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Title

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Journal

Dermatology Online Journal, 27(2)

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Publication Date

2021

DOI

10.5070/D3272052384

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Progressive nodular histiocytosis: an unusual disorder

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Abstract

Progressive nodular histiocytosis (PNH) is a rare type of non-Langerhans cell histiocytosis of the xanthogranuloma group. Less than 20 cases have been reported. We report here a novel case of PNH with dermoscopic description and post-surgical outcome. Our patient presented with pruritic papules and nodules with progression over two years. Dermoscopic examination of large lesions showed multiple telangiectases without ulceration. There was no mucosal involvement. Histopathological analysis of a papule showed a dermal infiltrate composed of histiocytes and many Touton giant cells; a nodule revealed a dermis occupied by spindle cells arranged in a storiform pattern. The nodules were resected and the largest surgical defect, on the forehead, was corrected with A-T advancement flap. The papules were treated with cryosurgery achieving adequate cosmetic outcome without recurrence.

Keywords: progressive nodular histiocytosis, non-Langerhans cell histiocytosis, xanthogranuloma group

Introduction

Progressive nodular histiocytosis (PNH) is an infrequent form of non-Langerhans cell histiocytosis (LCH) of the xanthogranuloma group, which includes juvenile xanthogranuloma, xanthoma disseminatum, benign cephalic histiocytosis, multiple adult xanthogranuloma, and generalized eruptive histiocytosis. It was first described in 1978 by Taunton [1-3]. Currently, fewer than 20 cases can be found on a PubMed search of reports indexed for

MEDLINE. Progressive nodular histiocytosis is defined by the progressive emergence of yellow-to-brown papules and pink-to-reddish nodules on the head, trunk, extremities, and mucous membranes. Facial involvement can be severe and lead to leonine facies and ophthalmological alterations [4-5]. Most reports of PNH describe adults but it can also affect the pediatric population. No direct association with malignancies has been reported although it can appear in patients with cancer history and may indicate recurrence of the tumor [5]. Histopathological examination of both papules and nodules is necessary for diagnosis because of differences in histiocyte morphology in both lesions. There is no standardized treatment for PNH and many therapeutic options such as laser, corticosteroids, methotrexate, and cyclophosphamide have been used with variable success and recurrence of lesions after discontinuation [6-7]. Reporting patients with PNH helps to improve recognition of the disease and communicate different approaches to management.

Case Synopsis

A 34-year-old man presented to our institution with multiple mildly itchy papules and asymptomatic nodules beginning on the head, and later involving trunk and upper extremities of two years' duration. These lesions continued to increase in number and size over time. The eruption showed a progressive course without signs of spontaneous resolution. The papules and nodules affecting the face caused cosmetic concerns. Other than his mild pruritus, the patient had no local or systemic symptoms. Family and medical history were negative.



Figure 1. Multiple yellow-brown papules and large skin-colored nodules on the trunk and upper extremities.

On examination, there were yellow-brown papules and large skin-colored and pink-red nodules on the face, trunk, and upper extremities (**Figure 1**). The nodules varied in size from 1-5cm and some showed an umbilicated surface. Dermoscopic examination of large lesions showed multiple telangiectases without ulceration (**Figure 2**). Oral and nasal mucosa were uninvolved.

A punch biopsy of a thoracic papule revealed a dense dermal infiltrate composed of histiocytes with granular and eosinophilic cytoplasm and many Touton giant cells, as well as scattered mononuclear inflammatory cells. Eosinophils were not observed (**Figure 3**). A presumptive diagnosis of juvenile xanthogranuloma was made and given the cosmetic concerns relating to facial lesions, the patient was scheduled for surgical resection of the larger nodules.

A large nodule on the forehead was resected (**Figure 4**). Histopathological analysis of the nodular lesion showed an atrophic epidermis and a dermis occupied by spindle cells arranged in a storiform pattern (**Figure 5**). There was no evidence of atypical cells or malignancy. Immunohistochemical analysis was positive for CD68 and negative for CD1a. Routine laboratory tests and lipids were normal. The surgical defect was corrected with an A-T advancement flap.

