic antihistamines. The symptoms preceded by abdominal, genital, and hand pruritus with nocturnal exacerbation of 3-month duration. Cutaneous examination showed that multiple tense blisters and bullae with diameter from 0.3 to 1.2 cm, which were filled with clear fluid and surrounded by erythema, were distributed over the

penile skin (Figure 1A). The Nikolsky sign was negative over the lesions. There were discrete nodules (Figure 1A) and papules distributed over the penis and the scrotum. Papules and vesicles presented on his abdomen, hands, wrists, and especially on the webs of the fingers (Figure 1B). There was no mucosal and facial involvement. Several of his close classmates had nocturnal itching lesions but without bullae. No other family members were similarly affected. Direct microscopy of scraping from the papules of digital webs revealed *S. scabiei* mites and eggs (Figure 2). No biopsy was taken. The patient was treated with topical 10% sulfur ointment alone, resulting in rapid improvement for the itching and gradual disappearance for the bullae. No recurrence occurred during a 5-year follow-up.

### LITERATURE REVIEW

Using keywords “bullous scabies,” we searched MEDLINE and PubMed on March 25, 2016, for all articles published in English or published with English abstract details, and searched the China National Knowledge Infrastructure (<http://cnki.net/>) for content written in Chinese using the above term. We also selected the cases if the references had details. All the published cases diagnosed as BS were recruited for the review, including the following data: patient's age at discovery, gender, lesional location(s), clinical features, pathological changes, and treatment and its outcome.

### RESULTS

All the reported cases, including the present case, are summarized in Table 1. Among them, four were selected from reference 21 of which we lacked the full text, and there still included a dilemmatic case reported by Balighi and others.<sup>36</sup> Of the 44 cases, 30 were male<sup>13–19,21,25–30,32,34–37,39,41–47</sup> and 14 were female.<sup>16,17,20–24,29,31,33,38,40,48–50</sup> The age range was from 1 to 89 years, with a median age of 70.6 years; it also showed that only seven patients were under 30 years (Figure 3).

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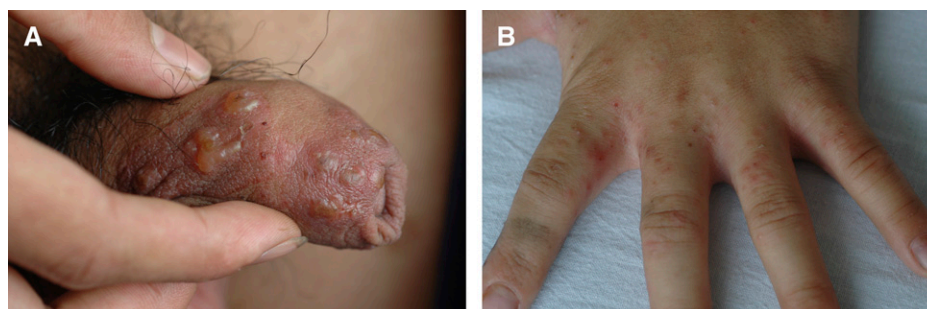


FIGURE 1. (A) Multiple tense blisters and bullae filled with clear fluid and surrounded by erythema, and discrete nodules on the penile skin. (B) Papules and vesicles on the hand, especially the webs of the fingers.

Bullous locations were described in 36 cases, varying from arms,<sup>14-20,22,24,27,30-33,35,37,38,40,46</sup> legs,<sup>16-20,22,24,25,27-30,35,37-40,46</sup> trunk,<sup>15,18,19,22,28,30,32,35,37,38</sup> genitals,<sup>15,16</sup> feet,<sup>31</sup> buttocks,<sup>28</sup> thighs,<sup>30,41</sup> neck,<sup>15</sup> inguinal folds,<sup>16,28</sup> and even generalized<sup>13,16,18,23,29,36,50</sup>; but facial or mucosa involvement had never been reported. The blisters were preceded by pruritus, and may have occurred on immunosuppressed individuals.<sup>17,22</sup> Recurrent BS was also described in a case.<sup>19</sup> No other associations were described except for a case of bullous pemphigoid (BP) subsequent to BS.<sup>38</sup>

