QUIZ SECTION

Red-yellow Papules and Nodules All over the Body: A Quiz

Jia-Wei LIU†, Jin-Di FENG† and Chun-Xia HE*
*Department of Dermatology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences and Peking Union Medical College, State Key Laboratory of Complex Severe and Rare Diseases, National Clinical Research Center for Dermatologic and Immunologic Diseases, Beijing, China. *Email: hcxpumch@foxmail.com*
†These authors contributed equally to this work.

A65-year-old woman presented with a 5-month history of progressive red-yellow papules and nodules with mild pruritus. The lesions first appeared on the abdomen 20 days after pacemaker implantation and gradually spread to the whole body. The patient's medical history was significant for lumbar disc herniation diagnosed 6 years ago, diabetes mellitus diagnosed 1 year ago with current insulin therapy and bradycardia presenting 6 months ago leading to a diagnosis of sick sinus syndrome and subsequent pacemaker implantation. The patient denies arthralgias or articular deformities, changes in urine output or voiding patterns, hoarseness or visual impairment. Physical examination revealed numerous yellowish, pea-sized, soft papules and nodules involving the scalp, face, trunk, extremities and mucosal sites including conjunctiva, oral cavity, pharynx, anus and vulva. Laboratory studies showed essentially normal complete blood count and peripheral blood smear with normal lipid profile. Liver function tests demonstrated elevated gamma-glutamyl transferase (GGT) at 342 U/L (normal<45 U/L) and elevated alkaline phosphatase (ALP) at 506 U/L (normal<135 U/L). Patch test for common contact allergens, including the metal series, was negative. Computed tomography revealed widespread small nodules in the lungs, subcutaneous tissue and kidneys. Endoscopy showed scattered yellow-white submucosal nodules in gastrointestinal mucosa (Fig. 1).

What is your diagnosis?

1: Disseminated adult xanthogranuloma.
2: Xanthoma disseminatum.
3: Eruptive xanthoma.
4: Multicentric reticulohistiocytosis.

See next page for answer.

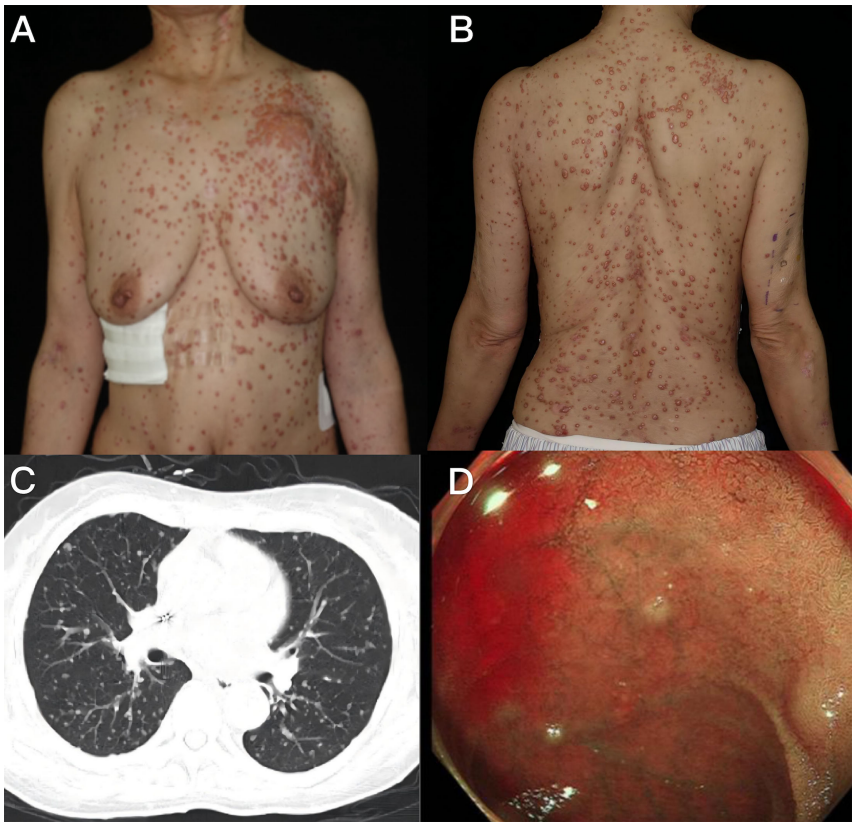

Fig. 1. Clinical manifestations, chest computed tomography and gastroenteroscopy findings: (A, B) Disseminated yellow papules and nodules on skin. (C) Chest CT showed diffuse pulmonary nodules. (D) Gastroenteroscopy showed scattered yellow-white submucosal nodules.

2026 ©Author(s). Published by MJS Publishing, on behalf of the Society for Publication of Acta Dermato-Venereologica. This is an Open Access article distributed under the terms of the Creative Commons Attribution-NonCommercial 4.0 International License (https://creativecommons.org/licenses/by-nc/4.0/).

