Juvenile Colloid Milium: Case Report and Literature Review

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ABSTRACT
Juvenile colloid milium (JCM) is a rare, chronic, benign but cosmetically disturbing degenerative dermatosis, characterized by the appearance of translucent papules on sun-exposed areas before puberty. The juvenile form of colloid milium is thought to be caused by an inherited susceptibility to ultraviolet (UV) light, transmitted in an either autosomal dominant or recessive manner, eventually leading to keratinocyte degeneration. The prevalence of JCM is unknown due to the scarcity of case reports. This paper describes the case of a 10 years old male patient diagnosed with JCM which, according to the information available so far, is the first such case reported in Romania.

Keywords: juvenile colloid milium, keratinocyte degeneration, UV susceptibility, translucent papules, sun-exposed areas.

INTRODUCTION
Juvenile colloid milium (JCM) is an exceedingly rare, chronic dermatosis characterized clinically by the presence of multiple, translucent, yellowish or flesh colored papules on sun exposed areas of prepubertal children. Its key histopathologic features consist of well circumscribed accumulations of amyloid-like amorphous, fissured, eosinophilic deposits within the superficial dermis, occupying and widening the dermal papillae (1). Similar to adult colloid milium (ACM), sun exposure appears to be an important factor in inducing such lesions in susceptible pediatric patients, but the two diseases show different pathophysiology and clinicopathological features. We document the case of a 10-year-old boy with JCM and summarize previous cases described in the literature.

CASE REPORT
A 10-year-old male patient from rural environment has been presented by his mother to our clinic for the evaluation of facial lesions consisting of multiple, small (0.2-0.5 cm), translucent...
papules, with an orange-yellow hue, occasionally hemorrhagic, located over the child’s nose, cheeks and upper lip (Figure 1). The lesions started to appear three years prior and they have been noted to exacerbate during summer months and to slowly progress over the years. The family history was unremarkable, with no similar cases amongst its members. A clinical suspicion of facial angiofibromas associated with tuberous sclerosis complex has been raised and, because of the lack of additional clinical features required to sustain this diagnosis, a cutaneous biopsy has been considered.

A cutaneous incisional biopsy specimen from the upper lip area was performed. It showed multiple widened dermal papilles projected above the skin surface (Figure 2a). These modified papillary structures were stuffed with an amorphous, eosinophilic, acellular material, including some clefts and dilated capillary vessels with infiltrated walls (Figure 2b). The epidermis on top was thinned and included numerous apoptotic keratinocytes and prominent cystoid bodies, some of them with a confluent appearance, giving rise to colloid masses that blended with the papillary dermal deposits (Figure 2c). The dermal deposits were in direct contact with and impinging the overlying epidermis, without the presence of a grenz zone. The deposits were PAS positive and Congo Red negative. Immunohistochemical staining for high molecular weight cytokeratins AE1/AE3, CK5/6 and 34betaE12 showed patchy positivity inside the colloid masses. Corroborated with the clinical setting, the histopathologic findings supported the diagnosis of juvenile colloid milium.

After rendering the final diagnosis, further clinical evaluation did not reveal other significant findings. The patient received recommendation and advice on sun protection measures, broad spectrum sun protection cream and vitamin C supplementation, 250 mg per day. At one month follow-up, the evolution was slightly positive, with a minor improvement of the preexisting small lesions and lack of appearance of new ones. CO2 laser treatment was further proposed, but the patient was lost to follow-up.

**DISCUSSION**

Colloid milium was first mentioned in 1866 and less than 150 additional cases have been later reported (2). Four clinical variants of colloid milium have been described. They include an adult onset type, which is the most frequently encountered form, a juvenile form, a nodular form (3) and a pigmented form (4).

According to our knowledge, 10 other cases of juvenile colloid milium have been reported in the literature so far (Table 1) (1, 5-12). In addition to the cases summarised in Table 1, other cases of juvenile colloid milium have been reported in studies concerning ligneous conjunctivitis (13-15). In one of the papers, the author revealed a link between ligneous conjunctivitis...
and hypoplasminogenemia and concluded that a correlation between juvenile colloid milium and hypoplasminogenemia could also be made. One patient who suffered from both conditions had indeed a homozygous mutation in the plasminogen gene (10). Worth mentioning is also that three of the 10 cases reported in the literature came from consanguineous parents. Furthermore, three cases of familial colloid milium were reported: two cases where both siblings were affected by this condition, respectively one case where father and daughter had this affliction.

