

Case Report

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# Multiple Adult Xanthogranuloma with Follicular Mucinosis-Associated Langerhans Cell Histiocytosis

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## Abstract

Langerhans cell histiocytosis and xanthogranuloma are both conditions characterized by increased histiocytic proliferation and are both more commonly seen in children. Nevertheless, the two are completely separate entities and have distinct differences in clinical presentation, histopathological appearance, prognosis, and therapy. Although adult forms of either disorder are rare, concurrent presentation of both is even more unusual. We report a 61-year-old man who presented with disseminated yellow-red papules coalescing into nodules, on a background of erythema and alopecia. Histopathology exhibited a dense dermal infiltrate of foamy histiocytes and lymphocytes in addition to follicular mucinosis with atypical folliculotropic cells. Appropriate staining revealed that the foamy histiocytes throughout the dermis represented a xanthogranulomatous process, while the folliculotropic proliferation represented Langerhans cell histiocytosis. Further work-up of this multiple adult xanthogranulomas with follicular mucinosis-associated Langerhans cell histiocytosis exposed underlying chronic myelogenous leukemia per bone marrow biopsy, which was likely either solely or partially an initiating factor in the eruption of multiple histiocytic process in this patient.

**Keywords:** Langerhans cell histiocytosis; Xanthogranuloma; Chronic myelogenous leukemia; Follicular mucinosis

## Introduction

Langerhans Cell Histiocytosis (LCH) is a rare disease characterized by the clonal proliferation of S100, CD1a, and langerin positive dendritic cells. Although the disease may occur at any age, it is more often diagnosed in children than adults. Extent of organ involvement may vary from single to multisystem, more commonly affecting bone, skin, pituitary gland, lymph nodes, spleen, liver, CNS, and/or lungs. Increased organ involvement correlates with worse prognosis and amplified therapeutic aggressiveness. Although choice of therapeutic regimen may vary, appropriate management always includes imaging and work-up as primary. This includes CMP, CBC with differential, TSH/T4, UA, coagulation studies, skeletal survey, abdominal and thyroid ultrasound, chest x-ray, and head CT. Methotrexate, vinblastine, thalidomide, azathioprine, cytarabine or etoposide +/- prednisone have been utilized as either mono- or combination therapies in the medical management of this condition [1,2].

Adult xanthogranulomas (XG) are benign tumors of factor XIIIa and CD68 positive histiocytic cells. In contrast to Langerhans cells, histiocytes in XG are negative for S100, CD1a, and Langerin. Juvenile XG tends to self-resolve, while adult XG is more often persistent. Multiple adult XG have been reported to be associated with lymphoproliferative malignancy [3]. Cosmetic debulking of lesions may be accomplished via surgery or carbon dioxide laser. Systemic retinoids have also been utilized for inhibition of tumor growth [3]. These two diseases have rarely been reported in combination and not in the adult population. We review a case of these entities co-existing in an adult below.

## Case Report

A 61-year-old Caucasian man presented to the clinic with a one year history of yellow-orange papules coalescing into nodules and plaques located on the scalp, face, neck, trunk, back, chest, abdomen, and extremities (Figures 1 and 2) Lesions were accompanied by a background of erythema and loss of hair. He reported pruritus of these lesions, but review of systems was otherwise negative. His past medical history was significant for cardiovascular disease and atrial fibrillation for which he was taking metoprolol-hydrochlorothiazide, diltiazem,



**Figure 1:** Multiple Adult Xanthogranulomas and Follicular Mucinosis-Associated Langerhans Cell histiocytosis - shoulder.



