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Abstract

Background: Follicular occlusion tetrad (FOT) is a clinical syndrome consisting of suppurative hidradenitis, acne conglobata, dissecting cellulitis of the scalp, and pilonidal sinus. FOT is a rare case that is mostly found in severe conditions resulting in resistance to therapy. Diagnostic accuracy and therapy for all components of FOT is extremely important.

Case: A 43-year old male presented with small, painful blisters and bumps filled with pus that had been ongoing for five years. We found pustules and erythematous nodules and multiple abscess with atrophic scars on the scalp, anterior and posterior trunks, abdomen, groin and gluteal regions on the facial region, we found multiple atrophic scars. The pus culture showed the presence of Escherichia coli, and fistulography examination revealed multiple cutaneous fistules and enterocutaneous sinus. The histopathological examination indicated rupture of hair follicles, follicular plugs, and infiltration of heavy-mixed infiltrate cells.

Discussion: The FOT diagnosis was established through medical history recording, physical and histopathological examinations, and fistulography. Upon medical history recording and physical examination, we found pustules and nodules in several hairy areas. The fistulographic examination showed some fistules and sinus tracts, and the histopathological examination showed adnexal tissue damage caused by occlusion of hair follicles and inflammation due to accumulation of keratin and debris. All these findings led to the FOT diagnosis.

Keywords: Acne conglobate, dissecting cellulitis, Suppurative hidradenitis, follicular occlusion syndrome, pilonidal sinus

Introduction

Pillsbury, Shelley, and Kligman first introduce the term “follicular occlusion triad” in 1956 [1]. This triad consists of suppurative hidradenitis, acne conglobate, and dissecting cellulitis of the scalp. This grouping is based on histopathological findings of these three diseases, which indicates follicular hyperkeratinization. In 1975, the fourth component of this syndrome, which is pilonidal sinus, was added into the triad, thus changing the term to follicular occlusion tetrad (FOT) [1].

Suppurative hidradenitis (SH) is also known as acne inversa, Verneuil’s disease, or pyoderma fistulans signifcica [1]. The first SH international symposium took place in Dessau, Germany in 2006, where the definition of SH as a recurrent chronic inflammation on hair follicles that usually occurs after puberty and manifests as a painful, deep-seated inflammation on body parts that are rich in apocrine glands, such as the axilla, groin, and anogenital region was formulated [2]. Suppurative hidradenitis is a lymphohistiocytic inflammation with granulomatous reaction and sinus and scar development of the hair follicles. SH predisposing factors are bacterial infection, hormonal (androgen), smoking, obesity, and genetic factors [3]. The latest study showed that the prevalence of SH is 1% out of 10,000 population samples in France [3], and around 1:600 in Caucasians [4]. The prevalence of this disease is higher in females with a ratio ranging from 2:1 to 5:1, but the reason behind this finding is still unknown. This disease is rarely found in the prepubescent or post-menopausal population. Suppurative hidradenitis is commonly found in the 23-year old population [3].

Acne conglobate is a severe and rare form of acne, often found in grown men without systemic manifestation [5]. Conglobate means round like ball, usually found on the anterior and posterior trunks and gluteal, buccal, neck, and shoulder regions [6]. The characteristic lesions are multiple papules with inflammation, soft nodules, and multiple abscesses, which usually conjoin and form sinuses. This condition usually occurs in the second and third decades of life and persists until the age of 40-50 [5].
Dissecting cellulitis (DC) of the scalp, also known as perifolliculitis capitis abscedens et suffodiens, is a rare, chronic inflammation of the scalp and is part of FOT [7]. The lesion usually starts as multiple nodules and is often found in the vertex and upper occipitalis regions. These nodules then rapidly change into fluctuative, baggy, and pus-filled nodules [8]. These lesions may spread to the posterior aspect of the head and may even affect all surfaces of the scalp, causing destruction of hair follicles and permanent cicatrical alopecia [7]. This condition is commonly found in adult males, especially in the darker-skin races, although this condition may also found in Caucasian males and females [8].

A pilonidal cyst also known as pilonidal sinus [9]. Pilonidal sinus as first introduced by Mayo in 1833. The term pilonidal, first described by Hodges (1880), is derived from the Latin term of “pilus” which means hair and “nidus” which means nest. A pilonidal sinus is a cystic structure along the coccygeus near the gluteal fold, located around 4-5 cm from the anus. These cysts usually contain hair and skin debris [10]. Most cases are asymptomatic, but infections and inflammation associated with the cyst may cause pain. A pilonidal sinus is more commonly found in men (80%). The highest incidence of this condition ranges from ages 15 to 24 years [11].

