Int J Legal Med (1998) 111 : 261–264

CASE REPORT

R. Hausmann · S. Hammer · P. Betz

Performance enhancing drugs (doping agents) and sudden death – a case report and review of the literature

Received: 4 November 1997 / Received in revised form: 3 March 1998

Abstract The case of sudden cardiac death of a 23-year-old body builder who used anabolic steroids combined with other performance enhancing drugs is reported. Postmortem investigations revealed cardiac hypertrophy, acute cellular necrosis and interstitial fibrosis of the myocardium. The side-effects and interactions of the substances used are discussed.

Key words Anabolic steroids · Multi-drug abuse · Body building · Sudden cardiac death

Introduction

Anabolic-androgenic steroid abuse is widespread among athletes in sports requiring increased strength, body weight and cardiovascular fitness [33, 50, 51]. The real incidence is hard to evaluate but results of the National Household Survey on Drug Abuse indicated that more than 1,000,000 Americans are current or former users [58, 59]. In Germany, the estimated number of juvenile users is about 100,000 [42]. Body builders reportedly use up to 4-10 times the recommended medical dose of such agents, often in combination with other stimulants and diuretics. Drug abuse in sports may be supported by underground books and magazines [4, 6, 12, 13, 22, 46] offering assistance in obtaining and administration of the drugs. Since unexpected death can occur due to different effects of the substances used [7, 10, 14, 17, 24, 27, 28, 34, 35, 38] the growing incidence of steroid use in athletes is also of interest for the forensic pathologist.

In the literature there are several studies reporting sudden cardiac death especially due to acute myocardial infarction following the use of anabolic steroids. However, death can also be explained by other effects especially if other substances are used simultaneously.

We describe the case of a 23-year-old man who had used anabolic steroids in combination with other stimulating agents according to the protocols recommended in underground literature [22, 46] and died of acute cardiac arrest without previous symptoms. The complex pathophysiological interactions and side effects of the different substances apparently responsible for the fatal outcome are discussed.

R. Hausmann (✉) · S. Hammer · P. Betz
Department of Forensic Medicine,
University of Erlangen-Nuremberg, Universitätsstrasse 22,
D-91054 Erlangen, Germany

Case report

In order to support his intensive training a 23-year-old body builder had taken an unknown amount of anabolic steroids combined with many other performance-enhancing drugs over a period of about 9 months. After visiting a dancing club he went to bed at 4 a.m. and 6 h later he was found unconscious and the resuscitation started by an emergency physician was not successful. The following drugs were found in the appartment:

1. Testex Leo 250 prolongatum i.m. (testosterone cyclopentilpropionate)
2. Primobolan Depot 100 mg i.m. (methenolone enantate)
3. Proviron 25 mg tablets (mesterolone)
4. Thybon 100 μg tablets (liothyronin hydrochloride)
5. Aldactone 100 mg tablets (spironolactone)
6. Clomifen 25 mg capsules
7. Contraspasmin 0.02 mg tablets (clenbuterol hydrochloride)

These substances are usually used by body builders for the following reasons:

Testex Leo and Primobolan are synthetic derivates of testosterone with both androgenic and anabolic effects.

Proviron is an anabolic steroid which does not inhibit gonadotropine secretion and thus prohibiting gynecomastia.

The thyroid hormone (T3) Thybon possesses cardiac stimulating and fat reducing effects.

Spironolactone is an aldosterone antagonist and prevents potassium loss. It is used for reducing the subcutaneous water content and in order to prevent potassium deficiency.

