International Journal of Biology and Life Sciences
ISSN: 2957-9511 | Vol. 9, No. 2, 2025

One Case of Diffuse Plane Xanthoma Associated with Laryngeal Obstruction and Dysphagia

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Abstract: A 28-year-old female patient with yellow plaques on the extended side of her limbs for more than 10 years gradually affected the face, neck, and armpits. She was admitted to the otolaryngology department for treatment due to "difficulty breathing, dysphagia, and hoarseness for 1 year". Histopathology of the axillary skin lesions showed mild atrophy of the epidermis, many foam-like histiocytes infiltrated in the middle and upper dermis, and occasional Touton giant cells. Otolaryngology and Dermatology: Inhalatory wheezing sound can be heard, II ° laryngeal obstruction, slight congestion of pharyngeal mucosa, bilateral tonsils II ° enlargement, slight congestion, and a few pus emboli can be seen. Bilateral pharyngeal lateral chords are significantly proliferated, approaching the midline, pharyngeal cavity is narrow, and both eyelids are surrounded by pale yellow or brownish red flat plaques. Dense red papules and pale-yellow nodules can be seen around the mouth; Brown red or light-yellow papules and small nodules can be seen in the neck, and yellow particles can be seen on the extended side of the joints throughout the body. Diagnosis: Generalized flat xanthoma. The patient has no related systemic symptoms, and their pharyngeal manifestations and lesions may be related to potential hematological diseases.

Keywords: Xanthoma; Diffuse Plane Xanthoma; Diffuse Normolipemic Plane Xanthoma; Laryngeal Obstruction; Dysphagia.

1. Introduction

In 1962, the medical community recognized a relatively rare condition known as diffuse normal plane jaundice (DPNX), a term first introduced by esteemed researchers Altman and Winkelmann. The histopathological hallmark of this unique condition is the extensive presence of foam cells—lipid-laden macrophages—whose quantities may vary in conjunction with lymphocytes and, occasionally, Touton giant cells. The potential association between DPNX and systemic diseases, particularly leukemia and various lymphoproliferative disorders, highlights the complexity associated with this condition. This article presents a notable case involving a patient who experienced laryngeal obstruction due to undiagnosed proliferation of laryngeal lymphoid tissue, likely related to her overall health issues, specifically multiple myeloma and monoclonal immunoglobulin disease. Additionally, the symptoms of throat obstruction may correlate with a yellow tumor observed on the patient's skin. Thus, the aim of this article is to report this remarkable case and briefly review the relevant literature on DPNX.

2. Case Introduction

The case described involves a 28-year-old female patient who was admitted after experiencing prolonged difficulties with breathing and swallowing, as well as hoarseness, for one year. The initial manifestations of her condition became apparent ten years prior, when she began developing yellow patches on the extensor surfaces of her joints for unclear reasons. Over time, the number and size of these rash-like lesions gradually increased, eventually affecting her neck, armpits, eyelids, and perioral region.

Seven years prior to her most recent admission, she sought treatment at the dermatology outpatient department of our hospital, where pathological samples were collected from the papules in her armpits. Pathological examination confirmed the diagnosis of a "yellow tumor." Approximately one year ago, the patient began experiencing symptoms such as difficulty breathing and swallowing, hoarseness, intermittent sore throat, and cold-like symptoms. As her condition deteriorated, she resorted to oral breathing and experienced nasal congestion. Despite multiple medical consultations and treatment attempts — including injectable medications and oral therapies — significant improvement in her symptoms was not achieved.

The patient's medical history indicated that she had previously been in good health, with no family history of genetic diseases, and no significant abnormalities were detected during a thorough systemic examination. Upon examination of her throat and skin, we observed inspiratory wheezing suggestive of second-degree laryngeal obstruction, along with mild congestion of the pharyngeal mucosa. The bilateral tonsils exhibited secondary swelling, accompanied by mild congestion and occasional purulent plugs. Furthermore, we noted significant symmetrical proliferation of the bilateral lateral pharyngeal cords, encroaching upon the midline and narrowing the pharyngeal cavity.

