Granulomatous Response due to Anabolic Steroid Injections

Angel Fernandez-Flores[1,2], Saul Valerdiz[2], Luis G. Crespo[3], Ramon Rodriguez[3]

[1]Service of Cellular Pathology, Clinica Ponferrada; [2]Service of Anatomic Pathology, [3]Service of General Surgery, Hospital El Bierzo, Ponferrada, Spain

Corresponding author:

Angel Fernandez-Flores, MD, PhD

S. Patología Celular, Clinica Ponferrada

Avenida Galicia 1

24400 Ponferrada, Spain

gpyauflowerlion@terra.es

Received: June 21, 2010

Accepted: April 8, 2011

SUMMARY Injected corticosteroids can sometimes lead to a granulomatous reaction. This is apparently also true for anabolic steroids, which are often used by bodybuilders, although we have not found any histologic report on such a phenomenon. We report a case of a granulomatous reaction in a 30-year-old male bodybuilder having undergone anabolic steroid injections. Foreign bodies typical of steroids were found, together with areas of calcification and ossification with lamellar bone. Multivacuolated macrophages were found in the fibrous tissue close to these areas of calcification and ossification.

KEY WORDS: steroids, anabolic, silicone, triamcinolone, foreign body, granuloma, cutaneous fillers

INTRODUCTION

Corticosteroid injections can give rise to secondary effects including cutaneous and subcutaneous granulomas. Anabolic steroids are a specific type of corticoids that are often injected by bodybuilders to increase their muscular mass. Although 'oil granuloma' is a well-known secondary effect of anabolic steroid injection, we have not found any report on morphological changes seen in granulomatous reaction to anabolic steroid injection.

CASE REPORT

A 30-year-old male presented to the Service of General Surgery complaining of several subcutaneous nodules. The examination showed several tumors on the breasts, trunk, arms and thighs. The superjacent skin was of normal color (Fig. 1, left). The tumors were hard and most were more easily identified when palpated (Fig. 1, right). The largest tumor (left arm) was 12 cm in diameter.

The patient said that he commonly practiced several sports that also included weightlifting. Ten years before, his trainers had given him intramuscular injections of anabolic steroids and he had also injected himself with similar substances including Dimetabol®, Testogan®, Winstrol®, Sustanon®, and Ganabol®.

For aesthetic reasons, the patient wanted removal of two nodules from the trunk. Two biopsies, one from each side (4 cm in diameter each), were sent to the Service of Anatomic Pathology. Morphological studies revealed the nodules to consist primarily of a fibrotic reaction with many calcified foci (Fig. 2, top left). The fibrotic areas contained many round empty spaces, as well as other acicular empty spaces (Fig. 2, bottom left). Many multivacuolated macrophages were also seen (Fig. 2, top right). In some areas, the vacuolated macrophages were in close proximity to the calcified and ossified areas (Fig. 2, bottom right). Some of the macrophages contained a refractile material that was not birefringent under polarized light (Fig. 3, top left). In some areas, the calcified foci were continuous with the ossified foci (Fig. 3, top right), with lamellar bone and fatty medulla without hematopoiesis (Fig. 3, bot-

Acta Dermatovenerol Croat
2011;19(2):103-106

Figure 1. One of the tumors evident in the patient (right thigh). The tumor was covered by skin of normal appearance and it was better palpated than seen.

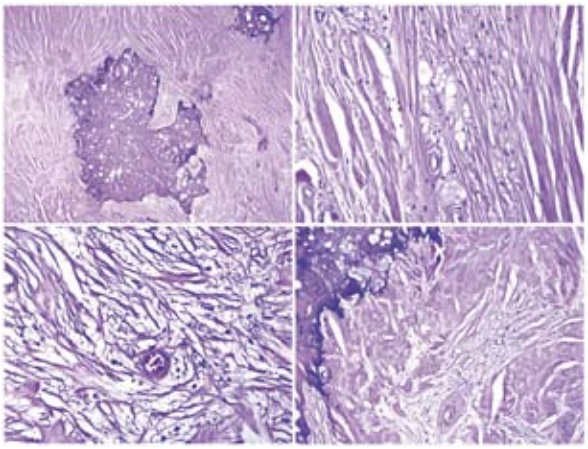

Figure 2. Top left: calcified foci in the areas of fibrosis. Top right: macrophages with vacuolar cytoplasm. In the collagen, some round empty spaces are also seen, as well as acicular spaces (bottom left). Bottom right: some of the macrophages were in close proximity to areas of calcification and ossification. HE; top left x2; top right x10; bottom left x20; bottom right x4.

tom left). Another type of foreign body, lobulated and with peripheral giant-cell reaction, was also seen (Fig. 3, bottom right). The largest of these particles was 0.625 mm in diameter and appeared similar to ones previously described after injection of triamcinolone (1). Under high power magnification, this material showed a multivesicular appearance (Fig. 4, top left). No histochemical staining was seen with orcein, Masson's trichrome, Ziehl-Neelsen, or Congo red. Periodic acid-Schiff (PAS) staining was positive in the multinucleated cells surrounding the particles, as well as in the material itself, with a globular pattern,