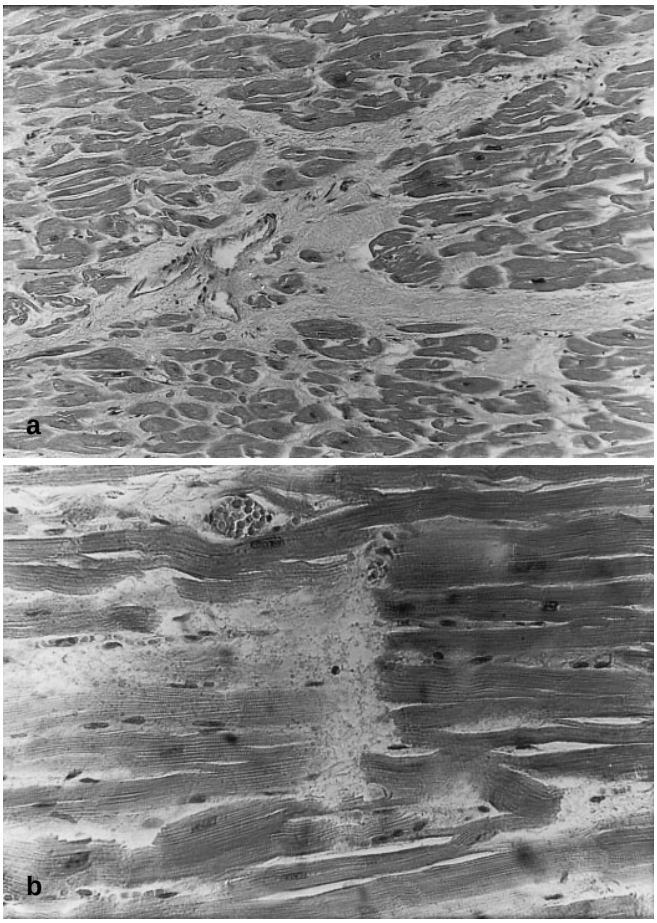

Fig. 1 Left ventricular myocardium of a 23-year-old body builder (H & E) with (a) interstitial fibrosis (190 ×) and (b) dehiscense of intercalated discs (480 ×)

Clomifen is thought to increase gonadotropin levels which are suppressed by high doses of androgenic steroids and thyroid hormones.

Contraspasmin has both β1 (cardiac stimulation) and β2 (anabolic) effects [8, 15, 39, 45, 47–49].

Autopsy findings

Body weight 94 kg, size 192 cm, muscular build. The autopsy revealed cardiac hypertrophy (heart weight 500 g), the right ventricle was dilated, the endocardium showed focal induration. The liver parenchyma was soft and fragile. Cerebral edema, acute vascular congestion in liver, spleen and kidneys were found.

Histological findings

The heart muscle showed an enlargement and nuclear polymorphism of the left ventricular muscle fibres. Furthermore disseminated focal necrosis with loss of nuclear staining, dehiscences of intercalated discs and an interstitial fibrosis (Fig. 1) were obvious. Capillary hyperemia, platelet aggregations and several fibrinous clots were found in the lungs, liver and kidneys. The liver epithelia showed nuclear fat-free vacuoles. Several small cystic blood-filled pools were scattered throughout the liver parenchyma, partly lined with epithelium (peliosis hepatis, Fig. 2).

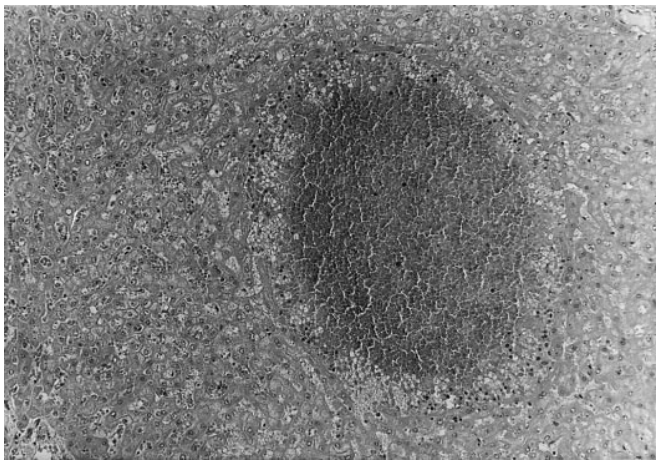

Fig. 2 Peliosis hepatis with several small, blood-filled pools in the liver parenchyma (H & E, 190 ×)