The patient displayed flat patches of light yellow or brownish-red around her eyelids, and dense red papules, along with pale yellow nodules, were observed in the perioral area. Similar yellow granules were also present on the extensor surfaces of her joints. Histopathological examination of the axillary skin revealed mild epidermal atrophy and extensive infiltration of foam-like histiocytes within the upper dermis, occasionally accompanied by Touton giant cells. These findings align with those seen in jaundice. During hospitalization, standard blood tests—including routine blood tests, urinalysis, and stool examination—revealed no significant abnormalities. Additionally, assessments of blood glucose levels, lipid profiles, and evaluations of liver and kidney functions were all within normal ranges. A chest CT scan and electrocardiogram were conducted, both yielding

unremarkable results.

The CT scan of the larynx revealed slight enlargement of the laryngeal cavity with uneven wall distribution in the supraglottic region, suggesting a potential diverticulum. Esophageal imaging showed multiple diverticula in the throat, indicating chronic inflammatory changes. Supplementary examinations, including fiber-optic nasopharyngoscopy, revealed purulent secretions in the nasopharynx, significant pharyngeal stenosis, disappearance of the epiglottis, and bilateral vocal cord congestion, although the mobility of the cords was preserved. Notably, bilateral pear-shaped dimples were not visible.

Overall, diagnosis encompasses chronic sinusitis, chronic pharyngitis, and laryngitis. Removal of lesion samples for additional pathological and immunohistochemical analysis confirmed the diagnosis of chronic inflammation with lymphoid tissue hyperplasia. Immunohistochemical results indicated chronic inflammatory changes in the mucosal tissue, with positivity for CD20 (follicular zone+), CD21 (FDCs+), CD3 (follicular interstitial zone+), and Ki-67 (germinal center+). Interestingly, molecular pathology results for EBER/ISH were negative; thus, we conclude that the diagnosis is diffuse flat xanthoma.

3. Discussion

Diffuse flat yellow tumor (DPX) is a rare, non-hereditary condition classified as a relatively uncommon variant of yellow tumor. Clinically, DPX typically presents as diffuse, flat, patchy yellow skin lesions localized on the eyelids, head, face, neck, trunk, and limbs, occurring particularly in individuals with normal blood lipid levels. [1] These lesions often first appear on the joints of the hands, elbows, and other extremities before extending to the neck and trunk.[2] Flat yellow tumors are categorized into familial and non-familial types. Those with a family history generally exhibit varying degrees of lipid metabolism disorders and systemic symptoms, whereas individuals without such a history typically present without significant symptoms.

Histopathologically, DPX is characterized by the presence of foam cells within the dermis, which may be accompanied by Touton giant cells, lymphocytes, and varying numbers of foam-like tissue cells.[3] Early lesions exhibit inflammatory cell infiltration, while advanced lesions demonstrate fibroblast proliferation. It is noteworthy that there is no significant correlation between histopathological findings and the classification or potential presence of Huangma disease. However, the histopathological results in this case correspond with the characteristics of typical jaundice.

The pathogenesis of diffuse neuroblastoma (DPNX) remains unclear. Some researchers propose that in cases of DPNX associated with immunoglobulin disease, monoclonal IgG binds to low-density lipoprotein (LDL) and promotes macrophage uptake.[4] Nonetheless, the absence of a clear correlation between DPNX and systemic diseases suggests that DPNX may emerge several years prior to the manifestation of other potential systemic disorders.[5] Thus, it is advisable to conduct long-term monitoring and regular laboratory assessments for myeloproliferative diseases.

