

# Yellow Urticaria in a Patient with Liver Disease

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## Abstract

**Background:** Yellow urticaria is a rarely reported phenomena that occurs in patients with hyperbilirubinemia that suffer an episode of urticarial rash. A variety of insidious etiologies of hyperbilirubinemia have been reported in cases of yellow urticaria making it an opportunity to catch serious liver or biliary disease early in its course. **Case Report:** We report a case of yellow urticaria that occurred in a 67-year-old male suffering from end-stage liver disease after he had received a transfusion of fresh frozen plasma. Physical examination and thorough history collection allowed the determination of the proper diagnosis and guided further clinical care. **Conclusion:** An occurrence of yellow urticaria necessitates that the clinician finds two diagnoses: the cause of hyperbilirubinemia, and the cause of urticaria. While striking in appearance, yellow urticaria may be most clinically significant when it prompts recognition of previously unknown hepatic or biliary pathology.

## Keywords

Urticaria, Allergy, Liver Disease, Transfusion Reaction

## 1. Introduction

Urticaria is a common dermatologic pathology characterized by pruritic wheals, commonly surrounded by reflex erythema, that resolves within 24 hours. These skin findings may be accompanied by angioedema, or sudden swelling of the lower dermis, that typically resolves within 72 hours. These skin findings can be caused by a wide range of insults such as allergy, infection, or physical stress, that provoke mast cell degranulation. Further characterization is still needed regarding some of this pathophysiology-particularly in relation to the cell signaling involved in the release of these vasoactive granules. Up to 50% of precipitating causes go undiscovered and may be referred to as “spontaneous”. In cases of acute spontaneous urticaria, a diagnostic workup to evaluate the specific etiology is not generally recommended given the often rapid resolution [1].

Yellow urticaria is a rare and likely under-reported variation of urticaria with a distinct central yellow coloration that has only been published about twenty times worldwide to date. Previous reports indicate that these occurrences are in the setting of a pre-existing hyperbilirubinemia due to hepatic or biliary pathology. The related hepatic diseases causing yellow urticaria in these cases ranged from infective hepatitis, alcohol-induced end stage liver disease, metastatic breast disease to the liver, and hemochromatosis-related liver cirrhosis. Scleral icterus was noted on physical examination in most of these cases as well. Skin biopsy was performed in several of the previously reported cases but is typically considered clinically unnecessary if there is a prompt resolution of symptoms. Like acute spontaneous urticaria, the key components leading to a diagnosis involve a detailed history and clinical examination of the patient. Treatment is also similar to that of common acute urticaria [2] [3]. This setting gives the dermatologic finding the potential to reveal a more serious unknown condition. This case reminds the reader to think carefully and consider a broad, thorough differential diagnosis when encountering unusual clinical findings.

## 2. Case Report

A 67-year-old Caucasian male was admitted for anemia secondary to gastrointestinal bleeding in the setting of alcoholic cirrhosis and Barcelona Clinic Liver Cancer stage-D hepatocellular carcinoma. Several days into his hospitalization, he reported itching on the bilateral anteromedial thigh minutes after the completion of a plasma transfusion following the transfusion of 1-unit packed RBCs and platelets hours earlier. Examination revealed a 20 cm × 15 cm and a 5 cm × 10 cm grouping of raised patches on the right and left thigh, respectively (**Figure 1**). Both patches demonstrated a thin, erythematous border with distinct central yellow coloration. The patient denied any other sudden onset symptoms including fever, chills, shortness of breath, wheezing, dizziness, or lightheadedness.



**Figure 1.** The left and right anterior thigh (left and right image respectively) as encountered upon initial examination after itching was reported by the patient.

Other examination findings were significant for slight jaundice, most notable in the sclera. No other rashes were seen on the rest of the body. The oropharynx was clear, and no wheezing was present. Of note, his previously measured total bilirubin was 6.8 mg/dL.