Postmortem laboratory findings

Urine was analysed for anabolic steroids and narcotics by enzyme immunoassay (EIA) and gas chromatography-mass spectrometry (GC-MS) after derivatisation (TMS = Trimethylsilyl). Significant concentrations of substances with effects on the central nervous system could not be found, but mesterolone, methandienone (anabolic steroid, syn.: methandrostenolone), testosterone, nandrolone (anabolic steroid) and clenbuterol were detected in the urine. The ratio of testosterone to epitestosterone in urine was 64:1 (IDAS, Doping Laboratory, Kreischa) and such abnormally high ratios are generally considered by the International Olympic Comittee (IOC) and other sports federations as proof of exogenous testosterone administration [25].

Discussion

There exist several reviews of the literature dealing with the abuse effects of anabolic-androgenic steroids (AAS) on various organ systems [23, 25, 30, 32, 36, 40, 56]. Myocardial infarction [11], sudden arrhythmic death and stroke [19] have been described in young steroid abusers. The first documented steroid-related cardiac death was reported by McNutt et al. in 1988 [38] and further cases associated with hyperlipidemia [21] or thrombotic occlusion of coronary arteries [16, 24] have been described. Myocardial infarction has also been reported in a weight lifter who used aspirin and testosterone simultaneously [17].

The effects of anabolic-androgenic steroids could be demonstrated both in studies on primary myocardial cell cultures [41] and in experimental animals [5, 29, 55]. In addition, quantitative electron microscopy showed an enlargement of the sarcoplasmatic space and a disbalance of the mitochondrial/myofibrillar ratio. When the administration of anabolic steroids and training were combined, some pathological alterations such as destruction of mitochondria and aberrant myofibrils, focal dehiscent intercalated discs and necrotic cells [3] or mitochondrial disruption and a decrease in myocyte capillary supply [53] have been found. There is also evidence of an increased collagen production in experimental animals given steroids [55].

Structural alterations to the heart have also been observed in humans. Luke reported the case of a 21-year-old, previously healthy, steroid-abusing weight lifter who died of cardiac arrest [34]. In addition to renal hypertrophy and hepatosplenomegaly, biventricular hypertrophy could be detected. The myocardium showed extensive fibrosis, small foci of necrosis and myocytes with contraction band necrosis. Further cases with widespread patchy fibrosis have been described by Kennedy [27] and Lynberg [35]. The myocardial fibrosis was thought to be caused by a lack of blood supply in a hypertrophic myocardium [26]. Melchert and Welder suggested four hypothetical models of AAS-induced adverse cardiovascular effects: an androgenic, thrombosis, vasospasm and a direct myocardial injury model [40]. In addition to steroid-related disorders of the cardiovascular system, liver diseases such as peliosis hepatis, cholestasis and hepatic tumors have been observed in steroid-abusing athletes [2, 9, 20, 44, 57]. The histomorphological findings of small cystic, blood-filled pools in the liver parenchyma in our case correspond to the diagnosis of peliosis hepatis and can be regarded as a further morphological evidence of steroid abuse. In accordance to the AAS-associated morphological alterations described in the literature, we found cardiac hypertrophy, an interstitial fibrosis and disseminated focal necrosis of the myocardium. Coronary stenoses due to arteriosclerosis, coronary thrombosis or dysplasia [60] which could have caused the myocardial alterations were not observed. Furthermore there was no evidence of cocain abuse which has also been discussed in connection with myocardial necrosis [18]. The histologically detectable dense aggregations of red blood cells and capillary fibrinous clots may be explained by erythropoietin stimulation by AAS [1], clomifen-induced platelet aggregation [16, 40, 52] or the diuretic effects of spironolactone.