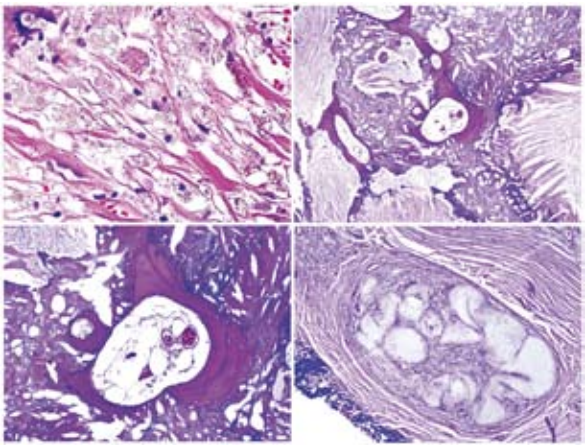

Figure 3. Top left: in some foci, the macrophages contained retractile cytoplasmic granules. Top right: areas of ossification were found, with lamellar bone as well as fat marrow without hematopoiesis (bottom left). Bottom right: pale multilobulated and vesiculated foreign bodies were also seen. HE; top left x20; top right x10; bottom left x20; bottom right x4.

and this positivity persisted even after diastase digestion (Fig. 4, top right). The same pattern was obtained with alcian blue pH 2.5 (Fig. 4, bottom left) and with colloidal iron (Fig. 4, bottom right). The inflammatory response, other than the presence of histiocytes, was mild and consisted mainly of a number of perivascular groups of lymphocytes.

Definitive diagnosis was a response to foreign body injection, consistent with steroids.

DISCUSSION

The injection of corticosteroids (commonly triamcinolone acetonide) is used for the treatment of many dermatologic diseases, such as scars, keloids, and others (2). This treatment is not free of side effects, which can include depigmentation, morphea-like changes (3), or even amaurosis (4). Several reports have also acknowledged a granulomatous response following the injection of corticosteroids (2,5-9). The aspect of this response is varied: it can mimic a rheumatoid nodule, vacuolated material surrounded by histiocytes (5,6), foreign body giant-cell reaction surrounding the basophilic (or eosinophilic) amorphous material (1,8), or histiocytes surrounding abundant extracellular lipid deposits (2). The histiocytes have been described as having a bubbly appearance (5).

The morphological features evidenced as secondary to corticosteroid injection have sometimes been described as mucin-like changes (5). This description is due to the histochemical staining of the substance

Acta Dermatovenerol Croat
2011;19(2):103-106

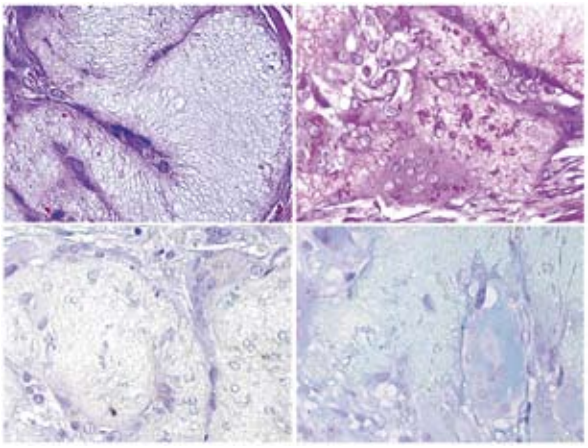

Figure 4. The vesicular features of the foreign bodies were better seen at high power (top left). The vesicles were positive with periodic acid-Schiff (PAS) (top right), alcian blue pH 2.5 (bottom left), and colloidal iron (bottom right). Positive vesicles were also seen in the cytoplasm of the macrophages (right, top and bottom). HE; top left x10; top right x20; bottom left x20; bottom right x20.

with alcian blue at pH 2.5 and to a moderate PAS-positivity (5). Not all studies have reported these properties (1,8). Our case showed indications of mucin-like histochemical properties in the cytoplasm of the macrophages, as well as in the substance itself. This granular amorphous material has been suggested to be the suspension medium rather than the corticoid itself (5,8), and the suspending vehicle may be the material that has some characteristics of acid mucopolysaccharides (10). Some have even suggested that the injected substance undergoes *in vivo* modifications (5). Our findings are in agreement with this type of claim, since the macrophages seem to be clearing the mucinous material.

Some previous studies have noted that the various microscopic features of the granulomatous response to corticosteroids do not significantly vary with the type of drug, dosage, technique of injection, anatomic sites, or intervals between injections (8). On the other hand, other studies found a number of morphological variations that depend on the type of corticosteroid injected (6).

