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Case Report

Progressive nodular histiocytosis with normal karyotypic analysis

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Abstract

Non-Langerhans cell histiocytoses (NLH) comprise a spectrum of diseases that includes sinus histiocytosis with massive lymphadenopathy, hemophagocytic lymphohistiocytosis, xanthogranuloma, and reticulohistiocytoma. Progressive nodular histiocytosis (PNH) is a rare NLH that microscopically mimics juvenile xanthogranuloma but presents with disseminated persistent and progressive papulonodules in adults. Herein, we describe a case of PNH presenting as diffuse, progressively enlarging papules, nodules, and pedunculated tumors in a 38-year-old male. The diagnosis is supported microscopically by the morphologic and immunohistochemical findings. Whereas conventional cytogenetic analysis of Langerhans cell histiocytosis and juvenile xanthogranuloma has previously been described, there are no reports of the karyotype of PNH. In our patient, conventional cytogenetic analysis of the tumor revealed a normal karyotype. Although these results may represent the overgrowth of normal stromal cells rather than lesional cells, we believe this to be an important finding, indicating karyotypic analysis will not allow for distinction between PCH and other NLH or Langerhans cell histiocytoses.

Introduction

Progressive nodular histiocytosis (PNH) is a rare NLH that microscopically mimics juvenile xanthogranuloma (JXG) but presents with disseminated, persistent and progressive papulonodules in adults. There are only thirteen reported cases in the literature. We describe a case of PNH in a 38-year-old white male. Cytogenetic analysis of tumor cells demonstrated a normal karyotype. This is the first description of the karyotype of PNH.

Case Report

A 38-year-old man presented with an eight-year history of over 100 progressively enlarging yellow-brown papules, sessile nodules, and pedunculated tumors involving his face, trunk, extremities, groin, and buttocks (**Figure 1**). His mucosal surfaces, palms, and soles were spared. Most of his tumors were asymptomatic, but some were tender, especially after trauma. His past medical history was non-contributory. There was no family history of any similar lesions. Laboratory studies included a normal lipid panel. Full-body computed tomography revealed mild splenomegaly.



Figure 1: Progressive nodular histiocytosis. A and B, Numerous papules, sessile nodules, and pedunculated tumors involving the face, trunk, extremities, groin, and buttocks.

Histopathology demonstrated a polypoid tumor produced by a dermal proliferation of non-atypical, epithelioid and spindled mononuclear cells with vacuolated and xanthomatous cytoplasm. The tumor included Touton giant cells and exhibited a storiform architecture with collagen fibrosis and admixed lymphocytes (**Figure 2A-C**). Mitoses were present but infrequent and not atypical. The spindle cells stained for CD68, vimentin, Factor XIIIa, CD163, and CD4. CD34 and CD45 were focally positive. The tumor cells were negative for CD1a, CD31, S-100 protein, and smooth muscle actin. Cultured tumor cells exhibited a normal karyotype (**Figure 2D**). Based on the age at onset, progressive course, and histology, a diagnosis of PNH was made.