Since the macroscopical and histological findings revealed no other relevant pathological alterations, a sudden cardiac arrest must be assumed to be cause of death. For an explanation the different effects of the enhancing drugs are of particular interest:

1. anabolics were found to cause a deep prolonged depression of the stimulation threshold of the human heart [54].

2. AAS, mesterolone and clomifen may elevate the levels of sodium, potassium, calcium and phosphate [43] and thereby increase the risk of atrial and ventricular fibrillation.

3. Clenbuterol accelerates the heart rate by β1- and β2-receptor stimulation [8, 15, 31, 37, 39, 47–49], thus raising the cardiac oxygen demand in combination with the effects of trijodthyronine (stimulation of contractility, elevation of cardiac output, heart rate).

The various effects of these substances on cardiac function itself and on electrolytic concentrations also influencing the cardiac system, can explain death due to sudden myocardial dysfunction on the basis of AAS-associated alterations of the myocardium.

Acknowledgements We thank Dr. D. Thieme and J. Grosse (IDAS, Doping Laboratory, Kreischa) for performing the chemical analysis.

References

1. Alen M (1985) Androgenic steroid effects on liver and red cells. Br J Sports Med 19:15–20
2. Antunes CMF, Stolley PD (1977) Cancer induction by exogenous hormones: possible androgen-induced cancer. Cancer 39: 1896–1898
3. Appel HJ, Heller-Umpfenbach B, Feraudi M, Weicker H (1983) Ultrastructural and morphometric investigations on the effects of training and administration of anabolic steroids on the myocardium of guinea pigs. Int J Sports Med 4:268–274
4. Bachmann M (1996) Clenbuterol – Das Mittel der Zukunft, 6. Auflage, Sportverlag Ingenohl, Heilbronn, pp 1993–1996
5. Behrendt H, Boffin H (1977) Myocardial cell lesions caused by an anabolic hormone. Cell Tissue Res 181:423–426
6. Blast from the past! Diuretics – bodybuilding's most dangerous drugs! (1996) Muscle Media 2000, 48:112–115
7. Bowmann SJ (1989) Anabolic steroids and infarction. BMJ 299:632
8. Choo JJ, Horan MA, Little RA, Rothwell NJ (1992) Anabolic effects of clenbuterol on skeletal muscle are mediated by β2-adrenoceptor activation. Am J Physiol 263:E50–E56
9. Creagh TM, Rubin A, Evans DJ (1988) Hepatic tumors induced by anabolic steroids in an athlete. J Clin Pathol 41(4): 441–443
10. Delbeke FT, Desmet N, Debackere M (1995) The abuse of doping agents in competing body builders in Flanders (1988–1993). Int J Sports Med 16:66–70
11. Dickhuth HH, Berg A, Baumstark M, Rokitzki L, Huonker M, Keul J (1989) Doping – auch ein allgemeinmedizinisches Problem. Fortschr Med 107:585–588
12. Duchaine D (1992) Underground steroid handbook (II) Update: 1992. HLR technical books, Venice
13. Duchaine D (1996) Underground bodyopus-militant weight loss & recomposition. XIPE Press, Carson City
14. DuRant RH, Escobedo LG, Heath GW (l995) Anabolic steroid use, strength training and multiple drug use among adolescents in the United States. Pediatrics 96:23–28
15. Emery PW, Rothwell NJ, Stock MT, Winter PD (1984) Chronic effects of β2-adrenoceptor agonists on body composition and protein synthesis in the rat. Biosci Rep 4:83–91
16. Ferenchick GS (1992) Anabolic/androgenic staoid abuse and thrombosis – is there a connection? Med Hypotheses 35:27–31
17. Faenchick GS, Adelman S (1992) Myocardial infarction associated with anabolic steroid use in a previously healthy 37-year-old weight lifter. Am Heart J 124:507–508
18. Fineschi V, Wetli CV, Di Paolo M, Baroldi G (1997) Myocardial necrosis and cocain – a quantitative morphologic study in 26 cocaine-associated deaths. Int J Legal Med 110:193–198
19. Frankle MA, Eichbag R, Zachariah SB (1988) Anabolic androgenic steroids and a stroke in an athlete: case report. Arch Phys Med Rehab 8:632–633
20. Goldmann B (1985) Liver carcinoma in an athlete taking anabolic steroids. J Am Osteopath Assoc 85:56
21. Graham S, Kennedy M (l990) Recent developments in the toxicology of anabolic steroids. Drug Saf 5:458–476
22. Grundig P, Bachmann M (1994) Anabole Steroide. Sportverlag Ingenohl, Heilbronn
23. Hartgens F, Kuipers H, Wijnen JAG, Keizer HA (1996) Body composition, cardiovascular risk factors and liver function in long term androgenic-anabolic steroids using bodybuilders three months after drug withdrawal. Int J Sports Med 17:429–433
24. Huie MJ (1994) An acute myocardial infarction occurring in an anabolic steroid user. Med Sci Sports Exac 26:408–413