ActaDV Acta Dermato-Venereologica ActaDV Advances in dermatology and venereology

ActaDV
Acta Dermato-Venereologica
ActaDV
Advances in dermatology and venereology

ANSWERS TO QUIZ

Red-yellow Papules and Nodules All over the Body: A Commentary

Acta Derm Venereol 2026; 106: adv-2026-0562.
DOI: 10.2340/actadv.v106.adv-2026-0562

***Diagnosis*: Disseminated adult xanthogranuloma**

Skin and gastrointestinal biopsies demonstrated spindle cells, epithelioid cells, lymphocytes and scattered Touton giant cells infiltration in middle dermis in a nodular pattern. Immunohistochemistry was positive for CD68, CD163 and Factor XIIIa, while negative for CD1a, S100, and Langerin (Fig. 2). We also performed skin lesion DNA and RNA sequencing in this patient. DNA sequencing of tissue samples is negative, while RNA sequencing identified a novel STOM::PDGFRB fusion gene resulting from t (1, 2)(q32;q33) translocation. PDGFRB rearrangement associated with the pathogenesis of chronic myelomonocytic leukaemia and atypical chronic myeloid leukaemia. Imatinib is a small-molecule selective tyrosine kinase inhibitor that exerts its therapeutic effect by occupying the adenosine triphosphate-binding sites of several tyrosine kinase molecules, including c-Kit, PDGFRα and PDGFRβ, thereby preventing phosphorylation of downstream protein substrates and inhibiting tumour cell proliferation (3).

Based on the RNA sequencing results from cutaneous tissue, the patient was treated with oral imatinib 100 mg daily, demonstrating significant lesion regression after 2 weeks of treatment. At 4-month follow-up, the cutaneous and pulmonary involvement showed complete regression, and ALP levels returned to normal range. However, follow-up spinal CT revealed multiple round hypodense lesions, consistent with post-treatment imaging changes following tumour regression from skeletal involvement Fig. 3. The patient continues on imatinib therapy.

Xanthogranuloma is a rare non-Langerhans cell histiocytosis that can be classified into juvenile xanthogranuloma (JXG) and adult xanthogranuloma (AXG) by age of onset. Seventy-five percent of JXG patients develop disease within the first year of life, while adult cases account for 10% of all cases, predominantly occurring between ages 20–30 years (4). The head and neck region is most commonly affected, followed by the upper trunk and upper extremities. Systemic involvement occurs in 5% of patients (5). Differential diagnoses include xanthoma disseminatum, eruptive xanthomas, tuberous xanthomas, and multicentric reticulohistiocytosis. Xanthoma disseminatum is characterized by significant mucosal and visceral involvement. Xanthoma disseminatum is generally not associated with elevated serum lipids. The eruption presented as disseminated yellow to reddish-brown papules, predominantly located in flexural areas and around the eyes. It commonly involves the skin, eyes, oral cavity, and respiratory mucosa, and may

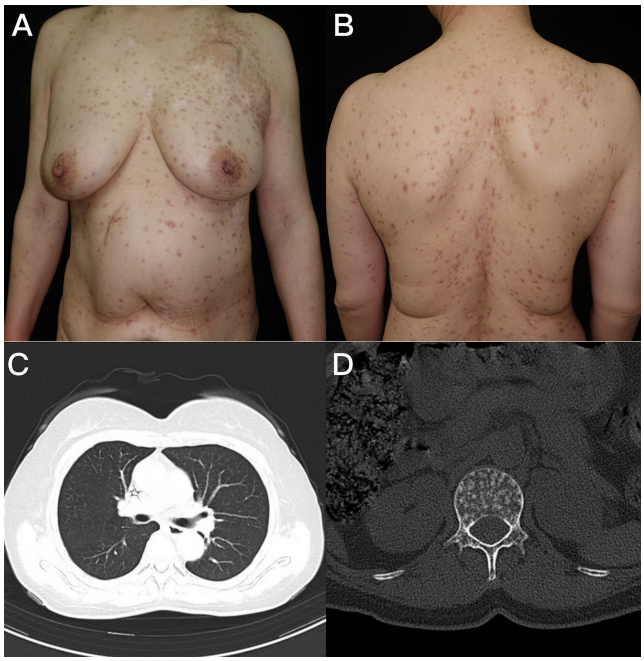

Fig. 3. Post-treatment presentation of the patient: (A, B) Post-treatment skin presentation showed remission of xanthogranuloma. (C) Chest CT showed clear pulmonary fields. (D) Spinal CT showed multiple hypodense lesions.