Based on the presence of papules and nodules, the progressive course of the disease, and characteristic histopathological findings of both papules and nodules, the diagnosis of PNH was determined. The patient continued to have surgical interventions for the nodules and cryotherapy for the papules. Adequate cosmetic outcome and no recurrence at two years' follow up was achieved after the excision and advancement flap on the forehead (**Figure 6**). No recurrence of treated papules or nodules has been noted at two years' follow-up. Nonetheless, as expected, new papules continue to appear progressively in the patient.

Case Discussion

Progressive nodular histiocytosis is an infrequent and impressive variant of non-LCH that affects the skin and mucous membranes [4]. Less than 20 cases have been reported, most were adults but children can also be affected [8]. It is important to recognize this misunderstood disease and aid in the correct classification of the various types of histiocytosis. Although PNH is a cutaneous histiocytosis, two



Figure 2: Dermoscopic evaluation shows a nodule with multiple superficial telangiectases without ulceration.

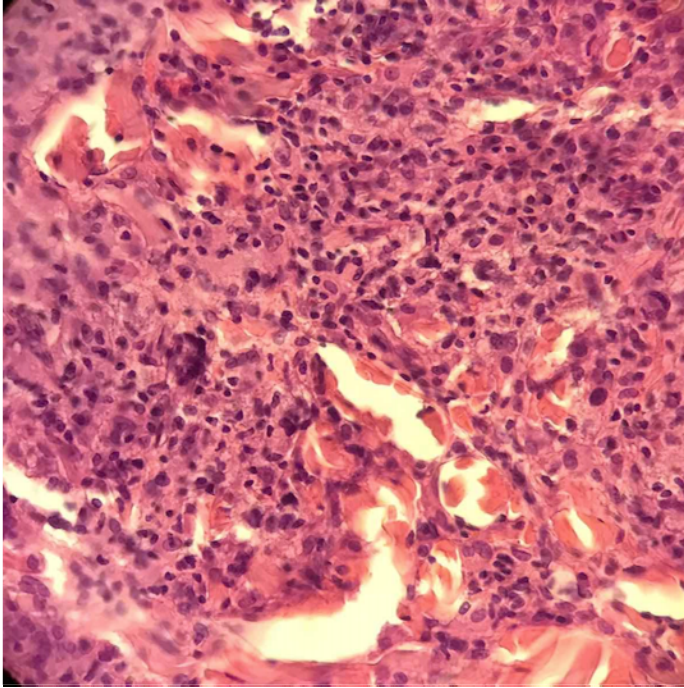


Figure 3. Histopathology of a papule revealed a dense dermal infiltrate composed of histiocytes with granular and eosinophilic cytoplasm, and many Touton giant cells, as well as scattered inflammatory cells. H&E, 40x.

patients with associated conditions and extracutaneous involvement have been reported; one with a hypothalamic tumor, and a second patient with hepatosplenomegaly, hypothyroidism, hyperuricemia, and hypocholesterolemia [9-11]. It is not clear if these associated conditions have a direct or incidental role with PNH.

The etiology and pathogenesis of LCH and non-LCH are not clear. Some reports support a reactive etiology and others communicate a neoplastic theory of histiocytes [9].

Clinically, PNH is characterized by the presence of yellow-brown papules and deep skin-colored and pink-red nodules with a progressive course without spontaneous regression. Lesions can be widely distributed over the body. There may be as many as hundreds, sometimes sparing the flexor areas and joints. However, the number of lesions does not correlate with the aggressiveness of the disease [12]. Multiple superficial telangiectases on the surface of large nodules, as noted in our patient, have been described. Ulceration or infection is uncommon [5]. Bulky masses over 20cm derived from many coalescing pedunculated nodules have been

reported [5,9,11,12]. Facial involvement is prominent and may result in leonine facies. Conjunctival, oropharyngeal, and laryngeal mucosa can be affected; involvement of the latter can lead to respiratory symptoms and hoarseness. Multiple lesions affecting the eyelids can lead to ectropion and visual disturbance [4,5,9]. Iron-storing nodules leading to anemia as a rare complication of PNH was reported in one patient [5].