Transfusion reaction protocol was initiated beginning with the transfusion being stopped. No errors were found on review of the blood product acquisition and administration. The patient received IV diphenhydramine, and urticarial patches were demarcated. Careful monitoring was performed for other allergic phenomena such as additional rashes, wheezing, and shortness of breath. No evidence of shock was noted. Within 2 hours, the patient reported resolution of the itching. Follow up examination showed evolution of the patches to large macules within the pen-markings. Yellow pigmentation persisted but without erythematous borders. He appeared otherwise clinically stable. Transfusion protocol reaction laboratory tests revealed: Hgb 7.1 g/dL, Hct 20.7%, WBC 4.4 K/uL, and plts 56 K/uL; this was improved from 6.6 g/dL, Hct 18.9%, WBC 4.1 K/uL and plts 44 K/uL respectively; haptoglobin < 10 mg/dL; and LDH 311 U/L. Peripheral smear was negative for any findings of hemolysis.

Further work-up after thorough physical examination was deemed unnecessary as isolated urticaria effectively rules out more serious classes of transfusion reaction [4] [5] [6]. The patient's yellow pigmentation slowly resolved over the next few days. Biopsy was not considered clinically necessary due to the rapid resolution of the urticaria and the stable condition of the patient. The patient remained stable for the rest of the admission and his plan of care continued unaffected. No further transfusions were required, and he was discharged to a sub-acute nursing facility several days later.

### 3. Discussion

Yellow urticaria is an uncommon but notable finding that can occur in patients with an underlying hyperbilirubinemia who suffer hypersensitivity reactions and mast cell degranulation [3] [7]. In this case, end-stage liver disease and hyperbilirubinemia were already known, leaving the insult that caused urticaria to be determined. It is important to determine the cause of yellow urticaria in the same fashion as in any other case of acute urticaria to avoid a potential recurrence in the future that may have been preventable. Due to its striking nature, the appearance of yellow urticaria in this case highlighted the pathology involved in the patient's clinical presentation. Differential diagnosis considerations for our hospitalized patient included transfusion reaction, adverse drug reaction such as to antibiotics, NSAIDs, and/or chemotherapy, food, and environmental allergens such as to adhesives or plastic tubing. Additional etiologies included in the differential diagnosis were infection, acute stress, physical irritation, and diseases with non-IgE mediated symptoms including vasculitis, cryoglobulinemia, lymphoma, and autoimmune diseases [8] [9].

Careful chart review indicated the patient was on a daily regimen of ciprof-

loxacin and neomycin as prophylaxis for spontaneous bacterial peritonitis. He had also started a course of ceftriaxone as a precaution for spontaneous bacterial peritonitis the day prior due to abdominal pain. It was also noted that the patient had received frequent transfusions over the past year, increasing his risk of sensitization and transfusion reaction to unmeasured blood antigens. He had not been pre-medicated to reduce the risk of transfusion reaction during this encounter. In this case the time frame of the reaction and its subsequent resolution without recurrence despite continued doses of antibiotics elevated the plasma transfusion as the most likely cause.

Reported biopsies of yellow urticaria have demonstrated the presence of olive colored bilirubin crystals in the reticular dermis, suggesting that they filter through the leaky capillary epithelium during the formation of the wheal [10] [11]. Crystal deposition may explain the persistent yellow pigmentation of affected skin after resolution of the wheal as crystals must be reabsorbed into extracellular fluid or consumed by resident macrophages [12] [13]. We feel that this pathogenesis of pigmentation is more likely than the commonly cited explanation of bilirubin's high affinity for elastase because no similar yellow pigment phenomena is seen in more common cases of extra-cellular fluid accumulation such as pitting edema.

This case demonstrates the need for clinicians to stay vigilant in the prevention of adverse reactions due to allergic causes or when performing interventions such as transfusions. Cases of urticaria including yellow urticaria may not be predictable but conducting a thorough history and clinical examination will likely allow the provider to promptly determine the cause and remove any offending agents. Mindfulness of the potential for yellow urticaria should be exercised especially in the setting of a patient with known liver disease or preexisting hyperbilirubinemia. This may also provide the clinician with the opportunity to detect early hepatic or biliary disease.

## 4. Conclusion

Yellow urticaria may be an important clue to a previously unknown hepatic or biliary pathology as it generally occurs in the setting of hyperbilirubinemia. Despite a striking appearance, the work-up and treatment for yellow urticaria are the same as common acute urticaria. We believe this case reminds the clinician to remain open to considering systemic processes when encountering unusual presentations.

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### 4.2. Informed Consent

The authors attest that the patient provided written informed consent for the purpose of this publication.

## Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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