Colloid milium is considered a rare entity, with no known figures on prevalence. The adult form seems to be more common in light-skinned

<table>
<thead>
<tr>
<th>Ref. number/Gender</th>
<th>Age of onset</th>
<th>Affected site</th>
<th>Family history</th>
<th>Personal history</th>
<th>Clinical aspects</th>
<th>Microscopic aspects</th>
<th>PAS</th>
<th>Congo Red</th>
<th>Immunohistochemistry</th>
<th>Ultrastructural findings</th>
</tr>
</thead>
<tbody>
<tr>
<td>(1) girl</td>
<td>7</td>
<td>Upper lip, nose</td>
<td>+</td>
<td>asthma</td>
<td>Small, yellow-brown translucent papules</td>
<td>Well circumscribed accumulations of amorphous, eosinophilic material developing immediately beneath the epidermis. Similar material was observed within the basal keratinocytes.</td>
<td>+</td>
<td>α-CK + in the periphery of the lesion, - in the center</td>
<td>Colloid was found in both the dermis and epidermis. In the epidermis, both intra- and extracellular deposits were present. The colloid material had a wavy, fibrillar structure with a diameter of 8.5 nm.</td>
<td></td>
</tr>
<tr>
<td>(1) boy</td>
<td>10</td>
<td>Upper lip, nose, infraorbital ridge</td>
<td>+</td>
<td>-</td>
<td>Small, yellow-brown translucent papules</td>
<td>Well circumscribed accumulations of amorphous, eosinophilic material. Similar material developed in basal keratinocytes</td>
<td>+</td>
<td>α-CK + in the periphery of the lesion, - in the center</td>
<td>Colloid was found in both the dermis and epidermis. In the epidermis, both intra- and extracellular deposits were present. The colloid material had a wavy, fibrillar structure with a diameter of 8.5 nm.</td>
<td></td>
</tr>
<tr>
<td>(5) girl</td>
<td>2</td>
<td>Lower eyelids, cheeks, extending onto the bridge of the nose</td>
<td>-</td>
<td></td>
<td>Numerous waxy yellow papules</td>
<td>Wide band of eosinophilic amorphous material filling the upper dermis. Mild perivascular inflammatory cell infiltrate</td>
<td>Weakly +</td>
<td>Focal positivity within the band of colloid</td>
<td>CK +</td>
<td></td>
</tr>
<tr>
<td>(6) boy</td>
<td>5</td>
<td>Eyelids, upper lip, cheeks, nose</td>
<td>-</td>
<td></td>
<td>Numerous small yellowish colored papules</td>
<td>Amorphous eosinophilic material in the upper dermis, situated immediately bellow an atrophic epidermis with eosinophilic round bodies present among the keratinocytes</td>
<td>+</td>
<td>Weakly +</td>
<td>CK +</td>
<td></td>
</tr>
<tr>
<td>(7) girl</td>
<td>7</td>
<td>Upper eyelids, nose, dorsal surfaces of both hands</td>
<td>+ (father)</td>
<td>-</td>
<td>Clusters of translucent yellow-tan 1-2 mm papules</td>
<td>Eosinophilic material occupying the dermal and reticular dermis with an overlying atrophic epidermis. Multiple necrotic keratinocytes</td>
<td>+</td>
<td>Weakly +</td>
<td>CK, AE1/AE3 + Collagen IV +</td>
<td></td>
</tr>
</tbody>
</table>

