Cancer Therapy & Oncology
International Journal
ISSN: 2473-554X

Juniper Publishers
key to the Researchers

Mini Review
Volume 15 Issue 5 - March 2020
DOI: 10.19080/CTOIJ.2020.15.555924

Cancer Ther Oncol Int J

Hormonal Manipulation in Men with Aggressive Fibromatosis (Desmoid Tumor)

Mérida-García Antonio*, Díaz-Serrano Asunción, Baldeón María Jesús, Álvarez José Valero, López Yolanda and De Portugal Teresa

Hospital Virgen de la Concha. Av. de Requejo 35, 49022 Zamora, Spain

Submission: February 20, 2020; **Published:** March 06, 2020

***Correspondence Author:** Antonio Mérida-García, Hospital Virgen de la Concha. Av. de Requejo 35, 49022 Zamora, Spain

Abstract

Desmoid tumors are most often developed by women. The role of hormones in these tumors is being studied. In this article, a review of the hormonal manipulation has been performed, focusing on the expression of androgen receptors and whether antiandrogen therapy could provide inhibitory effects on desmoid tumors, especially on men.

Introduction

Desmoid tumors, also called aggressive fibromatosis, are reported to account for 0.03% of all neoplasms [1]. These are developed by abnormal fibroblasts proliferation, originating from musculo-aponeurotic structures, most commonly seen in the anterior abdominal musculature. Desmoid tumors are usually well-differentiated, locally aggressive, non-metastatic tumors, which tend to infiltrate and compress surrounding structures. Most cases are sporadic, though there are some patients who develop these tumors within familial adenomatous polyposis (APC). The treatment of these tumors is based mainly on surgery and radiotherapy. Chemotherapy has not been properly explored due to two main reasons: control disease with local therapies, hormone therapy and/or NSAIDs, and low prevalence. To date, the hormone therapy consisted of antiestrogens. This article aims to discover the evidence on anti-androgen therapy by focusing on male patients.

Hormonotherapy in Desmoid Tumors

The incidence of desmoid tumors is higher in females than in males. Sex steroid hormones have been related to desmoid tumor development. It is known that oral estrogen therapy plays a role in its pathogenesis. During pregnancy tumor growth rate is higher and spontaneous regression have been described in menopausal and oophorectomized women [2,3]. Based on these facts, some single-arm trials and case reports using hormonal therapy have been published with favorable results [2-10]. The most frequently used drug was tomoxifen, but other hormonal agents have been found to be effective, such as toremifene, progesterone, medroxiprogesterone acetate, prednizolone, testolactone and gosereline. The most suitable endocrine manipulation, the optimal dose and the duration of the treatment remain unresolved. Clinical benefit with antiestrogen therapy in men has been described, however the limited sample size of the studies and the lack of randomized trials compromises the validity of the reported results.

Expression of Sex Steroid receptors in Desmoid Tumors

Expression of estrogen receptors (ER) has been reported in 25 to 75% of desmoid tumors (5,6,9–14). Some authors have also described progesterone receptors (PR) expression [5,6,9–14]. Ishizuka et al. examined androgen receptors (AR) expression profile in tissue samples from 27 patients with primary desmoid tumors (eight males and 19 females) [9]. ERα and ERβ immunochemistry expression was identified in 7.4% of cases, similarly for both sexes. PR expression was found in 25.9 and 33.3% for males and females, respectively. AR expression was detected on 52.9% of all desmoid tumors. No statistically significant correlation was described for sex and hormonal receptor immunoreactivity. For RT-PCR analysis, fresh frozen desmoid tissues were obtained from eight of the 27 patients (two males and six females). RT-PCR analysis demonstrated PR and AR expression in all cases. However, ERs messenger RNA (mRNA) was not detected by RT-PCR for any of them [9].

Androgen Receptors and the Role of Testosterone in Cellular Behavior

As we noted above, globally sporadic desmoid tumors are most frequent in women. However, it is not clear for APC. Smits et al. studied the desmoid tumor development in APC-mutant preclinical models and they reported a higher growth in male than in female during puberty. Therefore, it is concluded that the sex hormones are important in desmoid tumor development [15]. Recently, Hong et al. examined the role of testosterone in aggressive fibromatosis in both APC-mutant xenografts and human tumors by RT-PCR and Western Blot RNA analysis [16]. All 24 tissue samples expressed ARs, but a higher level of AR was described for males. Moreover, they tested tumor behavior in cell cultures from six human tumors (three from men and three from women) in androgen-free culture media and with different doses of dihydrotestosterone. An androgen dose-dependent increased in proliferation was observed, with higher rates in cultures from male patients. To confirm testosterone role in vivo, authors compared desmoid tumor growth in castrated and non-castrated APC-mutant mice. Tumor size and number of tumor nodules were reduced in castrated mice compared to non-castrated ones. Moreover, when testosterone was administered to castrated xenografts, desmoid tumor formation reached to be equal to non-castrated mice [16].

