CLINICAL IMAGES

Dermatologic & Ocular Findings in a 27-Year-Old Male

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A 27-year-old African American male presented to the office with a two-month history of intermittent chills without a fever. During this time, he experienced an unintentional weight loss of ten pounds. The symptoms progressed with the development of a painful rash of his bilateral knees. The rash was described as multiple, enlarging, red, painful, warm patches with a dry, flaky, non-pruritic outer edge. Beginning on the dorsum of his right foot, the rash spread to his bilateral shins and knees. After no resolution of the rash within two weeks, the patient sought medical attention.

Recent travel, household pets, sick contacts, sexual activity, occupational exposure, illicit drug use and over the counter or prescription medication usage was denied. He was currently employed as a postal worker. Review of systems was positive for bilateral knee pain, intermittent loose brown stools without diarrhea, fatigue, mild dyspnea on exertion and occasional nausea. One episode of non-bloody, non-bilious vomiting five days before his office visit was noted. Abdominal pain, melena, hematochezia, back pain, fever, cough, wheezing, rhinorrhea, pharyngitis, sinusitis, vision changes, eye pain, photophobia, headache, paresthesias, muscle weakness, oral or genital ulcers, or urethral discharge were all denied.

Physical examination revealed a thin, pale, non-toxic appearing male with normal vital signs. Unbeknownst to the patient, the right eye demonstrated a segmental bright red injection lateral to the cornea. (Figure 1). The conjunctiva was pale bilaterally. Over the patient's bilateral shins and knees were multiple light red, poorly circumscribed annular patches and nodules ranging in size from three to five mm in diameter. (Figure 2, Figure 3). The lesions were non-blanchable, exquisitely tender to palpation, and warm. There was associated +1 pitting edema of the bilateral lower extremities. Residual scaling was noted along the lower aspect of the shins where the initial lesions were resolving.

Initial laboratory study results revealed a significantly elevated C-reactive protein (CRP) of 115.20 mg/L (normal < 7.48mg/L) and erythrocyte sedimentation rate (ESR) of 120 mm/hr (normal 0 -20 mm/hr). Complete blood count results demonstrated a depressed hemoglobin of 7.3 g/dL (normal 13.7 – 17.5 g/dL) and mildly elevated white blood cell count of 13.1 K/uL (normal 3.8 – 10.5 K/uL). Remaining lab tests, including human immunodeficiency virus, antinuclear antibody, rheumatoid factor, rapid plasma regain, herpes simplex virus, and Lyme testing was negative. A chest x-ray was obtained and reported as normal. A digital rectal exam revealed brown stool positive for occult blood on stool guaiac testing.

QUESTIONS

1. What diagnosis are the skin findings most consistent with?

   A) Erythema Induratum

   B) Erythema Multiforme

   C) Erythema Nodosum

   D) Necrobiosis Lipoidica

2. What is the underlying diagnosis?

   A) Coccidiomycosis

   B) Sarcoidosis

   C) Sweet's Syndrome

   D) Ulcerative Colitis

[Answers and discussion can be found on page 28]

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FIGURE 1:

Right eye

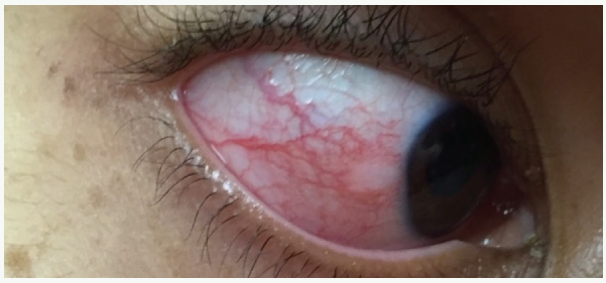


FIGURE 2:

Left leg

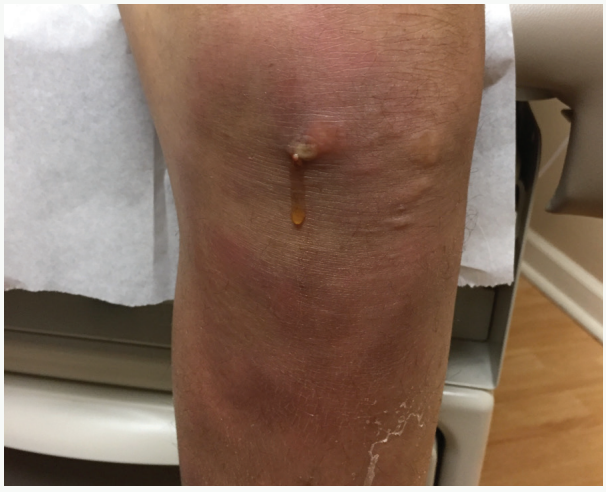
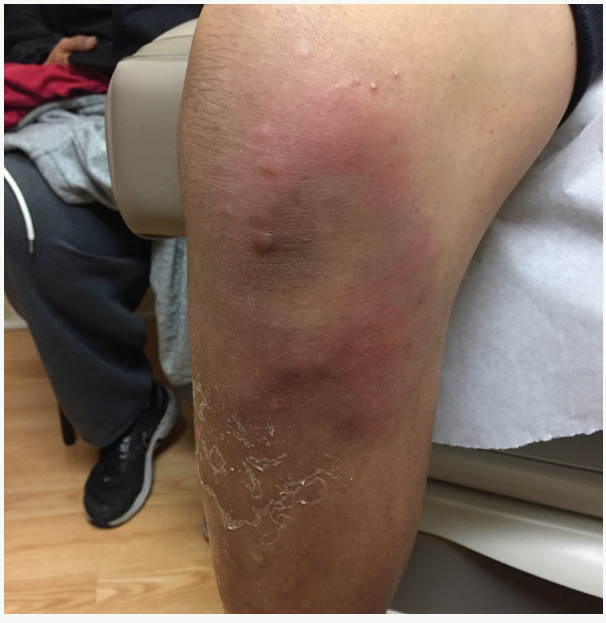


FIGURE 3:

Right leg



ANSWERS

1. What diagnosis are the skin findings most consistent with?

Correct answer: C) Erythema Nodosum

The skin findings discussed in the case study are consistent with Erythema nodosum. Erythema nodosum (EN) is a nodular erythematous eruption typically found on the extensor surfaces of the extremities. Erythema nodosum is associated with several diseases including autoimmune, infection and malignancy. Additionally, EN may develop from medications, particularly with sulfonamides and oral contraceptives.[1,2] Approximately 55 percent of cases of EN are idiopathic.[1,3]

Erythema induratum (EI) is characterized by tender, erythematous nodules of the posterior lower legs. Lesions are typically less than two cm in diameter and can present both unilaterally or bilaterally.[1] Erythema induratum more commonly affects women than men. Tuberculosis is the most common identifiable cause of EI.[1,4]

Erythema multiforme (EM) typically presents as round, erythematous papules that progress to classic target lesions characterized by an erythematous halo on the periphery and a dark red inflammatory zone and dusky central area. Lesions are typically symmetric on the extensor surfaces of the extremities and on the palms and soles. Erythema multiforme is commonly associated with a preceding acute respiratory infection, herpes simplex virus infection, or Mycoplasma pneumoniae infection.[1]

Necrobiosis lipoidica (NL) begins as oval, violaceous or red-brown nodules or plaques typically on the pretibial skin that expands slowly. The advancing border is red and the central area turns a characteristic waxy yellow-brown, often with ulceration and telangectasias.[1] Necrobiosis lipoidica is associated with diabetes mellitus. Studies have produced variable results to this linkage and anywhere from 11 to 75 percent of patients with NL either have or will develop diabetes mellitus.[1,5] Females are more commonly affected than males, and the most common presentations are in the third and forth decades of life.[1]

2. What is the underlying diagnosis?

Correct answer: D) Ulcerative Colitis

The underlying diagnosis is Ulcerative Colitis. Ulcerative colitis (UC) is a type of inflammatory bowel disease (IBD) characterized by inflammation limited to the mucosal layer of the colon. Major symptoms of UC include diarrhea, rectal bleeding, tenesmus, the passage of mucous, and abdominal pain.[2,6] Approximately one-third of IBD patients have at least one extraintestinal manifestation.[2]

