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Test Your Knowledge

GPP Quiz

Generalized pustular psoriasis (GPP) is a rare, severe, potentially life-threatening systemic chronic autoinflammatory disease. GPP has been included within the spectrum of psoriasis because it is sometimes observed in conjunction with plaque psoriasis, and because it involves the recruitment of T cells and neutrophils.

This quiz is intended to test your current knowledge of GPP and should enhance your understanding of the disease, with explanations of the correct answer included following each question.

1 True or false? GPP is a distinct entity from plaque psoriasis.
- **A.** True
- **B.** False

2 Which of the following is the main cytokine pathway involved in the pathogenesis of GPP?
- **A.** Interleukin (IL)-17
- **B.** IL-18
- **C.** IL-23
- **D.** IL-36

3 Liver function abnormalities have been reported in approximately what proportion of patients with GPP?
- **A.** 15%
- **B.** 25%
- **C.** 50%
- **D.** 75%

4 GPP is characterized by widespread eruptions of which of the following?
- **A.** Benign nodules
- **B.** Sebaceous cysts
- **C.** Herpes zoster lesions
- **D.** Sterile pustules

5 True or false? In the United States, no agents have been approved specifically for the treatment of GPP.
- **A.** True
- **B.** False

6 Which of the following statements about the economic burden of GPP vs plaque psoriasis is *correct*?
- **A.** Because GPP is associated with fewer comorbidities, patients require less intensive care
- **B.** Patients with GPP have a significantly decreased economic burden because of their lower direct medical and pharmacy costs
- **C.** In individual patients, the costs associated with plaque psoriasis are similar to those associated with GPP
- **D.** Rates of inpatient visits and hospitalizations are higher in patients with GPP

7 Which of the following events may trigger the development of acute GPP?
- **A.** Acute myocardial infarction
- **B.** Sleep apnea
- **C.** Sudden withdrawal of corticosteroids
- **D.** Uncontrolled diabetes

8 Which of the following is a common comorbidity associated with GPP?
- **A.** Down syndrome
- **B.** Dyslipidemia
- **C.** Herpes simplex virus
- **D.** Parkinson disease

9 In the differential diagnosis of GPP, which of the following major diagnoses should be *excluded*?
- **A.** Acrodermatitis continua of Hallopeau (ACH)
- **B.** Acute generalized exanthematous pustulosis (AGEP)
- **C.** Palmoplantar pustulosis (PPP)
- **D.** Sneddon-Wilkinson disease

10 Which of the following statements about the impact of GPP on quality of life is *correct*?
- **A.** Plaque psoriasis and GPP have a similarly negative impact on quality of life
- **B.** Patients with GPP experience less itching and fatigue than do those with plaque psoriasis
- **C.** The Dermatology Life Quality Index (DLQI) score is nearly 4 times higher (ie, more severe) in patients with a GPP flare than in those with plaque psoriasis
- **D.** Patients with plaque psoriasis experience more anxiety and depression than do those with GPP

Answer key

1: A. Although both conditions share "psoriasis" in their name, GPP is a clinically, pathologically, genetically distinct entity from plaque psoriasis.[1-3] GPP is associated with localized symptoms, such as pain, itching, and burning, as well as systemic signs and symptoms, including fever, swelling, malaise, joint pain, headache, and leukocytosis.[4-7]

GPP also differs from plaque psoriasis with respect to pathogenesis. GPP is characterized by innate immune inflammation and is considered a neutrophilic disease, whereas plaque psoriasis is characterized by adaptive immune responses and is considered an autoimmune disease.[1,2] Further, the primary cytokine pathway involved in the development of GPP differs from the major pathways involved in the development of plaque psoriasis.

About one-third of patients with GPP present with the lesions of plaque psoriasis, suggesting a common genetic component, but the majority do not exhibit such lesions, which is suggestive of a unique pathoetiology.[8]

2: D. IL-36 is a key driver of GPP, whereas the IL-17/23 axis plays a larger role in plaque psoriasis.[8] Although there are shared pathways between GPP and plaque psoriasis, with many cytokines playing a role, including tumor necrosis factor (TNF), IL-23, IL-17, and IL-36, the IL-36 pathway is involved predominantly in GPP pathogenesis.[3] In terms of genetics, mutations affecting the IL-36 pathway have been shown to be associated with the development of GPP but not with plaque psoriasis.[3] Although genetic studies highlight the importance of the IL-36 pathway in GPP pathogenesis, overactivation of the pathway in the absence of genetic mutations has also been shown to be associated with GPP.[3,9]