FOT is a rare case in the dermatovenereology department. In this report, the authors will discuss a case of FOT and hope this report can broaden our knowledge about establishing FOT diagnosis and how to appropriately manage this condition.

Case

A 43-year old male, working as a courier and living in Pasar Kliwon came to the Dermatovenereology Department of Moewardi Public Hospital Surakarta, Central Java, Indonesia and presented with a painful and foul-smelling scalp, armpits, chest, back, stomach, groin, and buttocks. Five years prior to presentation, these signs started with small, painful blisters and bumps filled with pus. This patient underwent three prior surgical procedures for the bumps on his face, neck, chest, armpits, and buttocks; two procedures occurred in 2011 and one occurred in 2014. All of the surgical procedures took place in other hospitals, but there was no improvement in his signs or symptoms. This patient reported a history of severe acne on his face since he was 20 years old, but now there were only scars on his face. The patient has a 10-year history of diabetes mellitus. He goes for his regular check-ups in the Internal Medicine Department of Moewardi Public Hospital and is taking metformin 500 mg three times daily, novorapid insulin 20-20-20 IU, and levemir [11] insulin 0-0-0-16 IU. The patient does not have history of hypertension, asthma, or heart disease. This patient has been a smoker for 20 years.

Upon physical examination, this patient looked moderately ill and fully alert (compos mentis). His blood pressure was 130/80 mmHg, whereas other vital signs were within normal. Based on visual analog scale (VAS) the pain score was 2, while his height was 160 cm, and his weight was 70 kg with a body mass index (BMI) of 27.3 kg/m², which indicated obesity. There were pustules, erythematous nodules, and multiple abscess with atrophic scars on his scalp, anterior and posterior trunks, and abdominal, inguinal, and gluteal regions. On the facial region, there were multiple atrophic scars (Figure 1).

Based on the laboratory examination, we found the fasting blood glucose level was 210 mg/dl (normal value 76-110 mg/dl), post prandial blood glucose level 309 mg/dl (normal value <160 mg/dl), HbA1c 13.3% (normal value 4-6%), and creatine 1.5 mg/dl (normal value 0.6-1.3 mg/dl). Based on the potassium hydroxide examination, we did not find hyphae or spores. Based on the Gram stain examination, we did not find hyphae or spores. Based on the Gram stain examination, we did not find hyphae or spores. Based on the Gram stain examination, we found Escherichia coli that was resistant to ampicillin, gentamycin, ciprofloxacin, and trimethoprim-sulfamethoxazole, and we were advised to use ceftazidime or amikacyn. We also did histopathological examinations from skin biopsies, which were collected from erythematous patch and abscess on the scalp, left armpit, and sacrococcygeus regions. The specimens then were stained with hematoxylin-eosin). From the scalp specimen, we found keratin plugs in the hair follicles and empty hair follicles. Most of them did not contain hair matrix, and there was no inflammation. From the armpit specimen, we found ruptured hair follicles and diffuse infiltration of neutrophils, lymphocytes, and erythrocytes (dominant) around and inside the hair follicles walls. From the sacrococcygeus specimen, we found epidermal atrophy, dermal edema, keratin cysts and a few inflammatory cells (Figure 2).

Figure 1: (A-C) Facial region: multiple atrophic scars. (D-J) Scalp, anterior and posterior trunk, inguinal, gluteal regions: pustules, erythematous nodules, and multiple abscess with atrophic scars.

Figure 2: (A,B) Axilla region low magnification: ruptured hair follicles and neutrophils, lymphocytes, and erythrocytes infiltration.
around and inside hair follicles walls. High magnification: the inside of hair follicles infiltrated by erythrocytes (dominant), lymphocytes, and neutrophils. (C,D). Sacrococcygeus region low magnification: epidermal atrophy. High magnification: keratin cysts. (E). Scalp region: follicular plugs of the hair follicles, empty hair follicles, most of them do not contain hair matrix, no inflammatory reaction found.

A thoracic X-ray demonstrated bronchitis. The sputum examination revealed no acid-fast bacteria. Based on the fistulography of the left and right armpits, we found multiple cutaneous fistules and found multiple enterocutaneous fistules in the thoracic and abdominal regions (Figure 3).

Figure 3: Fistulography examination. (A-C) thorax region (D) abdominal region: multiple enterocutaneous sinuses. (E,F) right and left axillar region: multiple cutaneous fistules.