Conclusion

The AR expression in desmoid tumors has been demonstrated in both sexes, but it seems to be a higher expression in men. Preclinical data suggest that antiandrogen drugs may play a role in desmoid tumors treatment, therefore it should be explored in clinical setting. Responses to antiestrogens have already been described in men, so antiandrogen therapy may also be considered in both sexes. In our opinion, personalized therapy based on the specific sex steroid hormone receptor expression should be studied.

References

1. Kotiligam D, Lazar AJF, Pollock RE, Lev D (2008) Desmoid tumor: a disease opportune for molecular insights. Histol Histopathol 23(1): 117–126.
2. Bus PJ, Verspaget HW, van Krieken JH, de Roos A, Keizer HJ, et al. (1999) Treatment of mesenteric desmoid tumours with the anti-oestrogenic agent toremifene: case histories and an overview of the literature. Eur J Gastroenterol Hepatol 11(10): 1179–1183.
3. Fiore M, Colombo C, Radaelli S, Callegaro D, Palassini E, et al. (1990) Hormonal manipulation with toremifene in sporadic desmoid-type fibromatosis. Eur J Cancer Oxf Engl 51(18): 2800-2807.
4. Janinis J, Patriki M, Vini L, Aravantinos G, Whelan JS (2003) The pharmacological treatment of aggressive fibromatosis: a systematic review. Ann Oncol Off J Eur Soc Med Oncol 14(2): 181-190.
5. Tsukada K, Church JM, Jagelman DG, Fazio VW, McGannon E, et al. (1992) Noncytotoxic drug therapy for intra-abdominal desmoid tumor in patients with familial adenomatous polyposis. Dis Colon Rectum 35(1): 29-33.
6. Waddell WR (1975) Treatment of intra-abdominal and abdominal wall desmoid tumors with drugs that affect the metabolism of cyclic 3',5'-adenosine monophosphate. Ann Surg 181(3): 299-302.
7. Fong Y, Rosen PP, Brennan MF (1993) Multifocal desmoids. Surgery 114(5): 902-906.
8. Altomare DF, Rotelli MT, Rinaldi M, Bocale D, Lippolis C, et al. (2010) Potential role of the steroid receptor pattern in the response of inoperable intra-abdominal desmoid to toremifene after failure of tamoxifen therapy. Int J Colorectal Dis 25(6): 787-789.
9. Ishizuka M, Hatori M, Dohi O, Suzuki T, Miki Y, et al. (2006) Expression profiles of sex steroid receptors in desmoid tumors. Tohoku J Exp Med 210(3): 189-198.
10. Jadrijevic D, Mardones E, Lipschutz A (1956) Antifibromatogenic activity of 19-nor-alpha-ethinyltestosterone in the guinea pig. Proc Soc Exp Biol Med Soc Exp Biol Med N Y N 91(1): 38-39.
11. Alman BA, Goldberg MJ, Naber SP, Galanopoulous T, Antoniades HN, et al. (1992) Aggressive fibromatosis. J Pediatr Orthop 12(1): 1-10.
12. Serpell JW, Tang HS, Donnovan M (1999) Factors predicting local recurrence of desmoid tumours including proliferating cell nuclear antigen. Aust N Z J Surg 69(11): 782-789.
13. Lim CL, Walker MJ, Mehta RR, Das Gupta TK (1986) Estrogen and antiestrogen binding sites in desmoid tumors. Eur J Cancer Clin Oncol 22(5): 583-587.
14. Bruzzone S, Girardi S, Jadrijevic D, Lipschutz A, Mardones E (1956) Antifibromatogenic potency of 9alpha-fluoro derivatives of progesterone. Nature 178(4547): 1396-1397.
15. Smits R, Kielman MF, Breukel C, Zurcher C, Neufeld K, et al. (1999) Apc1638T: a mouse model delineating critical domains of the adenomatous polyposis coli protein involved in tumorigenesis and development. Genes Dev 13(10): 1309-1321.
16. Hong H, Nadesan P, Poon R, Alman BA (2011) Testosterone regulates cell proliferation in aggressive fibromatosis (desmoid tumour). Br J Cancer 104(9): 1452-1458.

How to cite this article: Mérida-García Antonio, Díaz-Serrano Asunción, Baldeón María Jesús, Álvarez José Valero, López Yolanda,et al. Hormonal Manipulation in Men with Aggressive Fibromatosis (Desmoid Tumor). Canc Therapy & Oncol Int J. 2020; 15(5): 555924.
DOI: 10.19080/CTOIJ.2020.15.555924.

DOI: 10.19080/CTOIJ.2020.15.555924

How to cite this article: Mérida-García Antonio, Díaz-Serrano Asunción, Baldeón María Jesús, Álvarez José Valero, López Yolanda,et al. Hormonal Manipulation in Men with Aggressive Fibromatosis (Desmoid Tumor). Canc Therapy & Oncol Int J. 2020; 15(5): 555924.
DOI: 10.19080/CTOIJ.2020.15.555924.