Coccidiomycosis (San Joaquin Valley fever) is caused by direct exposure to soil containing the dimorphic soil-dwelling fungi Coccidiodes. It is seen in the southwestern United States. Sixty percent of infected individuals can present as asymptomatic, and 40 percent may have a primary focal pneumonia with symptoms of fever, cough, pleuritic chest pain, night sweats or profound fatigue.[2] The infection is followed by the development of EN in ten percent of females and four percent of males.[1] Mediastinal or hilar lymphadenopathy and unilateral infiltrate are commonly seen on chest x-ray. Serology and sputum cultures can help confirm the diagnosis.[1,2]

Sarcoidosis is an inflammatory disease characterized by the presence of noncaseating granulomas that can affect many organs and present with a wide range of symptoms. The lung is involved in greater than 90 percent of sarcoidosis patients with respiratory symptoms such as a cough and dyspnea being the most common. Chest x-ray findings include hilar adenopathy, infiltrate or fibrosis. Ocular, cutaneous, and constitutional symptoms are also common.[2] Erythema nodosum has been observed in up to 39 percent of sarcoidosis cases.[1]

Sweet's syndrome is a neutrophilic dermatosis characterized by abrupt onset of tender, erythematous red to red-brown plaques or nodules. The plaques and nodules have an annular or arciform pattern and primarily present on the head, neck and upper extremities (particularly the back of the hands and fingers).[1] Patients may also have fever, neutrophilia and a predominantly neutrophilic infiltration in the dermis of lesions.[2] As many as 86 percent of cases are idiopathic, occurring in women with a preceding respiratory tract infection.[1] Ten to twenty percent of cases are associated with a malignancy, predominately hematologic, especially acute myelogenous leukemia. Sweet's syndrome has also been found in systemic lupus, IBD, as a medication side effect (all-trans-retinoic acid, granulocyte colony stimulating factor) and solid tumors (especially the genitourinary tract).[1,2]

DISCUSSION

Erythema nodosum is a panniculitis that affects the subcutaneous fat in the skin.[1] The peak incidence is between the ages of 18 to 34 years with a female to male ratio of five to one.[1,7] It presents as painful, bilateral, subcutaneous nodules about two to six cm in size with poorly defined borders most commonly on the anterior lower extremities.[1] The extensor surfaces of the forearm, trunk, and thighs may be involved. Individual lesions typically last for two weeks, do not ulcerate and may be associated with swollen ankles. Prodromal symptoms of malaise, fatigue or symptoms of an upper respiratory infection may precede the skin eruption by one to three weeks.[1,7] Arthralgias occur in approximately 50 percent of patients and consist of erythema, swelling, tenderness over the joints and occasionally effusions.[1] Erythema nodosum commonly involves the knee, but any joint can be affected.[1,7] Rheumatoid factor typically tests negative with this disease process.[1]

Erythema nodosum represents a hypersensitivity reaction to a variety of antigenic stimuli.[1] It is idiopathic in up to 55 percent of cases. However, there are many possible causes. Erythema nodosum can be caused by infections by Streptococci, tuberculosis, Yersinia, and Coccidiomycosis, drugs such as sulfonamides, bromides, and oral contraceptives, systemic illnesses including sarcoidosis, IBD, and Hodgkin's disease and pregnancy.[1,2,7] The most common identifiable cause is streptococcal pharyngitis, responsible for approximately 28 to 48 percent of cases, followed by sarcoidosis, which causes 11 to 25 percent of cases.[3,7] The initial evaluation should include a throat culture, antistreptolysin titer, chest x-ray, purified protein derivative skin test, and erythrocyte sedimentation rate. Skin biopsy is not required in patients with typical presentations and the diagnosis can be made on clinical grounds alone. Patients with gastrointestinal symptoms should have a stool culture for Yersinia, Salmonella, and Campylobacter and stool guaiac test.[1,7]