Histopathological evaluation of papules demonstrates a dermal infiltrate of histiocytes with abundant, vacuolated clear cytoplasm and a variable number of multinucleated Touton giant cells. Lymphocytes, plasma cells, and eosinophils are usually found to be part of the infiltrate. Nodules show spindle cells arranged in a storiform pattern. In addition, a few Touton giant cells can be found and there is absence of mitotic activity and atypical cells [4-6].

Nofal et al. described four diagnostic criteria for PNH that included: 1) presence of two distinct types of skin lesions, with multiple occurrence and generalized distribution; 2) a progressive course; 3) histopathology consistent with xanthogranuloma, 4) immunohistochemistry consistent with non-LCH (CD68 positive, CD1a negative, S-100 protein negative). Criteria 1 and 2 are necessary for the specific diagnosis [4].

The main entity in the differential diagnosis of PNH are other non-LCHs within the xanthogranuloma group, usually sharing similar histological and immunohistochemistry findings [4,6]. Therefore,



Figure 4. Large nodule on the forehead before surgical resection.

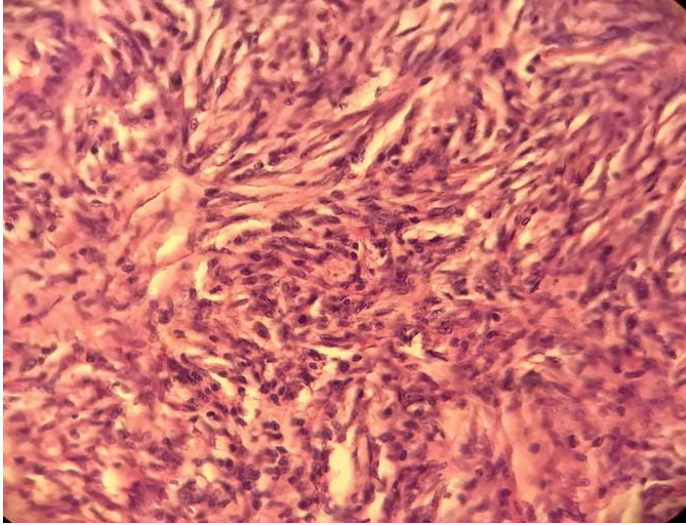


Figure 5. Histopathology of nodular lesion showed a dermis occupied by spindle cells arranged in a storiform pattern. H&E, 40x.

accurate diagnosis relies on thorough differences like the absence of spindle cells or spontaneous involution. In addition, the progressive nature of the disease and the simultaneous presence of the two distinct types of lesions, papules and deep nodules help to make the diagnosis [4,9]. Other features like patient's age, number and distribution of lesions, and associated systemic symptoms also may help to diagnose this entity and guide to differentiate it from juvenile xanthogranuloma [4].

Treatment for PNH is difficult and an effective one is not yet available. Excisional surgery for nodules that may cause disfigurement or impairment is recommended, but recurrences are not uncommon



Figure 6. Surgical defect corrected with A-T advancement flap without recurrence at two years' follow-up.

[5,13]. Ablative lasers like carbon dioxide and excimer have been used for nodules but recurrence within the scars was observed. Multiple sessions of cryotherapy for papules have been tried and may be a good treatment option for localized and small lesions [4,6,13]. Our patient had favorable results with cryotherapy for papules and excellent cosmetic results after surgical resection of nodules. Corticosteroid treatment as intralesional injection, pulse therapy, and continuous daily treatment (10-70mg/day oral prednisone) has been reported [5-7]. Electrodesiccation and curettage of disfiguring lesions has been reported in a pediatric patient with satisfactory cosmetic results [2]. Systemic chemotherapeutic agents like vincristine, cyclophosphamide, and prednisolone have been tried without success [4,13]. Oral methotrexate (15mg once/week) was reported successful in one case with complete resolution of lesions and symptoms after six months. The patient remained in remission for 18 months with treatment but recurrence was noticed after treatment suspension. Methotrexate was reintroduced and remission was obtained within three months of restarting therapy [7].