Continued on next page
TABLE 1. Reported juvenile colloid cases

<table>
<thead>
<tr>
<th>Case</th>
<th>Age</th>
<th>Location(s)</th>
<th>Family History</th>
<th>Description</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>(8) girl</td>
<td>57</td>
<td>Zygomatic prominence, bilateral, nose, perioral region</td>
<td>-</td>
<td>Small confluent brownish papules</td>
<td>Amorphous eosinophilic material that came from the epidermis and extended into the papillary dermis between elongated rete ridges. Eosinophilic round bodies were found within and between the keratinocytes. The colloid material contained histiocytes, melanophages and mast cells.</td>
</tr>
<tr>
<td>(9) girl</td>
<td>6</td>
<td>Cheeks, perioral, periorbital</td>
<td>+ (brother presented similar lesions)</td>
<td>Yellowish, translucent, firm, flat plaques and papules, arranged in a linear pattern, radiating centrifugally from the oral commissures.</td>
<td>Pale pink homogeneous material was present in the upper dermis, without the presence of a Grenz zone.</td>
</tr>
<tr>
<td>(10) girl</td>
<td>1</td>
<td>Nose, cheeks, temple, upper lip, lower eyelids</td>
<td>- (parents were relatives – third cousins)</td>
<td>Numerous, purpuric, small, discrete, translucent, yellowish grouped papules. The lesions started bleeding easily after minor trauma.</td>
<td>Well circumscribed accumulations of fissured amorphous eosinophilic material in the papillary dermis.</td>
</tr>
<tr>
<td>(11) boy</td>
<td>3 months old</td>
<td>Reumatoid arthritis, lupus erythematosus</td>
<td>Consanguineous parents</td>
<td>Yellowish translucent wavy papules</td>
<td>Amorphous eosinophilic hyaline material in the papillary dermis</td>
</tr>
<tr>
<td>(12) boy</td>
<td>6</td>
<td>Cheeks, nose, upper lip</td>
<td>Consanguineous parents</td>
<td>Translucent, amber brown, papules occasionally hemorrhagic</td>
<td>Nodular lamps of amorphous eosinophilic material deposited in the superficial dermis lifted the atrophic epidermis.</td>
</tr>
</tbody>
</table>

(DAko) CK + at the periphery. - in the center of the islands of colloid
Initially, tonofilaments become dense and clumped, but in time they lose their electron density. Later, electron-light filaments form wavy bundles and small whorls, that occupy the entire cell. Within the wavy filaments, some melanosomes, organelles and nuclear debris were found. In the epidermis, the degenerated cells seemed to be lined by a basal lamina-like layer, feature not present in the filamentous masses from the dermis. Occasionally, a random arrangement of the filaments, similar to that encountered in amyloid was observed.
individuals and in male patients. As it can be observed from the published literature, the juvenile form has its onset before puberty. Clinically the lesions are similar in all types of colloid milium, developing on sun-exposed areas such as the nose, cheeks, ears, periorbital region, posterior neck and the dorsal aspects of the hands as translucent or yellow-brown, waxy, solitary or confluent papules (3). JCM can resemble amyloidosis, syringomas, angiofibromas, retention cysts, milium or sarcoidosis. The appearance of JCM lesions has been linked with severe acute sunburn or chronic sun exposure (8). Unusual involvements have also been reported, with nodular colloid milium located on the conjunctiva and anterior orbit (15), upper eyelid (16), the oral cavity (17) or in association with liceous conjunctivitis or periodontitis (5). Both types of inheritance pattern, autosomal dominant and autosomal recessive, have been mentioned. It is believed that colloid milium is caused by the degeneration of elastic fibers in response to excessive exposure to ultraviolet rays (UV), petroleum and hydroquinone (18). The juvenile form is thought to arise in genetically predisposed individuals, secondary to the degeneration of UV-transformed keratinocytes.

JCM is microscopically characterized by amorphous eosinophilic deposits within the papillary dermis. The pathogenesis of JCM is somehow similar to macular amyloidosis, in which apoptotic keratinocytes give rise to dermal deposits of amyloid. Based on ultrastructural observations and on the fact that these deposits stain positive for cytokeratin, some investigators actually believe that JCM might represent a particular form of amyloid-K dermatosis (1, 8). In adult form, there is always some cleft formation inside the dermal deposits and a grenz zone can be appreciated, together with a scarcity of apoptotic keratinocytes. These findings suggest a different structure, origin and mechanism of formation of colloid deposits in adult colloid milium, namely a degeneration process of collagen and elastic fibers in the superficial dermis under the influence of UV radiation. Concerning the immunohistochemical staining methods, most of the JCM cases reported were positive for cytokeratin, while one author claims that some pancytokeratin, namely AE1/AE3 and EKH4, did not produce immunoreactivity inside the colloid material (8). As it was in our patient, another reported case stained positively with AE1/AE3 pancytokeratin (7).

The best treatment option for colloid milium has not yet been identified. Sunscreen use should be recommended for all patients. Published reports mention dermabrasion, cryotherapy, Er:YAG laser (19), CO2 laser (20) and other different ablative therapies for adult colloid milium, with various results.

CONCLUSION

Reported cases of juvenile colloid milium are very scarce, a PubMed search for “juvenile colloid milium” conducted by the authors in August 2018 revealing only 10 items after the exclusion of papers describing adult forms of the disease. According to the information available so far, this is the first case of juvenile colloid milium reported in Romania.

Conflicts of interest: none declared.
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REFERENCES