Erythema nodosum is self-limited, typically resolving within a few weeks without intervention. Quality evidence for treatment is lacking and most cases require only symptomatic relief with NSAIDs.[1,7] A typical regimen is 250 to 500 mg of naproxen twice per day as needed for pain.[7] Supportive measures include leg elevation, rest, and compression stockings or bandages help reduce edema and pain.[1,7] Any associated causes or underlying conditions should be treated if found.[1,7] Potassium iodide has been found to be an effective therapy in small, uncontrolled studies.[1,7] A supersaturated solution of potassium iodide drops (SSKI) at a dose of 300 to 900 mg per day orally for one month has been found to be effective.[1,7] A typical dose for adults with EN is 300 mg (six drops of SSKI 47 mg/drop) three times daily.[1,7] Iodine drops can be mixed in juice or water to dilute the bitter taste. Oral corticosteroids are effective but seldom necessary and underlying infection or malignancy should be excluded before their use.[1,7]

DIAGNOSIS

Ulcerative colitis is a type of IBD characterized by inflammation limited to the mucosal layer of the colon. Its incidence in North America is 2.2 to 19.2:100,000 and affects males and females equally. Age of onset is bimodal at 15 to 30 and 60 to 80.2 Patients can present with diarrhea, abdominal pain, hematochezia, tenesmus, fever, fatigue and weight loss. Extraintestinal manifestations include dermatologic (EN, pyoderma gangrenosum, psoriasis), rheumatologic (arthritis, ankylosing spondylitis), ocular (uveitis, episcleritis), hepatobiliary (hepatitic steatosis, primary sclerosing cholangitis), bone (osteoporosis) and thromboembolic disorders.[2,8]

Active disease is associated with elevated CRP, ESR, and platelet levels and a decreased hemoglobin. Fecal lactoferrin is a highly sensitive and specific marker for intestinal inflammation. Single contrast barium enema may show ulceration of mucosa and loss of haustration. CT scanning is not as helpful as endoscopy or barium enema. Diagnosis is confirmed by endoscopic biopsy. Findings range from erythematous mucosa with a granular surface in mild disease to edematous and ulcerated mucosa with pseudopolyps in severe or long-standing disease. Ulcerative colitis almost always involves the rectum and extends proximally to involve all or part of the colon. Forty to fifty percent of patients have disease limited to the rectum and rectosigmoid, 30 to 40 percent have disease extending beyond the sigmoid but excluding the whole colon and 20 percent have total colitis.[2]

First line treatment is with sulfasalazine or other 5-amino salicylic acids.[2,6] Oral corticosteroids and infliximab may be added to help achieve remission.[2,6] For patients needing hospitalization, intravenous corticosteroids, cyclosporine, or infliximab can be tried.[2,6] Once remission is achieved, the same agent is usually used as maintenance.[2,6] Azathioprine is an additional maintenance medication for those who required corticosteroids or cyclosporine for remission.[2,6] Complications of UC include hemorrhage, toxic megacolon, perforation, strictures, and colon cancer.[2] Patients with UC should have a screening colonoscopy eight to ten years after initial diagnosis.[6]

CASE CONCLUSION

Despite his limited abdominal complaints, this patient had multiple findings on presentation that were consistent with UC including weight loss, arthralgias, elevated inflammatory markers, anemia, blood in his stool and extraintestinal manifestations of EN and episcleritis. Erythema nodosum occurs in ten percent of UC patients.[2,8] Episcleritis occurs in three to four percent of IBD patients and is more commonly seen in Crohn's disease.[2,8] The patient was admitted to the hospital for treatment of his anemia and further evaluation. After receiving appropriate blood products, the patient underwent colonoscopy revealing inflammation of the mucosa from the rectum to the distal transverse colon characterized by edema, erythema, friability, granularity, pseudopolyps and ulcerations in a continuous and circumferential pattern consistent with UC. Biopsies confirmed active colitis.

After the diagnosis of UC was established, the patient was started on intravenous steroids and discharged on a biologic agent for long-term suppression. His skin lesions became less tender and resolved over the next week. His episcleritis also resolved over the course of the next few weeks.

AUTHOR DISCLOSURES:
No relevant financial affiliations.

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