The pathological findings included a subepidermal split with variable inflammatory infiltrate predominantly neutrophils, and eosinophilic spongiosis, or both<sup>17</sup>; which mimic the pathological features of BP.<sup>18</sup> However, intraepidermal blister was also reported.<sup>14</sup> The scabies mites or eggs could be found in the bullae occasionally.<sup>19,33</sup> Thirty-two patients had been studied by direct immunofluorescence (DIF); among them, 18 were positive and 14 negative. The most frequent presentations for DIF were linear IgG combined with complement 3 (C3) deposit (11/18), the rare conditions included combinative deposit of granular IgG, C3, and complement 4 (C4) (1/18); linear IgM combined with C3 (1/18); linear

deposit of IgG, IgM, and C3 (1/18), or only a single component deposition including granular IgG (1/18), linear C3 (1/18), or granular C3 (2/18). Nineteen of 24 patients showed negative results for indirect immunofluorescence (IIF), whereas five revealed circulating IgG binding to the dermoepidermal junction.<sup>24,30,43,44,48</sup> Seven of 23 patients showed negative results for both DIF and IIF.<sup>23,31-33,37,41,45</sup>

Forty patients were reported with therapeutic options, whom were cured by antiscabietic remedy, including topical gamma benzene hexachloride, sulfur ointment or cream, malathion, benzyl benzoate, permethrin or systemic ivermectin, or topical ointment combined with systemic ivermectin. Antihistamines, topical or systemic steroids, immunoglobulin, or cyclophosphamide alone, or in different combinations have been tried, showing poor response to BS besides palliative improvement of itching and/or lesions.<sup>14,16,35,36,40,41</sup> Interestingly, oral prednisolone was reported worsening the lesions in a case.<sup>21</sup>

## DISCUSSION

BS, also called BP-like eruption,<sup>15</sup> is an atypical manifestation of scabies, which may develop concurrently with, or after, the occurrence of scabietic lesions.<sup>26-28,51</sup> Despite the lack of histopathological examination for the present case, scabies mites were detected, and both the lesions and symptoms disappeared after antiscabietic therapy alone without recurrence during a 5-year follow-up; all these suggested that the diagnosis was BS.

The present results showed that BS has male predilection and mainly afflicts the elderly, especially patients older than 70 years; such an age group is the same in which BP mainly occurs. The reasons for elderly predominance, we speculate, are that older individuals have increased likelihood of bedridden status and stay in nursing homes, resulting in increased risk of scabies infection.<sup>52,53</sup> The exact mechanisms are not fully understood yet. The lesions may involve, except the mucosa and face, the whole body including arms, legs, trunk, genitals, feet, buttocks, thighs, neck, inguinal folds, and may even be generalized; but the trunk and extremities are the most commonly involved areas. Scabies mites and/or eggs may be detected from the lesions of BS, but not always. The pathological features of BS are similar to those of BP; however, true BP subsequent to BS had indeed occurred.<sup>38</sup> We considered that the case described by Balighi and others<sup>36</sup> was BS rather than BP, because of the positive detection of the scabies mites from the vesicobullous lesion, and the

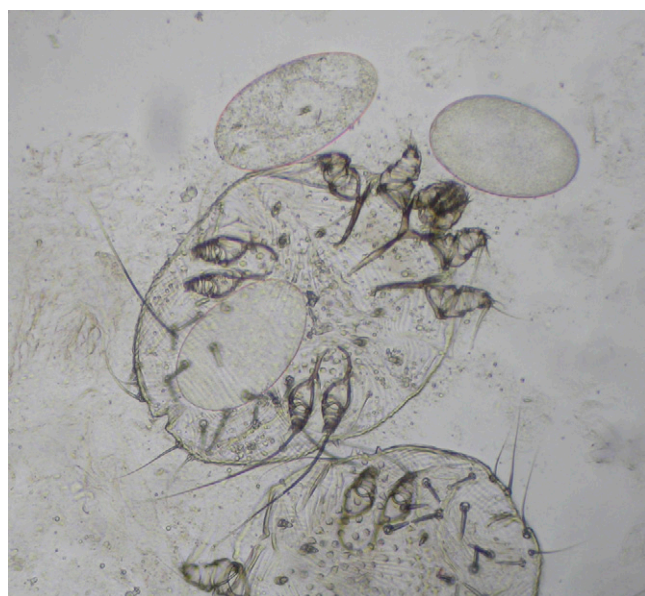


FIGURE 2. Scabies mites and eggs detected on the scraping from the papules.