**Figure 2:** Multiple Adult Xanthogranulomas and Follicular Mucinosis-Associated Langerhans Cell histiocytosis - scalp.

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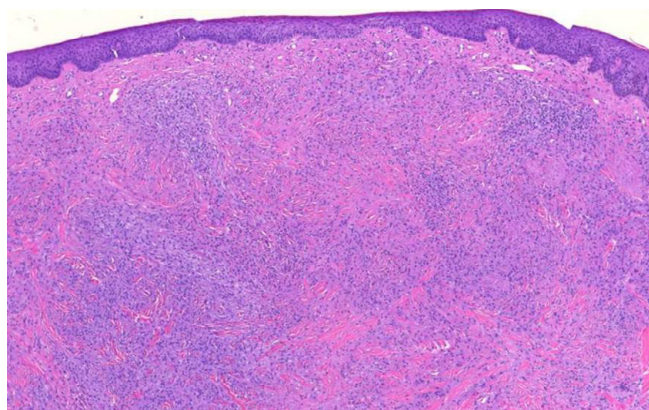
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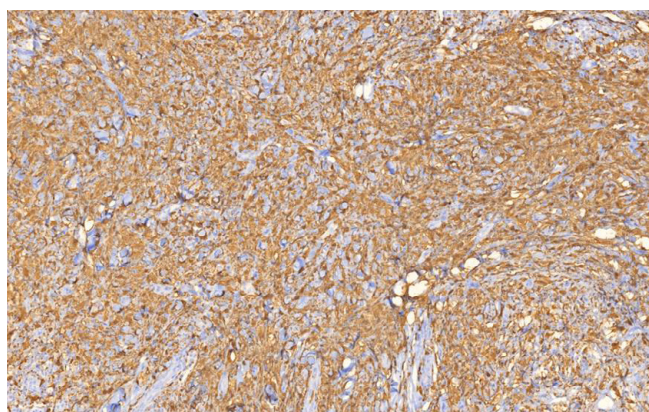
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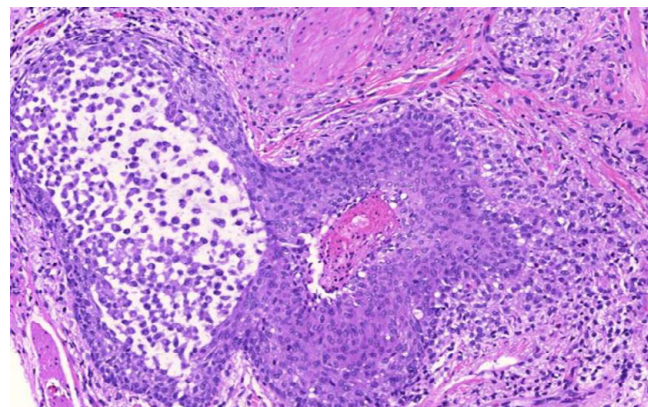
and warfarin. An active 20 pack year smoking history was also reported by the patient. His family history was positive for an unknown cancer in his mother, brother, and sister. Punch biopsies from the face, chest, and back all revealed two coexisting histiocytic processes. The first component demonstrated a dense dermal infiltrate of foamy histiocytes, lymphocytes and sprinkling of eosinophils (Figure 3). The foamy histiocytes found throughout the dermis were Factor XIIIa positive, CD68+ and were negative for S100, CD1a, and Langerin, consistent with a xanthogranulomatous process (Figure 4). The second component identified was follicular mucinosis and a proliferation of oval to round cells within the follicular epithelium that was positive for Langerin, S100, and CD1a (Figure 5). The staining pattern and morphology of the folliculotropic portion were consistent with a diagnosis of LCH. These LCH cells also showed strong nuclear positivity using an antibody specific to the BRAF V600E point mutation. Although this was suggestive of a clonal process, clonality could not be confirmed by sequencing technology. A diagnosis of multiple adult XG with follicular mucinosis-associated LCH was made. Patient's work-up was consistent with recommendations for both adult presentation of Langerhans cell histiocytosis and multiple adult XG. CBC with differential demonstrated a leukocytosis and thrombocytosis. Pan CT revealed diffuse bladder wall thickening, a 1.6 cm nodular lesion at the base of the bladder, and numerous ground-glass opacities scattered throughout the lungs. No lytic or blastic lesions were seen on skeletal survey (Figure 6). A mildly elevated alkaline phosphatase was found on chemistry panel but was



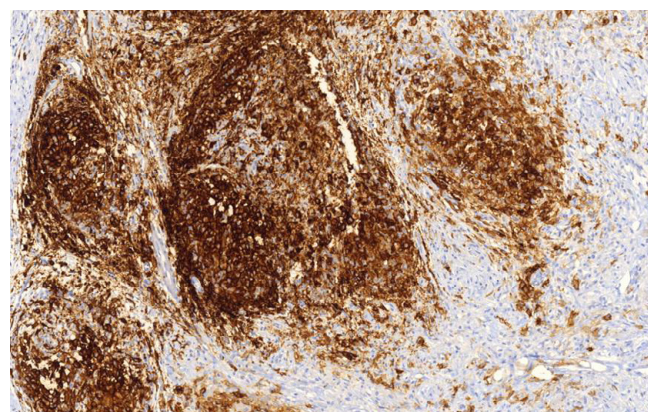
**Figure 3:** A dense dermal infiltrate of foamy histiocytes, lymphocytes and sprinkling of eosinophils consistent with the Multiple Adult Xanthogranuloma component (H&E x10).