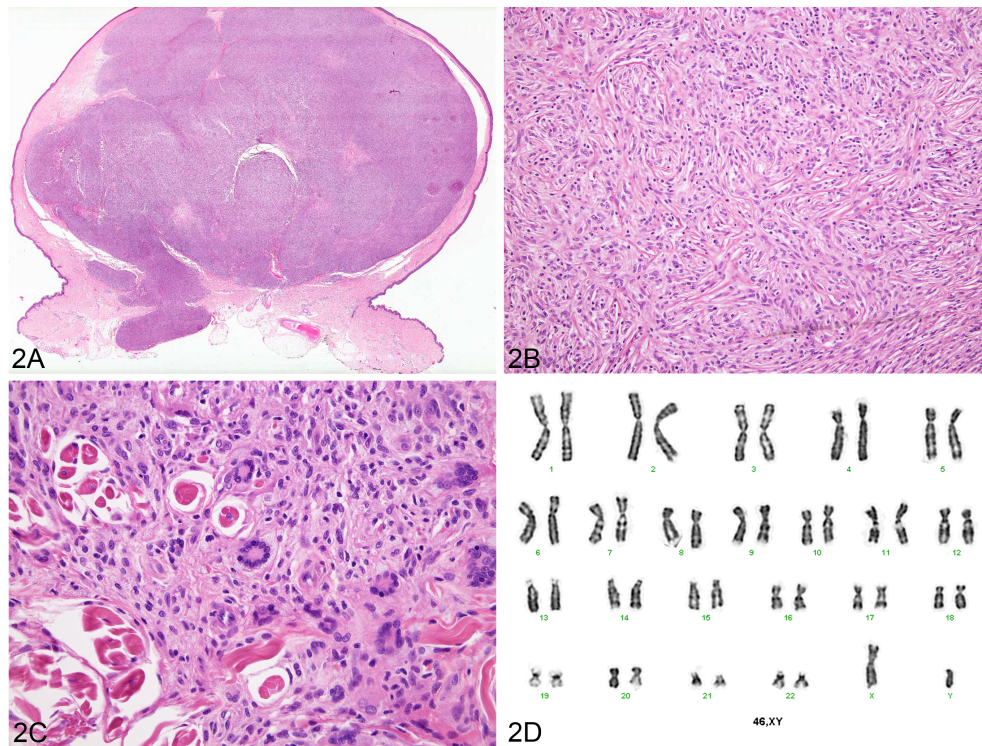


Figure 2: Progressive nodular histiocytosis, histology and karyotype. A. Low power view shows a well-circumscribed, pedunculated tumor replacing the reticular dermis; B. Higher power reveals a moderately cellular proliferation of non-atypical histiocytic and spindle cells with vacuolated and xanthomatous cytoplasm; C. Multinucleated and Touton giant cells as well as collagen trapping were present within the lesion; D. Conventional cytogenetic analysis revealed a normal male karyotype.

Discussion

Non-Langerhans cell histiocytoses (NLH) often vary in clinical presentation and histopathologic features, but they share a common lineage with tumor cells arising from the monocyte/macrophage [1]. The tumor cells lack Birbeck granules and are usually negative

for S100 protein, CD1a, and Langerin by immunohistochemistry, although rare cases with S100protein positivity have been reported [2]. They express markers of the monocyte/macrophage system, such as CD68 and HAM-56 [2,3].

Progressive nodular histiocytosis (PNH), also referred to as spindle cell xanthogranuloma, is a rare form of NLH. It is non congenital and non-familial [1]. First described by Taunton et al. in 1978, PNH is characterized by superficial papules and subcutaneous nodules and has been described in patients from 9-62 years old, with a mean age of 33 [2]. Although PNH is one of the cutaneous histiocytoses without systemic involvement, various associated conditions have been reported, including a case occurring in a 9-year-old girl with hypothalamic tumor [4], a 57-year-old male with CML and autoimmune thyroiditis [5], and cases with laryngeal [2,6], liver, and lung involvement [7].

The differential diagnosis includes multiple adult xanthogranuloma (MAXG) and juvenile xanthogranuloma (JXG). JXG remains the most important diagnostic challenge because its clinical and histologic presentation can be virtually indistinguishable from PNH. In its classic form as spontaneously regressing solitary, red to yellow-orange papules or nodules of varying sizes in young children, JXG is easily distinguished from PNH clinically. However, its presentation as multiple nodules in adults has also been described– a presentation which may be difficult to distinguish from PNH. Furthermore, the histologic features of these two entities are so similar that they are often considered as a spectrum of the same condition rather than separate diseases [8].

The etiology and pathogenesis of both Langerhans cell histiocytosis (LCH) and NLH are poorly understood. Whereas some support reactive etiology, others support a clonal, neoplastic theory. In attempts to further delineate this issue, the genomic alterations of LCH and JXG have previously been examined [11, 12]. To our knowledge, the karyotype of PNH has never been described. In our patient conventional cytogenetic analysis of the tumor revealed a normal karyotype. Although these results may represent the overgrowth of normal stromal cells rather than lesional cells, we believe this to be an important finding, indicating that karyotypic analysis will not allow for distinction between PCH and other NLH or LCH.

Treatment of PNH is difficult. There has been little success reported with intralesional and systemic corticosteroids, chemotherapeutic agents, or carbon dioxide laser [3,10]. Surgical excision appears to be the treatment modality of choice [3], which has proven effective in our patient. Whereas we have limited follow up of our patient, we are optimistic that serial excisions will offer satisfactory treatment, at least until a novel and curative approach can be found.

Conclusion

The etiology and pathogenesis of both Langerhans cell histiocytosis (LCH) and NLH are poorly understood. PNH may be clinically and histologically identical to other NLH, most importantly JXG. Conventional cytogenetic analysis of the lesions of PNH in our patient revealed a normal karyotype. Although these results may represent the overgrowth of normal stromal cells rather than lesional cells, we believe this to be an important finding, indicating karyotypic analysis will not allow for distinction between PCH and other NLH or LCH.

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