25. Karch SB (ed) (1996) Anabolic steroids. In: The pathology of drug abuse. CRC Press, Boca Raton New York London Tokyo, pp 407–429
26. Karch SB, Billingham M (1986) Myocardial contraction bands revisited. Hum Pathol 17:9–13
27. Kennedy C (1993) Myocardial infarction in association with misuse of anabolic steroids. Ulster Med J 62:172–174
28. Kennedy MC, Lawrence C (1993) Anabolic steroid abuse and cardiac death. Med J Aust 158:346–348
29. Kinson G, Lyberry R, Herbert B (1991) Influences of anabolic androgens on cardiac growth and metabolism in the rat. Can J Physiol Pharmacol 69:1698–1704
30. Kuipers H, Wijnen JAG, Hartgens F, Willems SMM (1991) Influence of anabolic steroids on body composition, blood pressure, lipid profile and liver functions in body builders. Int J Sports Med 12:413–418
31. Kurz H (1986) Sympathomimetika. In: Ammon HPT (ed) Arzneimittelneben- und Wechselwirkungen. Wissenschaftliche Verlagsgesellschaft, Stuttgart, pp 115–127
32. Lenders JWM, Demacker PMN, Vos JA, Jansen PLM, Hoitsma AJ, van't Laar A, Thien T (1988) Deleterious effects of anabolic steroids on serum lipoproteins, blood pressure, and liver function in amateur body builders. Int J Sports Med 91: 19–23
33. Liang MTC, Paulson DJ, Kopp SJ, Glonek T, Meneses P, Gierke LW, Schwartz FN (1993) Effects of anabolic steroids and endurance exercise on cardiac performance. Int J Sports Med 14:324–329
34. Luke JL, Farb A, Virmani R, Sample RH (1990) Sudden cardiac death during exercise in a weight lifter using anabolic androgenic steroids: pathological and toxicological findings. J Forensic Sci 35:1441–1447
35. Lynberg K (1991) Myocardial infarction and death of a body builder after using anabolic steroids. Ugeskr Laeger 153:587–588
36. Madea B, Grellner W (1996) Langzeitfolgen und Todesfälle bei Anabolikaabusus. Rechtsmedizin 6:33–38
37. McLeman PA, Edwards RHT (1989) Effects of clenbuterol and propanolol on muscle mass: evidence that clenbuterol stimulates muscle β-adrenoceptors to induce hypertrophy. Biochem J 264:575–579
38. McNutt RA, Ferenchick GS, Kirlin PC, Hamlin NJ (1988) Acute myocardial infarction in a 22-year-old worldclass weight lifter using anabolic steroids. Am J Cardiol 62:164
39. McRae JC, Skene PA, Connell A, Buchan V, Lobley GE (1988) The action of β-agonist clenbuterol on protein and energy metabolism in fattening wheter lambs. Br J Nutr 9:457–465
40. Melchert RB, Welder AA (1995) Cardiovascular effects of androgenic-anabolic steroids. Med Sci Sports Exerc 27:1252–1262
41. Melchert RB, Herron TJ, Welda AA (1992) The effect of anabolic-androgenic steroids on primary myocardial cell cultures. Med Sci Sports Exerc 24:206–212
42. Musshoff F, Daldrup T, Ritsch M (1997) Anabole Steroide auf dem deutschen Schwarzmarkt. Arch Kriminol 199:153–158