While not all skin xanthomas are associated with systemic diseases, Dermal Necrobiotic Xanthogranuloma (DNPX) is notably linked to systemic sexually transmitted diseases, particularly multiple myeloma and monoclonal immunoglobulin disorders. Additionally, other malignant hematological and lymphoproliferative diseases associated with DNPX include acute monocytic leukemia, chronic myelomonocytic leukemia, chronic myeloid leukemia, chronic lymphocytic leukemia, non-Hodgkin lymphoma, adult T-cell lymphoma/leukemia, Sézary syndrome, Waldenström macroglobulinemia, cryoglobulinemia, and Castleman's disease. The pathogenesis of DNPX remains incompletely understood; however, in cases associated with immunoglobulin disorders, it is hypothesized that monoclonal IgG binds to circulating low-density lipoprotein (LDL), facilitating the formation of antibody-LDL complexes that are more readily engulfed by macrophages. It is noteworthy that DNPX may manifest several years prior to the onset of these hematological conditions; thus, continuous monitoring with regular laboratory evaluations is recommended for the detection of myeloproliferative diseases.

Currently, several treatment modalities are available for DNPX. In cases with localized involvement, excision of a single lesion may be performed. Other therapeutic options include skin abrasion and laser ablation therapy. Notably, the Erbium: YAG laser has been effectively utilized in the treatment of facial yellow tumors. As of now, the patient displays no significant systemic symptoms, and the hematologist has been made aware of the diagnostic findings. A comprehensive evaluation for potential malignant tumors will be conducted in this patient. Furthermore, this case underscores the importance of recognizing that skin lesions may serve as initial manifestations of significant hematological disorders, highlighting the necessity for clinicians to be familiar with this rare condition.

In this case, the patient exhibited multiple diverticula in the throat and larynx, along with hyperplasia of lymphoid tissue, leading to grade II laryngeal obstruction and swallowing difficulties. Pathological findings indicate chronic inflammation along with lymphoid tissue proliferation, suggesting that laryngeal obstruction related to inflammation or lymphocyte proliferation is atypical and often associated with underlying conditions.

Pharyngeal lymphoid tissue hyperplasia is frequently associated with systemic diseases, particularly multiple myeloma and monoclonal immunoglobulin disease.[6] Despite the lack of related systemic symptoms, initial evaluations raised suspicion of potential blood disorders. Unfortunately, the patient declined further treatment and examination, leaving the underlying cause unresolved. We plan to follow up through telephone communication and encourage regular medical check-ups.

The etiology of laryngeal obstruction and swallowing difficulties in this patient remains ambiguous, as there is no significant association with common clinical causes. Systemic diseases frequently linked to xanthomatosis, such as leukemia and lymphoproliferative disorders, warrant consideration. [1] Cases associated with multiple myeloma and monoclonal immunoglobulin disease are also prevalent. [6] Furthermore, the literature indicates that mucosal tissues beyond the skin — including the throat, oropharynx, cornea, gastrointestinal tract, and bladder—can all develop lesions similar to jaundice.[7, 8] Given the considerable incidence of gastrointestinal jaundice, it is plausible that the laryngeal mucosal lesions observed in this patient may be related to cutaneous jaundice.s[9, 10]

In dermatology, diffuse normal lipid level jaundice (DPNX) is a rare condition first described by Altman and Winkelmann in 1962. This condition is characterized by extensive foam cell infiltration in the skin, accompanied by varying quantities

of lymphocytes and, occasionally, Touton giant cells. The association of DPNX with various systemic diseases, particularly lymphocytic proliferative disorders such as leukemia and multiple myeloma, necessitates further investigation. This article aims to present a specific case of DPNX in a 28-year-old female patient who experienced laryngeal obstruction due to previously undiagnosed hyperplasia of lymphoid tissue, potentially related to her health issues, including multiple myeloma and monoclonal immunoglobulin disease.

The terminological distinction between "flat xanthoma" and "xanthoma" elucidates the presence of skin xanthomas characterized by yellow deposits, which may manifest as flat macular lesions or slightly raised plaques. Xanthoma represents the most prevalent type of skin xanthoma, primarily affecting the inner canthus of the eyelids, although it can also present on the neck, trunk, and limbs. It is essential to note that while these lesions are often associated with conditions such as hypercholesterolemia and hyperlipidemia, their presence does not definitively imply lipid metabolism abnormalities. For instance, approximately 50% of patients with localized eyelid xanthomas may exhibit normal lipid levels, underscoring that xanthomas can occur independently of systemic lipid disorders. This case study details instances of Huangyuan tumor and other related conditions, such as disseminated Huangyuan tumor and histiocytosis, highlighting the critical importance of comprehensive clinical evaluation within these contexts.