Discussion
Suppurative hidradenitis, acne conglobate, and perifolicullitis capitis abscedens et suffodiens and pilonidal sinus are all components of FOT. The pathogenesis of this syndrome is still unknown, but evidence suggests that all four components of FOT have the same pathological process, which starts with follicular occlusion in areas containing apocrine glands [12]. Because of the accumulation of the material inside, the follicles stretch and then rupture. Keratin and bacteria from the ruptured follicles then initiate granulomatous and neutrophilic responses, which are considered primary inflammatory processes with secondary bacterial infections (usually by Staphylococcus aureus or S.epidermidis) [13]. In several cases, a cellular immune response defect has been found and is considered a predisposing factor for infection. Histopathological examination of new lesions shows perifolicullitis with neutrophil, lymphoid cell, histiocyte, plasma cell, and giant cell infiltration causing destruction of the adnexa glands. In chronic cases, epidermal sinuses and extensive fibrosis can be found [14].

Suppurative hidradenitis (SH) was discovered in 1854 by Aristide Verneuil, and it has been associated with sweat glands since then. However in 1921, the association between SH and apocrine glands was established [15]. In this disease, we can find follicular epithelial defects, and these may correlate with the pathogenesis of acne vulgaris. However, sebum production does not increase in SH [16]. Based on the Second Congress of the SH foundation in San Francisco in March 2009 [17], suppurative hidradenitis has been defined as chronic and recurrent follicular inflammation, which usually occurs after puberty and shows painful deep-seated inflammatory lesions in the areas containing apocrine glands; the predilection locations are on the armpits, groin, and anogenital regions.

The diagnostic criteria of SH based on the SH foundation congress consist of three parameters:
1. Typical lesions consist of painful nodules, ‘blind boils’ on new lesions, abscesses, sinus, scars, and ‘tombstone’ open comedons on secondary lesions.
2. Typical topography consists of armpits, groins, perineal and perianal areas, buttocks, under and between the breasts folds.
3. Chronic and recurrent.

To establish the diagnosis of SH, all of the criteria above must be fulfilled [17]. Suppurative hidradenitis (SH) can be classified into three stages for each area, according to Hurley’s classification as shown in (Table 1).

Table 1: Hurley’s classification [15].

<table>
<thead>
<tr>
<th>Stage</th>
<th>Characteristic</th>
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<tbody>
<tr>
<td>I</td>
<td>Solitary or multiple abscess, without sinus and cicatrix</td>
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<tr>
<td>II</td>
<td>Recurrent abscess with sinus and cicatrix. Solitary or multiple, extensive and separated lesion</td>
</tr>
<tr>
<td>III</td>
<td>Conjoin lesions, diffuse or almost diffuse, multiple conjoined sinuses with abscess in all area</td>
</tr>
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Hurley’s classification is extremely useful in classifying cases and their therapies. SH risk factors according to Naldi are smoking and obesity. Smoking (>70%) and an increase in BMI significantly appear as factors that cause a worsening of SH. Other risk factors for SH are genetic and hormonal factors [15-18]. Abnormal apocrine gland secretion is expected to be the trigger of SH [2]. Sartorius et al [19] Modified the SH score (SHS) so that it can be used in daily practice.

The SHS contains Four Components:
1. Areas involved,
2. Amount and the type of lesion in each area,
3. The furthest distance between two adjacent lesions and
4. The presence of normal skin among the lesions.

In a study conducted by Sartorius et al [19], this scoring method was proven to be relevant for showing the relationship between SH and BMI severity and smoking. According to Revuz [15], the Sartorius score is also useful in several therapeutic studies and represents the low quality of life as an effect of this disease. SH treatment depends on the stage of the disease (according to Hurley’s classification), frequency of exacerbations, and the patient’s goal. Total recovery can be achieved only by extensive surgical excision with secondary wound healing, but this procedure is used only for stage III or a severe stage II disease [2,15]. Therapy for the acute state of this disease including antiseptic and topical clindamycin [1,15] and systemic antibiotics such as amoxicillin, cephalosporin, clindamycin, rifampycin, or penicillin-M. Amoxicillin-clavulanic acid has the potential to be an effective regimen if given within
the first hour after early symptoms occur [15]. Intralosial steroid therapy (such as 5-10 mg triamcinolone) has been suggested to speeds up process the involution of early lesion [1,15]. High doses of systemic steroids can be used to reduce pain and inflammation. In chronic states, we can use a combination of antibiotics such as clindamycin-rifampycin, metronidazole, or a high dose of zinc gluconate [15]. Other choices of modality therapy includes laser therapy with Intense Pulsed Light (IPL) twice a week for one month, photodynamic therapy with 20% 5-aminolevulinic acid every week for one month combined with IPL or blue light, and/or a ND:YAG long-pulse laser, which is used twice a month in Hurley stage II [2]. In this case, the painful abscesses on the armpit(s), groin, and gluteal regions were ongoing for five years. SH risk factors in this patient were a 20-year smoking history and a BMI of 27.3 (indicating obesity). Based on the physical examination, we found pusules, erythematous nodules, and diffuse-edged multiple abscesses on the armpits, groin, and gluteal regions. Based on the fistulography of the thorax and abdomen, we observed multiple enterocutaneous sinuses, and from the fistulography of the right and left armpits we observed multiple cutaneous fistules. Thus, we classified this patient into SH stage III based on Hurley’s classification.