43. Neumann F, Schenck B (1987) Pharmakotherapie mit Hormonen. In: Forth W, Henschler D, Rummel W (eds) Pharmakologie und Toxikologie. Bibliographisches Institut & F. A. Brockhaus, Mannheim Wien Zürich, pp 396–423
44. Overly WL, Dankhoff JA, Wang BK, Singh VD (1984) Androgens and hepatocellular carcinoma in an athlete. Ann Int Med 100:158–159
45. Palm D, Hellenbrecht D, Quiring K (1987) Pharmakologie des noradrenergen und adrenergen Systems. In: Forth W, Henschler D, Rummel W (eds) Pharmakologie und Toxikologie. Bibliographisches Institut & F. A. Brockhaus, Mannheim Wien Zürich, pp 124–168
46. Philipps WN (1991) Anabolic reference guide (Sixth Issue). Mile High Publishing, Golden
47. Reeds PJ, Hay SM, Doward PM, Palmer RM (1988) The effect of β-agonists and antagonists on muscle growth and body composition of young rats. Comp Biochem Physiol 89:337–341
48. Rothwell NJ, Stock MJ (1985) Modification of body composition by clenbuterol in normal and dystrophic mice. Biosci Rep 5:755–760
49. Rothwell NJ, Stock MJ (1987) Effect of a selective β2-adrenergic agonist (clenbuterol) on energy balance and body composition in normal and protein deficient rats. Biosci Rep 7:933–940
50. Sachtleben TR, Berg KE, Elias BA, Cheatham JP, Felix GL, Hofschire PJ (1993) The effects of anabolic steroids on myocardial structure and cardiovascular fitness. Med Sci Sports Exerc 25:1240–1245
51. Salke RC, Rowland TW, Burke EJ (I985) Left ventricular size and function in body builders using anabolic steroids. Med Sci Sports Exerc 17:701–704
52. Sano T, Motomiya T, Tamazaki H (1983) Influence of lipids on platelet activation in vivo. Thromb Res 31:675–684
53. Soares J, Duarte J (1991) Effects of training and an anabolic steroid on murine red skeletal muscle – a stereological analysis. Acta Anat (Basel) 142:183–187
54. Svorcik C, Bicikova L (1978) Effects of drugs on the stimulation threshold of the human heart. Cor Vasa 20:184–195
55. Takala T, Ramo P, Kiviluoma K (1991) Effects of training and anabolic steroids on collagen synthesis in dog heart. Eur J Appl Physiol 62:1–6
56. Tseng Y, Rockhold R, Hoskins B (1994) Cardiovascular toxicities of nandrolone and cocaine in spontaneously hypertensive rats. Fund Appl Toxicol 22:113–122
57. Westaby D, Ogle SJ, Paradinas FJ, Randell JB, Murray-Lyo IM (1977) Liver damage from long-term methyl-testosterone. Lancet 261:263
58. Yesalis C, Anderson W, Buckley W, Wright J (1990) Incidence of the non-medical use of anabolic-androgenic steroids. In: Anabolic steroid abuse. National Institute on Drug Abuse, Rockville, pp 97–112
59. Yesalis C, Kennedy N, Kopstein A (1993) Anabolic-androgenic steroid use in the United States. JAMA 270:1217–1221
60. Zack F, Terpe H, Hammer U, Wegener R (1996) Fibromuscular dysplasia of coronary arteries as a rare cause of death. Int J Legal Med 108:215–218