TABLE 1  
Summaries of the published bullous scabies

| No. | Published year | Age | Gender | Location of bullous lesions               | IIF/DIF result             | Therapy  | Author                   | Reference |
|-----|----------------|-----|--------|---|----------------------------|--|--------------------------|-----------|
| 1   | 1974           | 1   | M      | Generalized                               | ND/ND                      | 1% GBH   | Bean                     | 13        |
| 2   | 1981           | 9   | F      | Generalized                               | ND/ND                      | 10% Benzyl benzoate  | Ponce-Navarez and others | 50        |
| 3   | 1981           | 13  | F      | Generalized                               | ND/ND                      | 10% Benzyl benzoate  | Ponce-Navarez and others | 50        |
| 4   | 1989           | 34  | F      | Generalized                               | —/—                        | 10% Benzyl benzoate  | Viraben and Dupre        | 23        |
| 5   | 1991           | 67  | M      | Arms, abdomen, genitals                   | —/Granular IgG             | 1% GBH   | Bhawan and others        | 15        |
| 6   | 1991           | 76  | M      | Neck, back, arms                          | —/Linear IgG, C3           | 1% GBH   | Bhawan and others        | 15        |
| 7   | 1992           | 76  | F      | LD  | ND/ND                      | 1% GBH   | Kurosawa and others      | 49        |
| 8   | 1993           | 36  | F      | Arms and legs                             | IgG/Linear C3              | 1% Malathion   | Ostlere and others       | 24        |
| 9   | 1993           | 69  | M      | Legs                                      | —/Granular IgM, C3         | 1% GBH   | Parodi and others        | 25        |
| 10  | 1993           | 74  | M      | LD  | ND/—                       | LD   | Shirlene-Jay and others  | 42        |
| 11  | 1993           | 74  | M      | Chest                                     | —/ND                       | 1% GBH, 1% lindane   | Said and others          | 26        |
| 12  | 1994           | 84  | F      | LD  | IgG/Linear IgG, C3         | LD   | Ezaki and others         | 48        |
| 13  | 1995           | 66  | F      | Arms and legs                             | —/Granular C3              | 25% Benzyl benzoate  | Veraldi and others       | 20        |
| 14  | 1995           | 73  | M      | Arms and legs                             | —/Granular C3              | 5% Permethrin  | Haustein                 | 27        |
| 15  | 1996           | 76  | M      | Trunk, legs, inguinal folds, and buttocks | —/Linear IgG, C3           | 5% Permethrin, 1% GBH, 6% sulfur   | Slawsky and others       | 28        |
| 16  | 1997           | 73  | M      | Legs                                      | ND/—                       | 25% Benzyl benzoate  | Clyti and others         | 46        |
| 17  | 1997           | 89  | F      | Arms and legs                             | ND/—                       | 25% Benzyl benzoate  | Clyti and others         | 46        |
| 18  | 1999           | 64  | M      | LD  | IgG/Linear IgG, C3         | LD   | Kambara and others       | 43        |
| 19  | 2000           | 81  | M      | LD  | IgG/Linear IgG, C3         | LD   | Inoue and others         | 44        |
| 20  | 2000           | 70  | F      | Legs                                      | ND/—                       | 5% Permethrin/oral ivermectin  | Bosch-Garcia and others  | 29        |
| 21  | 2000           | 72  | M      | Generalized                               | ND/—                       | 5% Permethrin/oral ivermectin  | Bosch-Garcia and others  | 29        |
| 22  | 2001           | 76  | M      | Trunk and thighs                          | —/Granular IgG, C3, and C4 | 1% GBH   | Bornhovd and others      | 30        |
| 23  | 2001           | 89  | M      | Trunk and extremities                     | IgG/linear IgG and C3      | 1% GBH   | Bornhovd and others      | 30        |
| 24  | 2003           | 52  | M      | LD  | —/—                        | 5% Permethrin  | Brar and others          | 45        |
| 25  | 2003           | 4   | M      | Left hand                                 | ND/ND                      | 5% Permethrin  | Shahab and Loo           | 17        |
| 26  | 2003           | 34  | M      | Trunk and limbs                           | ND/—                       | 5% Permethrin lotion   | Kaur and Thami           | 19        |
| 27  | 2005           | 30  | F      | Trunk, arms, and legs                     | ND/ND                      | 5% Permethrin  | Jena and others          | 22        |
| 28  | 2006           | 42  | M      | Lower trunk, arms, and legs               | ND/—                       | 1% Lindane   | Ansarin and others       | 18        |
| 29  | 2003           | 71  | M      | Arms, legs, and trunk                     | —/Linear IgG, C3           | Oral ivermectin  | Nakamura and others      | 21        |
| 30  | 2006           | 72  | M      | LD  | —/Linear IgG and C3        | Oral ivermectin  | Galvany and others‡      | 47        |
| 31  | 2006           | 52  | M      | Generalized                               | —/Linear IgG and C3        | Oral ivermectin and prednisolone   | Balighi and others*      | 36        |
| 32  | 2008           | 65  | M      | Trunk and arms                            | —/—                        | Sulfur 20% in yellow soft paraffin   | Wozniacka and others     | 32        |
| 33  | 2009           | 70  | F      | Arms                                      | —/—                        | 10% Sulfur ointment, and hydrocortisone  | Marciniak and others     | 33,†      |
| 34  | 2010           | 87  | F      | Arms and feet                             | —/—                        | Topical lindane  | Serra and others         | 31        |
| 35  | 2010           | 72  | M      | Genitals and inguinal folds               | —/Linear IgG and C3        | Oral ivermectin, topical compounds (permethrin, triamcinolone acetate, gentamycin)             | Rossell and others       | 16        |
| 36  | 2011           | 79  | M      | LD  | ND/—                       | Benzyl benzoate 20%  | Roxana Stan and others   | 34        |
| 37  | 2013           | 54  | M      | Trunk and limbs                           | ND/linear IgG and C3       | 10% Sulfur ointment  | Chen and Luo             | 35        |
| 38  | 2013           | 26  | M      | Both hands                                | ND                         | 5% Permethrin lotion and a single 12-mg dose of oral ivermectin along with oral antihistamines | Gutte                    | 14        |
| 39  | 2014           | 65  | M      | Trunk and extremities                     | —/—                        | 20% Sulfur ointment  | Zhang and others         | 37        |
| 40  | 2015           | 78  | F      | Trunk and extremities                     | ND                         | 10% Sulfur ointment  | Huang and others         | 38        |
| 41  | 2015           | 23  | M      | Right foot                                |                            | 5% Permethrin  | Maan and others          | 39        |
| 42  | 2015           | 87  | M      | Arms and legs                             | ND/Linear IgG, IgM, and C3 | 12.5% Sulfur and 5% permethrin   | Akin Belli and others    | 40        |
| 43  | 2015           | 73  | F      | Thighs                                    | —/—                        | 10% Sulfur cream   | Su and others            | 41        |
| 44  | 2010           | 15  | M      | Genital folds                             | ND/ND                      | Topical sulfur ointment  | Present                  | Present   |

