Nodular colloid degeneration of the skin: Report of three cases with review and update

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ABSTRACT

Nodular colloid degeneration (NCD) is a rare dermatological disorder and uncommon type of colloid milium. The degeneration may be related to sun exposure. In this report, three cases, all presenting as multiple plaques and nodules over the nose and the face are depicted. Histologically, these nodular masses were homogeneous, with eosinophilic-cleaved materials expanding the papillary dermis and extending into the deep dermis. Periodic acid Schiff (PAS), crystal violet, and methyl-violet stains highlight the colloid material. All the three cases were finally diagnosed as NCD. NCD could be considered in any case with facial nodules and a long history of sun exposure. We suggest the long-term sun exposure as an etiologic factor; thus sun protection would be the most preventive and available treatment.

Key words: Colloid milium, histochemistry, nodular colloid degeneration

INTRODUCTION

Nodular colloid degeneration (NCD) is a rare cutaneous deposition disorder characterized by a single large nodule or multiple soft to rubbery plaques or nodules occurring over sun-exposed regions. Colloid material deposits in the upper dermis characterize the disorder.[1] NCD can be differentiated from amyloidosis by histochemistry and immunohistochemistry. Histologically, there are masses of amorphous, eosinophilic material expanding the papillary dermis, resembling amyloid.[2] NCD is a rare disease; only eight cases have been reported so far in the English literature [Table 1]. We present three cases of NCD all occurring as papules, plaques, and nodules over sun-exposed areas, including nose and cheeks.

CASE REPORTS

Case 1
A 48-year-old man presented with bilateral nodules over the nasal alae with adjacent papules that had been gradually growing during several past years [Figure 1a]. The patient underwent curettage biopsy and dermabrasion, but after 6 months, the lesions persisted. The excised lesion was submitted for histopathologic evaluation under clinical differential diagnoses of sebaceous hyperplasia, granuloma faciale, sarcoidosis, and giant colloid milium.

Case 2
A 54-year-old woman with a purple plaque over the right nostril and a round nodule over the nose since two years [Figure 1b]. An erythematous papule on the left cheek also noted. The clinical differential diagnoses were cystic basal cell carcinoma and sarcoidosis. A biopsy was performed and sun protection advised, but no improvement was noted after two years follow up.

Case 3
A 55-year-old woman presented with asymptomatic purple plaques over the right cheek with overlying and adjacent translucent papules [Figure 1c]. The lesions started with papules spreading to form the plaques. Dermoscopy revealed yellow amorphous structureless areas with accentuated follicular openings [Figure 1d]. A clear fluid came out by piercing the lesions using a fine needle. A biopsy was drawn from the plaque, and the clinical differentials offered were eccrine Hidrocystoma, colloid milium, mucinosis, sarcoidosis, and pseudolymphoma.
Histopathology

Histopathologic examination revealed nodular, homogeneous, and eosinophilic materials expanding papillary dermis with extension into deep dermis [Figure 2a]. There are some clefts through the colloid materials dividing material into smaller islands. Scattered nuclei of fibroblasts were aligned along the cleaved colloid [Figure 2b]. Histochemistry study revealed reactivity of colloid materials with PAS, methyl-violet and crystal-violet [Figure 3a-c], and weak reaction with Congo-red staining. Elastin staining shows clumped fragments of elastin fibers among colloid materials [Figure 3d]. The epidermis was

**Table 1: Summary of reported cases of nodular colloid degeneration in the English literature**

| Author            | Age/gender | Location       | Lesion type (numbers) | Size (cm) | Treatment                  |
|-------------------|------------|----------------|-----------------------|-----------|----------------------------|
| Labadie           | 47/F       | Forehead       | Nodule (1)            | 5×2.6×0.6 | NA*                        |
| Sullivan et al.   | 43/M       | Forehead, cheeks| Plaque, nodule (50)   | 0.4-5     | NA                         |
| Kawashima et al.  | 74/M       | Head, chin     | Nodule (6)            | 0.5-3     | NA                         |
| Dupre et al.      | 51/M       | Cheek          | Plaque (1)            | 2         | NA                         |
| Patterson et al.  | 59/M       | Neck, extremities| Nodule               | NA        | NA                         |
| Preston et al.    | 43/M       | Penis          | Plaque (1)            | 2         | No treatment               |
| Mittal et al.     | 40/F       | Face           | Papule, plaque, nodule| 0.2-0.5   | Combi laser therapy        |
| Choi et al.       | 76/M       | Face           | Plaque (1)            | 3×1.5     | Sun protection             |
| Patient 1         | 48/M       | Nose           | Papule (15), plaque (1), nodule (2) | 0.2-0.4 | Dermabrasion+Sun protection |
| Patient 2         | 54/F       | Nose           | Papule (1), plaque (1), nodule (1) | 0.4 | Dermabrasion+sun protection |
| Patient 3         | 55/F       | Cheek          | Papule (1), plaque (4) | 0.3 | Piecing+sun protection     |

*NA: Not available references: 3,4,6,7,11-14
flattened and separated from nodular deposition by a grenz zone of collagen tissue.

DISCUSSION

Colloid degeneration of skin is a distinct clinicopathological entity characterised by colloid deposits in the dermis, of which three clinical variants are recognized: juvenile colloid milium (JCM), adult colloid milium (ACM), and NCD. Typically, adult colloid milium occurs in sun-damaged skin of fair and middle-aged individuals. The juvenile type is similar to ACM and starts before puberty. NCD reveals single or multiple plaques or nodules reaching up to 5 cm in size with a slightly lumpy surface. The most commonly affected sites are the sun-exposed areas particularly face, ears, neck, and dorsal hands.

The major histologic differential diagnosis includes nodular amyloidosis. Histochemistry and immunohistochemistry examination is helpful to distinguish colloid from amyloid. The colloid in all types shows a positive reaction with PAS and negative reaction with alcian-blue. In ACM and NCD, Congo-red stain is positive and results in green birefringence sometimes with weak reaction. The colloid in JCM shows no reaction with Congo-red, and produces fluorescence with Thioflavine-T. Variable reactions with methyl-violet and crystal-violet are reported. Another method to differentiate colloid from amyloid is that colloid does not react with Pagoda-red and other cotton dyes. Immunohistochemically, colloid and amyloid are positive for amyloid-p protein, although this protein could be seen in normal elastic fibers and actinic elastosis. Amyloid frequently reacts with light-chain immunoglobulin, to which colloid shows no reaction. Negative reactivity with cytokeratin also distinguishes colloid from amyloid, although cytokeratin may be positive in JCM.

Ultrastructurally, the colloid in NCD and ACM is composed of 1.5-2 nm, wavy branching filaments randomly arranged in amorphous material. The filaments are much shorter and smaller than amyloid, which are 6-10 nm straight filaments. In the juvenile type, there are tightly packed bundles of curvy shortened filaments, 8-10 nm in thick, arranged in a whorled pattern. The fibrillar structure is like that of amyloid, although negative staining with Congo-red distinguishes it from amyloid.

Although NCD is a rare disease, it should be considered in any cases with facial nodules and history of long-term sun exposure. We suggest the long-term exposure to sun as an etiologic factor in our cases. No successful treatment is available; therefore, sun protection would the most preventive treatment as of now.

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