CASE REPORT

Progressive nodular histiocytosis: a rare type of xanthogranuloma

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Abstract
Progressive nodular histiocytosis is a rare non-Langerhans histiocytosis. It tends to occur in adult with progressive course that differentiates from other groups of xanthogranuloma. The clinical presentation is characteristic and disfiguring of the face is not uncommon. Extracutaneous involvement and metabolic association were reported in a few cases. Treatment is unsatisfactory and follow-up is suggested for possible complication. Herein, we reported a typical case of the disease.

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Introduction
Progressive nodular histiocytosis (PNH) is a subgroup of xanthogranuloma and belongs to the class of non-Langerhans cell histiocytosis. It was first described by Taunton et al.1 in 1978. It predominantly affects the young adult in their 3rd–4th decades of life. The patient usually presents with multiple yellowish-brown, variable-sized papulonodules involving mainly the head, neck, trunk, and the limbs.2 The lesions tend to progress without spontaneous resolution. It is characterized histologically by diffuse infiltrate of spindle-shaped histiocytes with whorl-like growth pattern, admixed with xanthomatized histiocytes and Touton giant cells. Herein, we reported a typical case of the disease.

Case report
A 46-year-old man presented with numerous pedunculated asymptomatic papulonodules over face, trunk, and the upper limbs. The lesions varied from 0.3 cm to 2 cm and were firm in consistency. Telangiectasia on an erythematous to yellowish background can be easily appreciated. The nodules have developed since 6 years ago, beginning from face to trunk. He ever received skin biopsy when the lesions were only several and scattered over the face. Juvenile xanthogranuloma was told. However, the nodules increased in a progressive fashion without spontaneous regression. The face gradually showed a leonine feature (Figure 1). His respiratory pattern is smooth and there are no dysphagia, hearing impairment, or signs of ocular involvement. There is no family member sharing similar cutaneous presentation. The laboratory survey disclosed hypertriglyceridemia to as high as 334 mg/dL and a normal cholesterol level. A skin biopsy taken from the largest nodule on face revealed diffused dermal infiltrate, composed of spindle cells with variable foamy cytoplasm and multinucleated giant cells, especially the Touton type (Figure 2). The spindle cells comprised nearly 90% of the cells and showed a storiform arrangement. There was no cellular atypia and mitotic activity was absent. The histiocytes stained positive for CD68 and the spindle cells were negative for smooth muscle actin and desmin. For the cosmetic purpose, the patient later underwent surgical excision of the larger nodules on face.

Discussion
PNH is a rare entity and there were only 15 cases reported in the literature to date. The typical histology is proliferation of storiform, spindle-shaped histiocytes, confining to the dermis but it may involve as deep as the muscle layer. Xanthomatous, vacuolated histiocytes or multinucleated giant cells may be abundant. The histiocytes are positive for the macrophage/dendritic cell marker such as CD68 and negative for S100 and CD1a, suggesting the origin of non-Langerhans cell. The histological findings resemble several xanthogranulomatous diseases, such as juvenile xanthogranuloma, papular xanthoma, benign cephalic histiocytosis, generalized eruptive histiocytosis, and xanthoma disseminatum. Chu3 had...
suggested a possible continuity of the diseases as a spectrum. However, the differential diagnosis is still possible on clinical ground. Juvenile xanthogranuloma usually onsets before the age of 6 years and mostly shows a spontaneous resolution. Although several cases of xanthogranuloma were reported to occur during adulthood, the lesion was usually solitary.\(^4\) Benign cephalic histiocytosis and generalized eruptive histiocytosis are usually self-limited as well, whereas xanthoma disseminatum has a predilection for the flexural

Figure 1 (A) Multiple pedunculated papulonodules mainly over face, showing a leonine feature. (B) Also scattered nodules involve the trunk. (C) Close view of the nodule shows yellowish appearance with telangiectasia.

Figure 2 (A) Whorls of spindle-shaped histiocytes admixed with foamy histiocytes and multinucleated giant cells infiltrate the entire dermis [hematoxylin and eosin (H&E); original magnification, \(\times40\)]. (B) Touton (arrow) and foreign body (arrow head) giant cells can be easily appreciated (H&E; original magnification, \(\times200\)). (C) CD68 stains positive for the histiocytes (original magnification, \(\times200\)).
area with frequent visceral organ involvement. The progressive course and typical pedunculated nodules characterize the PNH. However, early diagnosis may be difficult when the lesion number is few and therefore long-term follow up is necessary for the suspected cases. Our patient with protracted clinical course and characteristic histological feature is a typical case of PNH.

PNH is regarded as solely a cutaneous disease without tendency of extracutaneous involvement. Systemic survey is required only when symptoms are present. However, Glavin et al reported a case with a 7-year history of the progressive skin nodularities showing biopsy-proved extensive laryngeal and pharyngeal involvement that cause dyspnea and dysphagia. Another case report suggests the hypothalamic involvement with precocious puberty and growth failure. Gonzalez Ruiz et al also imply a possible correlation between chronic myeloid leukemia and long-lasting PNH. The association between lipid metabolism and PNH is obscure. Although most of the patients with PNH are normolipemic like those with juvenile xanthogranuloma, coexisting lipid dysfunction was reported. Hypercholesterolemia was noted in a 34-year-old woman with PNH for 7 years. Gonzalez Ruiz et al demonstrated another patient with PNH for 26 years showing hypothyroidism and hypercholesterolemia. Our patient presented with hypertriglyceridemia and a normal serum cholesterol level. Whether dyslipidemia is a collision phenomenon or does it play a role in developing PNH requires further evidence.

Treatment of PNH is usually unsatisfactory. Surgical excision provides temporary relief, but local recurrence is very likely. Systemic corticosteroid, cyclophosphamide, radiotherapy, or chemotherapy, such as vincristine, tends to be ineffective. However, long-term follow-up is still necessary for early detection to avoid possible complication.

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