DIF = direct immunofluorescence; F = female; GBH = gamma benzene hexachloride; IIF = indirect immunofluorescence; LD = lack data; M = male; ND = not done; — = negative.

\*The case is dilemmatic whether it is a bullous scabies or scabies-induced bullous pemphigoid.

†We do not understand the text clearly except the gender and age.

‡The case was diagnosed on 2006 and the article was published on 2010.

excellent response to medications. Although China has about 20% of the world population and is a developing country, only five cases of BS, including the present one, had been reported up to date,<sup>35,37,38,41</sup> and three were described by our

group,<sup>35,38</sup> we considered that BS may have been largely misdiagnosed or neglected as a diagnosis in China before.

The mechanisms of bullae formation for BS remain unknown. Superinfection was considered to play an important



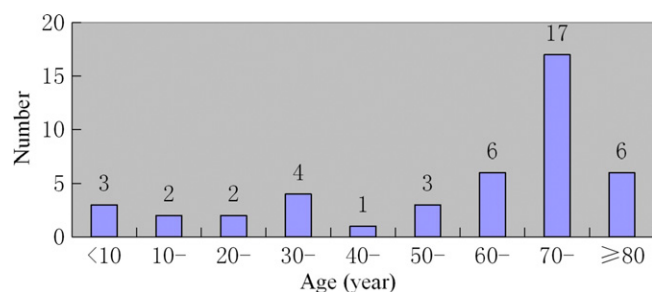


FIGURE 3. The age distribution of patients with bullous scabies shows that more than a half of patients are older than 70 years.