**Figure 4:** Factor XIIIa positivity (IHC x20, specimen in Figure 3).



**Figure 5:** Follicular distortion and mucinosis resulting from clonal proliferation of distinctly different dendritic cells consistent with the Follicular mucinosis-associated Langerhans cell component (H&E x 20).



**Figure 6:** S-100 positivity (IHC x20, specimen in Figure 5).

otherwise unremarkable. Triglycerides, total cholesterol, and LDL were within the reference range. SPEP showed a normal electrophoretic pattern. Upon discovery of leuko- and thrombocytosis, along with the bladder mass, the patient was referred to oncology and urology. Oncology performed a bone marrow biopsy that revealed a diagnosis of chronic myelogenous leukemia (CML). Patient was initially placed on vinblastine with prednisone for 3 months but was stopped due to neuropathy. This was followed by minimal response to etoposide and an infusion reaction to clofarabine after 1 dose. Imatinib was given for the CML. The disease has been refractory to a complete resolution at this point. The patient refused urologic evaluation of bladder mass.

## Discussion

Overall, we found the patient's clinical and histopathological presentation to be highly unusual. While the patient's advanced age of 61 years makes either one of these diagnoses atypical, the co-existence of both within the same middle aged patient further confounds the picture. Evaluating the patient's comorbidities of coronary artery disease, 20 year smoking history, CML, lung findings on chest CT, and bladder mass on pelvic CT, it was difficult to determine the relationship, if any, of these to one another and/or to the patient's skin findings.

We considered the xanthogranulomas to be a reactive process from the LCH or CML. Follicular mucin in this case was a reaction



to the LCH proliferation and was responsible for the notable loss of hair. Review of literature suggests that the patient's underlying CML is the most likely culprit. Shoo et al reports a case of adult XG presenting simultaneously with B-cell acute lymphoblastic leukemia [3]. Other hematologic conditions reported in association with adult XG include essential thrombocytosis, chronic lymphocytic leukemia, large B cell lymphoma, and monoclonal gammopathy. Hematologic conditions reported in association with childhood XG include CML, acute lymphocytic leukemia, monocytic leukemia, histiomonocytic reticulosis, and juvenile myelomonocytic leukemia [4].

Still, the connection between the simultaneously occurring LCH is not explained by the revelation of CML diagnosis. While we acknowledge that it may be pure coincidence, there have been other reports of simultaneous LCH and diffuse xanthogranulomas found in literature. Patrizi A et al as well as Bains et al presented cases of LCH patients, who during chemotherapy, presented with juvenile xanthogranuloma [5,6]. The notion regarding this phenomenon is that the coexisting dendritic cell lesions are therapy-related due to manipulation of cytokines by chemotherapeutic agents. However, Tran DT et al reports a 19 year old woman who presented with LCH and simultaneous juvenile XG, without apparent associated chemotherapy, suggesting a biological association between XG and LCH [7]. Furthermore, it is also important to consider whether or not the patient's co-existing bladder mass has a role in his presentation, the definitive diagnosis of which is still to be determined. Although the bladder is not one of the organs most commonly affected by LCH, and although XG is more often reactive to lymphoproliferative malignancies than solid tumors, the presence of this co-existing entity cannot be ignored as either a potential contributory or unusually coincidental player. We acknowledge that further work-up

and diagnosis of this is necessary for further conclusions to be made.

In summary, the diagnosis of biopsy proven concurrent LCH and multiple XG in our patient represents a relatively rare presentation. Although literature reports multiple adult xanthogranulomas in association with lymphoproliferative disorders as well as cases of LCH in children that later presents with juvenile xanthogranulomas following chemotherapy, to our knowledge this is the first case of follicular mucinosis-associated LCH presenting simultaneously with multiple adult xanthogranulomas in a middle-aged patient.

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