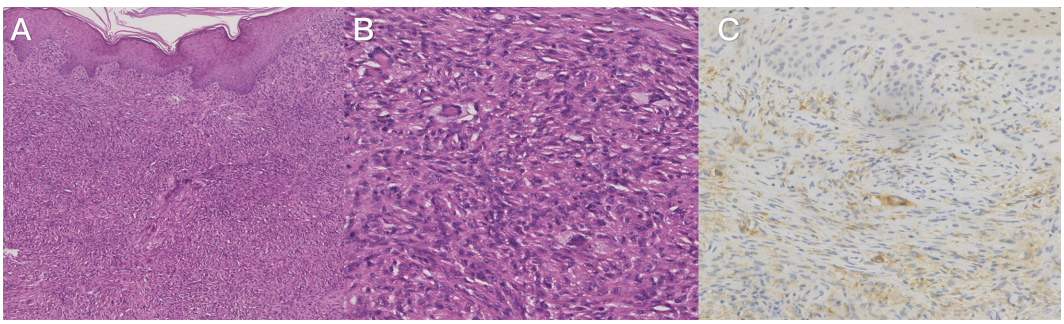

Fig. 2. Histopathologic findings: A, Histopathologic examination (original magnification ×50) of the skin lesions showed spindle cells, epithelioid cells and Touton giant cells in a nodular pattern. B, Histopathologic examination (original magnification ×200) of the skin lesions showed spindle cells, epithelioid cells, and Touton giant cells. C, CD68 staining (original magnification ×200) showed diffuse CD68-positive.

ActaDV Acta Dermato-Venereologica ActaDV Advances in dermatology and venereology

also affect the adenohypophysis, hypothalamus, and dura mater. Patients may present with characteristic mucocutaneous lesions, visual impairment, dysphagia, hoarseness, dyspnoea, and diabetes insipidus (6). Eruptive xanthomas present as red to yellow papules measuring 1–5 mm in diameter, typically distributed on the extensor surfaces of the extremities. Eruptive xanthomas are associated with primary or secondary hypertriglyceridaemia, with triglyceride levels commonly exceeding 3000 mg/dL (1). Tuberous xanthomas manifest as pink-yellow papules or nodules on the extensor surfaces of extremities, particularly over the elbows and knees. They are associated with autosomal dominant hypercholesterolaemia (7). Multicentric reticulohistiocytosis presents as periarticular firm small nodules, accompanied by joint pain and deformity. Histopathology reveals characteristic ground-glass multinucleated giant cells (8).

Non-Langerhans cell histiocytosis (NLCH) is relatively rare. Traditional systematic therapy relies mainly on chemotherapy. In recent years, genetic testing and targeted therapy have been applied to NLCH treatment with favourable outcomes. Previous studies reported BRAF mutations and other gene mutations in the MAPK pathway in NLCH patients, supporting targeted inhibition as rational therapy (2, 9). The MEK inhibitor trametinib has been used in the treatment of juvenile xanthogranuloma and other NLCH and achieved promising outcomes (10). This report describes imatinib treatment in an AXG patient with an identified PDGFRB rearrangement, highlighting the importance of molecular profiling in patients with NLCH.

REFERENCES

1. Durrington P. Dyslipidaemia. Lancet 2003; 362: 717–731. https://doi.org/10.1016/S0140-6736(03)14234-1
2. Janku F, Diamond EL, Goodman AM, Raghavan VK, Barnes TG, Kato S, et al. Molecular profiling of tumor tissue and plasma cell-free DNA from patients with non-langerhans cell histiocytosis. Mol Cancer Ther 2019; 18: 1149–1157. https://doi.org/10.1158/1535-7163.MCT-18-1244
3. Roskoski R Jr. Properties of FDA-approved small molecule protein kinase inhibitors: a 2020 update. Pharmacol Res 2020; 152: 104609. https://doi.org/10.1016/j.phrs.2019.104609
4. Collie JS, Harper CD, Fillman EP. Juvenile Xanthogranuloma. In: StatPearls. Treasure Island (FL): StatPearls Publishing LLC; 2025.
5. Dehner LP. Juvenile xanthogranulomas in the first two decades of life: a clinicopathologic study of 174 cases with cutaneous and extracutaneous manifestations. Am J Surg Pathol 2003; 27: 579–593. https://doi.org/10.1097/00000478-200305000-00003
6. Mija LA, Zhu CK, Mukovozov I. A systematic review of clinical features and treatment outcomes of xanthoma disseminatum. J Cutan Med Surg 2024; 28: 572–576. https://doi.org/10.1177/12034754241274356
7. Zak A, Zeman M, Slaby A, Vecka M. Xanthomas: clinical and pathophysiological relations. Biomed Pap Med Fac Univ Palacky Olomouc Czech Repub 2014; 158: 181–188. https://doi.org/10.5507/bp.2014.016
8. Luz FBGasparTAPKalil-Gaspar N, Ramos-e-Silva M. Multicentric reticulohistiocytosis. J Eur Acad Dermatol Venereol 2001; 15: 524–531. https://doi.org/10.1046/j.1468-3083.2001.00362.x
9. Durham BH, Lopez Rodrigo E, Picarsic J, Abramson D, Rotemberg V, De Munck S, et al. Activating mutations in CSF1R and additional receptor tyrosine kinases in histiocytic neoplasms. Nat Med 2019; 25: 1839–1842. https://doi.org/10.1038/s41591-019-0653-6
10. Aaroe A, Kurzrock R, Goyal G, Goodman AM, Patel H, Ruan G, et al. Successful treatment of non-Langerhans cell histiocytosis with the MEK inhibitor trametinib: a multicenter analysis. Blood Adv 2023; 7: 3984–3992. https://doi.org/10.1182/bloodadvances.2022009013