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Multiple Pilomatricoma in the Context of Previous Seminoma: Discussion on the Possible Relationship

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SUMMARY Multiple pilomatricomas are rare. In the literature, they have been associated with many conditions, although the most common association is with myotonic dystrophy. We present a new association not previously described in the literature, observed in a 28-year-old male with three pilomatricomas, who had been diagnosed with seminoma 15 months before the current diagnosis of multiple pilomatricomas. Concerning the current association, as well as many of those described in the literature, we also discuss whether they might be more than mere coincidences, maybe explained by some molecular alterations.

KEY WORDS: multiple pilomatricomas, seminoma

CASE REPORT

We present a 28-year-old male patient who came to the hospital with a complaint of several subcutaneous nodules. Fifteen months before, the patient had been diagnosed with classic seminoma of 1.5 cm in size, pT1, N0, M0, S0, of the left testis (Fig. 1). Radical left orchydectomy was then performed. No signs or symptoms of recurrence were present.

Current exploration revealed three subcutaneous, hard nodules, distributed in the right forearm, left arm and left buttock. The biggest of the nodules measured 1.3 cm. The three lesions were removed and morphological study showed them to correspond to typical pilomatricomas, with classic shadow cells (Fig. 2). All of them presented focal calcification, and two of them (left arm and buttock) also presented focal ossification.

DISCUSSION

Multiple pilomatricomas (MP) are a rare event (1-4), accounting for 2% to 3.5% of the reported cases of pilomatricoma (4). The concept of MP includes either simultaneous presentation or presentation of different tumors in the same patient at some time intervals (4). Up to 31 lesions in the same patient have been reported (5). Some histologic variants such as the perforant (6) or giant (7) variants have also been described in the form of MP (8). Ossification in pilomatricoma is not such a rare event since it can be observed in up to 15% to 20% of cases (9).

MP have been associated to myotonic dystrophy (5,10-13), Churg-Strauss and Rubinstein-Taybi syndrome (14,15), spina bifida (16), sternal cleft and mild coagulative defect (17), trisomy 9 (18), or celiac disease (1).

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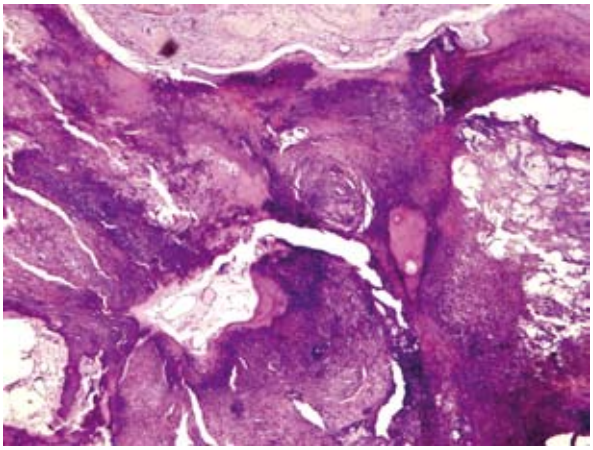

Figure 1. Histologic image of classic seminoma diagnosed in the patient 15 months before the current diagnosis of multiple pilomatricoma (hematoxylin-eosin, X40).

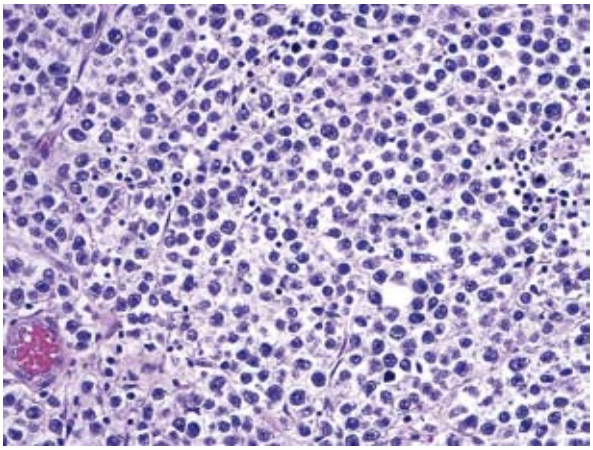

Figure 2. Image of one of the pilomatricomas in the patient, showing classic shadow cells and focal ossification (hematoxylin-eosin, X2.5).

The question is whether so much attention in the literature is due to any specific association between PM and any of these diseases, or it is, on the contrary, just the result of mere coincidences.

Although the reason why some patients develop MP is unknown, some argue that mutations in beta-catenin may explain at least some cases (3). Earlier, some authors found that pilomatricoma (not necessarily MP) was associated with alterations in the beta-catenin gene (19,20). Different mutations have been described. The most constant one seems to be that of the CTNNB1 gene, which appears in up to 100% of cases in some series (20). A heterozygote missense mutation at codon 32 (D32Y) has been a common finding to a lower percentage of pilomatricomas in some series (20,21).

One of the targets of the beta-catenin pathway is the gene that encodes c-MYC, which ultimately relates the whole pathway to adenomatous polyposis coli. Curiously, multiple pilomatricomas have been occasionally associated to Gardner syndrome (22). Other coincidences between MP and other diseases that have been described in the literature could also perhaps be related in the future to beta-catenin alterations. For instance, beta-catenin has been demonstrated to be reduced in celiac disease (23). Moreover, the Wnt pathway (which is closely related to the beta-catenin function) can be altered by valproic acid, causing spina bifida (24). On the other hand, it has been demonstrated that a mutation in cysteine protease calpain 3 (CAPN3) can cause muscle dystrophy (25), and CAPN3 controls the membrane expression of beta-catenin (25).

Coincidentally, beta-catenin is also altered in seminoma. Whereas testicular carcinoma in situ and intratubular germ cell neoplasia express beta-catenin, the latter is absent in seminoma in some studies (26). Other groups, nevertheless, found expression of beta-catenin in a significant percentage of the seminomas studied (27); however, following what is usually found in pilomatricomas, the immunoexpression of the protein is seen in cases of the gene mutation (21), owing to the abnormality of beta-catenin degradation (28,29).

All this might turn in the future, many of the associations described in the literature between MP and other conditions, including the current case, from mere coincidences into pathogenically related processes.

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