3: C. Liver function abnormalities have been reported in about half of all patients who experience an acute episode of GPP.[10,11] These abnormalities consist mainly of mild to moderate cholestasis or cytolysis, thus raising the possibility of specific liver/biliary involvement by the inflammatory process.[5] The abnormalities tend to return to normal with the remission of GPP.[11]

4: D. GPP presents as the rapid onset of widespread, erythematous, inflamed skin that is studded with 2- to 3-mm sterile pustules.[12] The pustules may expand and coalesce into irregular "lakes of pus." During pustulation, clinical findings associated with systemic inflammation may be observed. Patients appear systemically ill, with high-grade fever, chills, malaise, and anorexia. Erythroderma may occur. After 1 to 2 days, the pustules typically resolve, with residual erythema and desquamation.[12] Repeated cycles of pustulation can occur in those with active disease.

Cutaneous symptoms associated with GPP may include pain, burning, and pruritus. Mucosal findings include a geographic or fissured tongue, cheilitis, and ocular involvement (eg, conjunctivitis, uveitis, iritis). Extracutaneous findings may include nail abnormalities, arthralgias, jaundice, and lower-extremity edema.[12]

5: A. The current range of treatment options for GPP is limited, with clinicians typically selecting agents that are used to treat plaque psoriasis. To date, no specific treatment for GPP or any of its subtypes has been approved in the United States. Therefore, GPP is currently treated with general, psoriasis regimens.[2,13]

6: D. Studies of the economic burden of GPP show that patients with the disorder have more comorbidities than do those with plaque psoriasis and thus require more intensive care.[1] The medication burden for both dermatologic symptoms and comorbidities among patients with GPP exceeds that among those with plaque psoriasis.[14] Available data suggest that patients with GPP experience ≥1 flare that results in hospitalization every 1 to 5 years.[15] According to a US claims database analysis, 2 common disorders that are more likely to be treated along with GPP are anxiety and depression. Patients with GPP are also more likely to have a higher concomitant medication burden, with a greater use of antihypertensive, psychiatric, and opioid agents reported.[16]

7: C. Substantial evidence has shown that the withdrawal of systemic corticosteroid therapy can precipitate GPP.[7] There are reports of the induction of disease on withdrawal of cyclosporine. Other systemic drugs have been implicated occasionally as well, including terbinafine, propranolol, bupropion, lithium, phenylbutazone, salicylates, and potassium iodide.

Other triggers can include the following[7]:
- Upper respiratory tract infections
- Psychological stress
- Hypocalcemia (may also arise as a consequence of GPP)
- Pregnancy

8: B. Common comorbidities observed with GPP include metabolic disorders, such as dyslipidemia, obesity, hypertension, and diabetes mellitus.[4] Other conditions reported along with GPP include metabolic syndrome, ophthalmologic involvement, inflammatory bowel disease, cholestasis, and neutrophilic cholangitis.

9: B. In patients who present with signs and symptoms of GPP, the major diagnosis to exclude is AGEP.[12] Clinically, it may be difficult to distinguish AGEP from GPP. A main clue is a history of recent drug ingestion, with approximately 90% of all cases of AGEP associated with medication (most often certain types of antibiotics and calcium channel blockers). The main features of AGEP include acute widespread appearance of pinhead-sized sterile pustules, with erythema, edema, fever, and leukocytosis. AGEP has a more abrupt onset and a shorter duration than GPP. It does not recur and is not associated with plaque psoriasis.

ACH and PPP are localized forms of GPP. Sneddon-Wilkinson disease, also known as subcorneal pustular dermatosis, may be considered in the differential diagnosis but is not observed as frequently as AGEP. Occurring predominately in middle-aged or older patients, Sneddon-Wilkinson disease is associated with underlying malignancies (most commonly multiple myeloma and immunoglobulin A [IgA] monoclonal gammopathy) and pyoderma gangrenosum.

10: C. GPP has been shown to have a greater impact on patient quality of life compared with plaque psoriasis.[14,15] A recent study from the CorEvitas Psoriasis Registry showed that patients with GPP reported more severe pain, itching, and fatigue compared with individuals with plaque psoriasis.[17]

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