Acne conglobate is a form of severe nodulo-acne, which is mostly found in male teenagers. The lesions consist of comedo, papules, pusules, nodules, abscess, and scars. The predilection locations are on the back, buttocks, chest, abdomen (rarely), shoulder, neck, face, upper arms, and thighs. These comedos often have multiple orifices. Inflammatory lesions are usually bigger in size, soft, and dark-colored, and these lesions usually secrete foul-smelling serous or purulent material. Multiple sinus ducts are a common finding. After this acne heals, keloid or atrophic scars may form. The main etiology of acne conglobate remains unknown, but a karyotyping XYY defect may be responsible for the severity of acne conglobate. The relationship between this disease with a specific phenotype of human leukocyte antigen (HLA) has not yet been proven. Phenotype HLA -A and -B were evaluated from 65 patients with conglobate acne; among them, normal antigen frequency was found. Other patients with acne conglobate and suppurative hidradenitis have been studied, and four out of six patients have cross-reacting antigen HLA-B7 (which include HLA-B7, -Bw22, -Bw27, -Bw40, and -Bw42), and all of them have HLA-Dw4 [21]. Acne conglobate often disturbs social life because of its chronic nature, severity, and treatment difficulties. Secondary infections caused by Gram-positive bacteria and scar development are common findings. Based on histopathological examination, infiltrate around the hair follicles, which may cause damage in normal dermis layer, is commonly found [22]. Several treatments have been used, including high-dose antibiotic therapy, intralesional and systemic corticosteroids, incision, excision, and debridement surgery [20]. Isotretinoin causes dramatic results in some patients. In severe cases, a high dose of 2 mg/kg/day for 20 weeks may be needed. However, because of the severe flare-ups that occur with early isotretinoin usage, 0.5 mg/kg/day must be given as the initial dose, and systemic corticosteroids are often needed before starting isotretinoin therapy. Isotretinoin can be used concurrently with prednisone, which is the drug of choice for severe acne conglobate [20,22]. In addition to that therapy, an acne conglobate case, which has been successfully treated using a combination of laser ablation CO2 twice a week for three months, was reported. The goal of the therapy in that case was to eradicate the sinus, and then use topical tretinoin 0.1% to prevent new acne lesions. In that case report, it was stated that this therapy combination gives cosmetic improvements, and it was also stated that there was no recurrence one year after treatment. In our case, there were scars, but no new acne lesions, on the patient’s face, indicating that facial treatment was unnecessary.

Dissecting cellulitis (DC) of the scalp is a rare, chronic suppurative disease of the scalp. This disease mostly occurs in grown, dark-skinned men with ages ranging from 20 to 40 years [13, 24]. This disease may occur concurrently with acne conglobate, suppurative hidradenitis, and pilonidal sinus. The clinical manifestations of DC are keloid, perifollicular and follicular pustules, nodules, abscesses, and multiple sinuses, which may develop into scarring alopecia [24]. The specific etiology of this uncommon condition is still unknown, but it is expected that this mechanism is caused by follicular occlusion. Accumulation of sebaceous material causes follicular dilatation and rupture and local neutrophilic and granulomatous responses. Secondary infections may occur, but are not the main cause of FOT [25]. Dissecting cellulitis (DC) has a tendency to cause severe alopecia, fluctuant nodules, and sinus tracts. This characteristic makes DC different from acne keloidalis nuchae [12]. Because of its chronic nature and possibility of relapse, DC is difficult to treat. Smoking is a significant risk factor and one that worsens the condition [26]. There are several choices of DC therapy starting with systemic antibiotics such as rifampycin, minocyclin, clindamycin, metronidazole, or dapsone to acitretin, isotretinoin, systemic corticosteroids (such as 40-60 mg prednisone daily), high doses of zinc sulphate, and finally, surgical and laser therapies [13, 25]. There is a report about a severe DC case that responded to intravenous TNF-α antibody infliximab therapy [26]. Surgery can be chosen as one of the DC therapies. Incision and drainage of the lesion is the first step to do. Surgical excision is considered in severe or recalcitrant cases. Extensive excision on the affected areas and skin graft with split thickness skin graft can be considered. A combination of tissue expansion, radical excision, and isotretinoin has been proved useful [13]. In this case, the patient has abscess on his vertex region, which is a predilection location of DC.