Yellow tumors can be classified pathologically into primary and secondary types. Primary yellow tumors are further categorized into familial and non-familial variants. Familial types typically present with systemic manifestations and disorders of lipid metabolism, while non-familial yellow tumors tend to be sporadic and often lack significant systemic involvement.

Secondary xanthomatosis arises due to abnormal lipid metabolism associated with various diseases, such as diabetes mellitus and lymphoma. The precise etiology of DPNX (Diabetic Polyneuropathy with Xanthomatosis) remains elusive; however, it is posited that elevated blood lipid levels result in lipid deposition in tissues. This accumulation prompts tissue macrophages to engulf lipids, forming foam cells that subsequently aggregate to create xanthomas.

Clinically, yellow tumors manifest as yellow, brownish-yellow, orange-yellow, or reddish-yellow papules, nodules, and plaques. These lesions are typically asymptomatic and exhibit considerable variability in appearance. Specific clinical forms include: Xanthomas of the Eyelids: Commonly observed in middle-aged women, these lesions present as soft, well-defined patches or plaques, symmetrically distributed, primarily located at the medial canthus of the upper eyelid. Tendon Xanthomas: These lesions predominantly occur in the Achilles tendon and extensor tendons of the hands and feet. They are characterized by soft nodules that do not adhere to the overlying skin, frequently seen in patients with familial hyperlipidemia. Nodular Yellow Xanthomas: Capable of developing on extensor surfaces of joints, these may present as small, soft miliary papules to larger, fibrous nodules that can coalesce into plaques. Explosive Xanthomas: These lesions appear unexpectedly on the extensor surfaces, exhibiting acute inflammation, erythema, and tenderness, often associated with hypertriglyceridemia. Flat Yellow Tumors: These may occur throughout the body as macules or plaques and can include various subtypes such as diffuse flat yellow tumors and cholestatic flat yellow tumors.

Management strategies for yellow tumors primarily focus on dietary modifications aimed at reducing fat and sugar intake, in conjunction with pharmacological interventions to manage lipid levels. Patients with hyperlipidemia may benefit from oral statins, which have demonstrated efficacy in lowering cholesterol levels. For smaller yellow tumors, treatment options may include electrocoagulation, cryotherapy using liquid nitrogen, and laser therapy, including carbon dioxide lasers. In cases of larger yellow tumors, surgical excision may be indicated to improve prognosis and alleviate symptoms. Regular monitoring of blood lipid levels and follow-up assessments are essential to address potential complications, particularly cardiovascular and neurological issues associated with hyperlipidemia.

The prognosis for patients with yellow tumors is variable and influenced by factors such as age at onset, extent and location of lesions, and response to treatment. With appropriate dietary and medical management, many patients may experience significant improvement or even complete resolution of symptoms. Nonetheless, the risk of recurrence persists, especially if underlying systemic lipid disorders are inadequately managed. In cases of familial hypercholesterolemic xanthomatosis, heightened susceptibility to early-onset atherosclerosis underscores the necessity for patients to adhere to a structured follow-up plan emphasizing cardiovascular health from an early age.

Declarations

Conflict of interest All authors declare that they have no conficts of interest.

Human Rights

The authors declare that the work described has been carried out in accordance with the Declaration of Helsinki of the World Medical Association revised in 2013 for experiments involving humans as well as in accordance with the EU Directive 2010/63/EU for animal experiments.

Informed Consent and Patient Details

The authors declare that they obtained a written informed consent from the patients and/or volunteers included in the article and that this report does not contain any personal information that could lead to their.

Statement

All references mentioned in the Reference List are cited in the text.

Acknowledgments

The authors received no financial support for the research, authorship, and/or publication of this article. This work did not receive any grant from funding agencies in the public, commercial, or not-for-profit sectors.

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