role in some patients with a positive culture of *Staphylococcus aureus*.<sup>18</sup> In patients with positive deposition of C3 and various immunoglobulins, it was considered that the bullae may result from the direct injury or secretion of lytic enzymes by the scabies mites, which alters the basement membrane zone (BMZ) antigen resulting in autoantibody formation and inducing inflammatory reaction<sup>18</sup>; or mite proteins may have cross-reactivity with BMZ antigens and lead to the production of the autoantibodies, activating immunoreaction and producing the bullae.<sup>20</sup> In patients with negative DIF, id reaction, also called autoeczematization, to scabietic mite was considered as the mechanism of bullae.<sup>18</sup> Bornhove and others<sup>30</sup> considered that persistence of scabies led to a specific immune response with activation of Th2 cells, resulting in increase of interleukin-5 and eosinophilia, and causing BS. However, the present results found that 18 of 32 BS patients had positive finding of DIF with linear-granular IgG and/or C3 alone or in various combinations, whereas only five of 23 revealed circulating IgG on IIF study. The previous study demonstrated that positive epidermal immunofluorescent staining does not indicate absolutely an autoimmune bullous disease<sup>54</sup>; the value of positive immunofluorescent staining in BS needs further studies. Because of the deposition of immunoglobulin and C3 in the BMZ, the detection of circulating IgG in some patients, and the excellent response to antiscabietic treatments, BS can be considered a scabies-induced immune response.<sup>35</sup> But, it is still hard to understand why the lesions of BS had poor response to immunosuppressants, and the lesions could occur on the immunosuppressed individuals,<sup>17,22</sup> or even progressed after treatment with prednisolone.<sup>21</sup> It is also unclear why BS does not occur more often although scabies is a common disease, and why it has male predilection.

Because of the lack of defined diagnostic criteria, the diagnosis of BS should be considered for any bullous eruptions accompanied by papules and nocturnal itching, and the itching responds well to antiscabietics, but resists immunosuppressants, regardless of the histopathology and scraping findings. We suggest that the patient diagnosed as BS may have a follow-up as long as possible so that true BP can be excluded. The doctors also should pay attention to the possibility of recurrent BS.<sup>19</sup> Moreover, as circulating antibodies against BP180 and/or BP230 had been detected in some of the scabietic patients with bullous eruptions,<sup>38,51</sup> and persistent circulating antibodies against scabies antigens have been identified in dogs and foxes by enzyme-linked immunosorbent assays,<sup>54</sup> we support the opinion that some of the bullous lesions occurring in scabies are true BP.<sup>38,51</sup>

The differential diagnoses include BP, pemphigus, arthropod bite reaction, acute contact dermatitis, and bullous impetigo,<sup>17</sup> as well as epidermolysis bullosa acquisita. As both clinical and pathological features of BS resemble those of BP,<sup>17</sup> even when the skin scrapings are positive for scabies, it is still hard to differ true BP from BS,<sup>16,21</sup> and to exclude the possibility of scabies and concomitant BP.<sup>21</sup> It is also reported that patients suffering from scabies have an increased risk for BP.<sup>52</sup> In fact, true BP subsequent to scabies or to BS have been reported.<sup>9,38,51,55</sup> Usually, the facts that the detection of scabies mites and/or its eggs from scraping, good response to antiscabietic treatment, and/or the patients with either negative or low values of circulating IgG,<sup>16,21</sup> are important clues for the diagnosis of BS. Nakamura and others<sup>21</sup> considered that IIF study is more important than DIF to distinguish BS from BP. We considered, if possible, that circulating antibodies against either BP180 or BP180 and BP230 might be tested, for which the positive results support the diagnosis of BP. On the basis of the clinical manifestations and pathological changes, other differential diagnoses are not difficult to exclude.

The therapies of BS are similar to those of classical scabies including systemic and topical treatments. In patients with poor response or allergic reaction to topical treatment, systemic ivermectin is an option. Because resistance of common scabies to permethrin and lindane has been reported,<sup>3,4,6</sup> the doctors should pay more attention to the patients of BS with poor response to the medications, although such a condition has never been reported before. For recurrent BS, multiple applications must be administered.<sup>19</sup> Immunosuppressants seem to be of no benefit to BS. In rare conditions, oral prednisolone may worsen the lesions.<sup>21</sup> As a matter of fact, doctors always select drugs based on their personal predilection, local availability, and the cost.<sup>3,5</sup>

## CONCLUSIONS

BS is a rare subtype of scabies that commonly afflicts the elderly with a median age of 70.6 years. The lesions may involve the whole body except the mucosa and face. Its clinical and histopathological features mimic those of BP. No defined diagnostic criteria for BS have been proposed. A diagnosis of BS should be considered for any bullous eruptions accompanied by papules and nocturnal itching that respond well to antiscabietics but are resistant to immunosuppressants, regardless of the histopathology and scraping findings. The treatments for BS are similar to those of classical scabies.

## CONSENT

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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