Anabolic steroids are synthetic chemical derivatives of testosterone (11). They are sometimes used by bodybuilders to increase their muscular mass. Various surveys have estimated that 9% to 40% of regular gymnasium attendees use anabolic steroids (12-14). Adverse effects of repeated injections of anabolic steroids include fibrosis, dystrophic calcification, and oil granulomas at the injection sites. Nevertheless, we have not found any report on morphological changes on the granulomatous reaction due to anabolic steroids. Neither have we found any case of secondary ossification as part of the response, even though, as some have remarked, virtually any process that calcifies may secondarily ossify (15). Reports on secondary ossification with other foreign substances, such as silicone, are more common (16). There is an interesting case of a bodybuilder having developed a calcified gluteal mass due to the injection of anabolic steroids; however, the authors explain that the calcification was the result of repeated traumatic injuries to the muscle (11). In this respect, it is interesting how, in our case, immediate transition from the vacuolated histiocytes to the calcified and ossified areas could be found.

Another type of substance that has been reportedly injected by body-builders is sesame seed oil, resulting in one case in calcification (17). This aspect, nevertheless, was different from the current case, as it was characterized by a cystic lesion encapsulating the oily material and by fibrous membranes with foreign body reaction (17).

In addition to the histiocytic infiltrate, our case also showed a mild infiltrate of lymphocytes. This fact (the paucity of inflammatory cells) has also been noted in other studies (2). In some areas, the granulomatous response seen in the present case mimicked a similar response that has been described in aluminum granuloma (18), which may have arisen due to an aluminum component in the injections used.

CONCLUSION

However, although many morphological patterns can be associated with aluminum granuloma, ossification would seem to be an uncommon one.

Acknowledgment. We thank Dr Luis Requena, PhD (Fundación Jiménez Díaz, Madrid, Spain) for his diagnostic advice.

References

1. Kaur S, Amanjeet, Thami GP, Mohan H. Intralesional steroid induced histological changes in the skin. Indian J Dermatol Venereol Leprol 2003;69:232-34.
2. Joshi R. Incidental finding of skin deposits of corticosteroids without associated granulomatous inflammation: report of three cases. Indian J Dermatol Venereol Leprol 2008;74:44-6.
3. Holt PJ, Marks R, Waddington E. 'Pseudomorphoea': a side effect of subcutaneous corticosteroid injection. Br J Dermatol 1975;92:689-91.
4. Baran RL. Untoward reaction to injections of insoluble corticosteroids. Arch Dermatol 1974;110:465.

5. Santa Cruz DJ, Ulbright TM. Mucin-like changes in keloids. Am J Clin Pathol 1981;75:18-22.
6. Weedon D, Gutteridge BH, Hockly RG, Emmett AJ. Unusual cutaneous reactions to injections of corticosteroids. Am J Dermatopathol 1982;4:199-203.
7. Bhawan J. Steroid-induced 'granulomas' in hypertrophic scar. Acta Derm Venereol 1983;63:560-3.
8. Balogh K. The histologic appearance of corticosteroid injection sites. Arch Pathol Lab Med 1986;110:1168-72.
9. Thomas EL. Potential complication from injection of corticosteroids. Ophthalmic Surg 1987;18:154.
10. Kelly EW Jr. The effects of triamcinolone on human skin. J Natl Med Assoc 1963;55:510-4.
11. Al-Ismail K, Torreggiani WC, Munk PL, Nicolaou S. Gluteal mass in a bodybuilder: radiological depiction of a complication of anabolic steroid use. Eur Radiol 2002;12:1366-9.
12. Perry HM, Wright D, Littlepage BN. Dying to be big: a review of anabolic steroid use. Br J Sports Med 1992;26:259-61.
13. Korkia P. Use of anabolic steroids has been reported by 9% of men attending gymnasiums. BMJ 1996;313:1009.
14. Bolding G, Sherr L, Elford J. Use of anabolic steroids and associated health risks among gay men attending London gyms. Addiction 2002;97:195-203.
15. Walsh JS, Fairley JA. Calcifying disorders of the skin. J Am Acad Dermatol 1995;33(5 Pt 1):693-710.
16. Fodor J, Udvarhelyi N, Gulyas G, Kasler M. Ossifying calcification of breast implant capsule. Plast Reconstr Surg 2004;113:1880-2.
17. Darsow U, Bruckbauer H, Worret WI, Hofmann H, Ring J. Subcutaneous oleomas induced by self-injection of sesame seed oil for muscle augmentation. J Am Acad Dermatol 2000;42(2 Pt 1):292-4.
18. Chong H, Brady K, Metze D, Calonje E. Persistent nodules at injection sites (aluminium granuloma) – clinicopathological study of 14 cases with a diverse range of histological reaction patterns. Histopathology 2006;48:182-8.

Orizol cream - for removing sunspots; year 1929.
(From the collection of Mr. Zlatko Puntijar)