The prognosis of PNH is variable with recurrence after interruption of systemic treatments. Long-term follow up of patients with a multidisciplinary approach is recommended to prevent complications. New onset of PNH in a patient with cancer history could indicate recurrence of the malignancy [13].

Conclusion

Progressive nodular histiocytosis is rare and is a poorly understood disorder, as with other non-LCHs. Clinical diagnosis of PNH can be challenging and sometimes not possible because of its similarities with other non-LCHs of the xanthogranuloma group. Histopathology and immunohistochemistry are vital for diagnosis. This case is interesting because it describes and shows the characteristic dermoscopic features of nodules reported in literature and clinical images of an early disease with excellent outcome after surgical treatment. It also demonstrates that an

early diagnosis can prevent disfigurement. Recurrences of lesions are not uncommon and because of the progressive behavior of the disease life-long follow up is recommended.

References

1. Taunton D, Yeshurun D, Jarratt M. Progressive Nodular Histiocytoma. *Arch Dermatol*. 1978;114:1505-08. [PMID: 214042].
2. Guidolin L, Noguera-Morel L, Hernandez-Mart A, et al. A Case with Juvenile Xanthogranuloma and Progressive Nodular Histiocytosis Overlap. *Pediatr Dermatol*. 2017;34:e102–e103. [PMID: 28297144].
3. Williams A, Thomas A, Singh Kwatra K, Jain K. Progressive Nodular Histiocytosis Associated with Eale's Disease. *Indian J Dermatol*. 2015;60:388–90. [PMID: 26288410].
4. Nofal A, Assaf M, Tawfik A, et al. Progressive nodular histiocytosis: a case report and literature review. *In J Dermatol*. 2011;50:1546–51. [PMID: 22098005].
5. Hilker O, Kovneristy A, Varga R, et al. Progressive nodular histiocytosis. *Journal der Deutschen Dermatologischen Gesellschaft*. 2012;11:301–07. [PMID: 23231636].
6. Kunimoto K, Uede K, Furukawa F. Progressive nodular histiocytosis. *J Dermatol* 2010;37:1071–73. [PMID: 21083716].
7. Huet F, Brenaut E, Costa S, et al. Progressive nodular histiocytosis improved by methotrexate. *Eur Dermatol*. 2017;27:661–63. [PMID: 29165296].
8. Glavin FL, Chhatwall H, Karimi K. Progressive nodular histiocytosis: a case report with literature review, and discussion of differential diagnosis and classification. *J Cutan Pathol*. 2009;36:1286–92. [PMID: 19878386].
9. Amin S, Riddle C, Fraga GR, et al. Progressive nodular histiocytosis with normal karyotypic analysis. *Dermatol Online J*. 2013;19:18577.. [PMID: 24011326].
10. Gonzalez Ruiz A, Bernal Ruiz AI, Aragoneses Fraile H, Peral Martinez I, García Muñoz M. Progressive nodular histiocytosis accompanied by systemic disorders. *Br J Dermatol*. 2000;143:628-31. [PMID: 10971342].
11. Beswick SJ, Kirk JMW, Bradshaw K, Sanders DSA, Moss C. Progressive nodular histiocytosis in a child with a hypothalamic tumour. *Br J Dermatol*. 2002;146:138–40. [PMID: 11852916].
12. Kiyohara T, Makimura K, Miyamoto M, et al. Progressive Nodular Histiocytosis with Large Nodules and a Bulky Mass. *Acta Derm-Venerol*. 2019;99:610–11. [PMID: 30226532].
13. Chapman LW, Hsiao JL, Sarantopoulos P, Chiu MW. Reddish-Brown Nodules and Papules in an Elderly Man. *JAMA Dermatol*. 2013;149:1229-30. [PMID: 23945611].

Potential conflicts of interest

The authors declare no conflicts of interests.