Pilonidal sinus is a chronic inflammatory process of the skin, which is caused by keratin plugs and debris. Clinical manifestation of pilonidal sinus consists of penetration of the dermal layer by holes. Several factors affecting the incidence of pilonidal sinus are male, at the onset of puberty, family history of pilonidal sinus, and obesity [27]. In addition to those factors, an occupation involving driving/riding, remaining in a seated position for a long period of time, and bad personal hygiene increase the risk of this disease [28]. All of these factors contribute to the development of pilonidal sinus through variations of hair textures and skin changes [27]. Hair penetration into the subcutaneous layer has been found through dilated hair follicles, even though there are no follicles are found inside the cysts. The sinus develops into a short tract so that the hair may penetrate down to the subcutaneous layer. A reaction to foreign objects may cause an abscess and development of granuloma. The pathophysiology of this condition has been described by Putey and Scarff. There are three important events that occur in the development of pilonidal sinus:

1. Hair invasion,
2. Hair penetration and
3. Susceptible skin [29].
Pilonidal sinus is often found in the sacrococcygeus region of men with hirsutism. Other location predilections are the umbilicus, armpit(s), scalp, ears, nose, eyelids, genitalia, and interphalangeal spaces. From the histopathological examination, elongated sinus tracts on granulated tissue with layered squamous epithelial are a common finding. These sinuses terminate on a bulbous expansion in the lower dermis and subcutaneous layers, which contain a chronic abscess cavity [30]. Therapy given for pilonidal sinus consists of infection eradication therapy with oral antibiotics and sinus excision [12]. A surgical procedure remains the primary therapy choice even though the recurrence risk for chronic pilonidal sinus is around 5%-20% [31]. The clinicians in Aarhus, Denmark stated that the Nd-YAG laser can be used as a treatment for chronic pilonidal sinus without abscess [31]. In our case, the lesions were found in a predilection location (the sacrococcygeus region). The histopathological examination demonstrated keratin cysts in the epidermis, which supported the diagnosis of pilonidal sinus.

The differential diagnosis for this case is a carbuncle. A carbuncle is even more extensive with deeper inflammation, which occurs when there is a suppurative process (multiple, confluence furuncle). Painful lesions usually occur on the back of the neck, posterior trunk, and thighs. Patients may experience fever and malaise. The affected areas are red-colored with indurations and multiple pustules, which rapidly appear on the surface of the skin and then become dry around the hair follicles. The initial lesions are in grayish yellow color with irregular holes in the middle of it. These lesions may cause granulated tissue and scars, which usually appear purplish in color in the affected areas. Based on histopathological examinations, multiple abscesses separated by connective tissue trabeculae, dermis, and hair follicular infiltrate are common findings [32]. In our case, four components of FOT each with characteristic skin lesions were found. Based on the histopathological examination, we found hair follicular occlusion and rupture, whereas the carbuncle does not show this kind of histopathological finding. Therefore, a differential carbuncle diagnosis can be excluded.

The diagnosis of FOT can be established from a series of medical history recordings and physical, laboratory, and other supportive examinations such as fistulographic and histopathological. In our case, we had four components of FOT, including suppurative hidradenitis, acne conglobate, dissecting cellulitis, and pilonidal sinus.

**Summary**

A case of a 43-year old man has been described. From the anamnesis, we found small, painful blisters and bumps filled with foul-smelling pus on the scalp, armpits, chest, back, groin, and buttocks. Based on the physical examination, we found pustules, erythematous nodules, and multiple abscesses with atrophic scars on the scalp, anterior and posterior trunks, and abdominal, ingunal, and gluteal regions. On the facial region, we found multiple atrophic scars. Based on the fistulographic examination, we found multiple cutaneous fistules and enterocutaneous sinuses. Based on the histopathological examination, we found ruptured hair follicles, follicular plugs, and mixed inflammatory cell infiltration.

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