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Desmoid tumors – a characterization of patients seen at Mayo Clinic 1976–1999

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Abstract

Desmoid tumors occur with high frequency in individuals with Familial Adenomatous Polyposis (FAP). Because of this, individuals developing desmoid tumors may be referred for genetic risk assessment. Determining whether a person has a FAP-related desmoid tumor or a sporadic desmoid can be challenging. We sought to characterize the patients who were seen at our institution to determine if there were clinical differences in presentation between FAP-associated and sporadic desmoid tumors. We searched the Mayo Clinic-modified H-ICDA (Hospital adaptation of the International Classification of Diseases) diagnostic codes for all diagnoses of desmoid tumors in patients seen between 1976 and 1999. Charts were reviewed to determine accuracy of diagnosis, age when seen, gender, site of tumor, and presence of polyposis. A total of 454 patients (174 males and 280 females) met the search criterion. Of the 447 patients on whom all data was obtained, 70 had FAP and 377 had no evidence of FAP. The female/male ratio for FAP cases was 1.12 compared to female/male ratio of 1.71 for non-FAP cases. ($P = 0.17$). Location of development of desmoid tumors was correlated with but not specific for distinguishing FAP from non-FAP desmoids. Abdominal desmoids comprised the majority of FAP desmoids and extra-abdominal desmoids comprised the majority of non-FAP desmoids ($P < 0.001$) but age was not a discriminating factor. Using Bayesian analysis, we demonstrate how these findings can assist genetic professionals in their evaluation of patients with desmoid tumors by providing prior probabilities of FAP based upon clinical presentation.

Abbreviations: AFAP: attenuated familial adenomatous polyposis; *APC gene:* adenomatous polyposis coli gene; FAP: familial adenomatous polyposis; H-IDCA: Hospital adaptation of the International Classification of Diseases, adapted for the United States

Background

Desmoid tumors are locally aggressive but histologically benign neoplasms that are often classified as deep fibromatoses [1]. Despite their non-malignant classification, the common finding of local infiltration and risk of recurrence following excision leads to a significant increase in morbidity and mortality.

Desmoids can occur at the site of any fascia, but they commonly develop at the muscle. Multiple studies have shown that 37–50% occur in the abdominal region [2–5]. The shoulder girdle, chest wall and inguinal regions are the most prevalent extra-abdominal sites.

Sporadic desmoid tumors are very rare, estimated to occur in two to five persons per million per year. They account for approximately 0.03% of all neoplasms [6]. In contrast, desmoid tumors form in 3.5–32% of individuals with the autosomal dominant disorder, Familial Adenomatous Polyposis (FAP). Using an FAP desmoid risk of 32%, leads to up to a relative risk of 1067 compared to the general population [7–13].

Desmoids can be found at any age and have been documented from infancy to 67 years [14, 15]. There appears to be a higher incidence of desmoids diagnosed in women, particularly of reproductive age [2–4, 10, 11]. However, the magnitude of the female to male ratio is

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debated. The role of gender with respect to desmoid tumor development in the FAP population is also controversial.

Little has been written comparing the desmoids that arise in patients with FAP with those that arise apparently sporadically. Health professionals evaluating isolated cases of desmoid tumors in otherwise healthy appearing individuals face a challenge in determining prior probability of FAP, future disease potential and the need for further clinical evaluation or genetic testing. We were interested in determining if there were differences in the presentations of desmoid tumors with respect to gender, age, or tumor site that might help distinguish patients with desmoid tumors in FAP compared to non-FAP-associated desmoid tumors. We also were interested in understanding the proportion of desmoid tumors seen at this tertiary care institution that were FAP-related.

Methods

We searched the Mayo Clinic-modified H-ICDA (Hospital adaptation of the International Classification of Disease for the United States) diagnostic codes for all diagnoses of desmoid tumors in patients seen between 1976 and 1999. Charts were reviewed to determine the accuracy of diagnosis, age when first seen for desmoid consultation at Mayo Clinic, gender, site of tumor, and presence of polyposis or colon cancer in the patients or their relatives. We cannot be sure that some patients considered to have sporadic disease might not have had undiagnosed or undocumented FAP.

Results

A total of 454 patients comprising 174 males and 280 females met this search criterion. Seven patients (two males and five females) were excluded from analysis due to incomplete data or inability to categorize tumor location. Of the remaining 447 patients (172 males and 275 females), 70 had FAP (15.7%) and 377 had no evidence of FAP. The previously reported predominance of desmoids among women *versus* males was seen in our study population (61.5% *versus* 38.5%). Of the male cases, 19.2% had FAP compared to 13.5% of the female cases. Thus, the female/male ratio for FAP cases was 1.12 compared to the female/male ratio of 1.71 for non-FAP cases, suggesting a more equal distribution of desmoids among males and females with FAP. However, this finding was not statistically significant ($P = 0.17$). These data are summarized in Table 1.

Approximately 67% of the desmoids diagnosed in individuals with FAP were in the abdomen, whereas just 11% of the desmoids diagnosed in non-FAP patients were in the abdomen. In contrast, limb desmoids were diagnosed in 34.7% of non-FAP patients and just 1.4% of FAP patients. Overall, abdominal desmoids comprised the majority of FAP desmoids and extra-abdominal desmoids comprised the majority of non-FAP desmoids ($P < 0.001$) (Table 2).

The average ages of desmoid tumor consultation ranged from approximately age 34–40. There were no significant differences in ages between development of desmoids in FAP and non-FAP settings (Table 3).

Comments

We were interested to learn whether there might be clinical features that help distinguish desmoid tumors in FAP from the desmoid tumors that arise sporadically. Although statistically rare, determining the clinical differences between desmoids in these two settings would be of great benefit to genetic counselors and other health care providers. The results of this study indicate that the location of development of desmoid tumors is correlated with but not specific for distinguishing FAP from non-FAP desmoids ($P < 0.001$). Abdominal desmoid tumors comprised the majority of FAP desmoids (67%) and extra-abdominal desmoids comprised the majority of non-FAP desmoids (89%).

Multiple studies have found a higher incidence of desmoids diagnosed in women, particularly of reproductive age. The magnitude of the female to male ratio is debated and has not been adequately studied within the FAP population. Our study noted a female predominance of desmoid tumors for both FAP and non-FAP desmoids. The female/male ratio was closer to 1 in FAP than non-FAP patients (1.12 *versus* 1.71) but the difference was not significantly different ($P = 0.17$).

Individuals with FAP have an average age of colorectal cancer onset of 39 years, which is almost three decades younger than the average age of colorectal cancer in the general population. Given the significant increased risk of desmoids among individuals with FAP, we were interested in the age of desmoid tumor formation among this same population. We found that the age at presentation was not significantly different between desmoid tumors in patients with FAP *versus* those without FAP seen at Mayo Clinic.

Genetic testing for FAP is available clinically. Approximately 80–90% of classically affected individuals will be found to carry an alteration in the *APC* gene located on chromosome number 5. The majority

Table 1. Frequency of desmoid tumors in male and female patients stratified by FAP *versus* non-FAP status.

	Non-FAP (%)	FAP (%)	Total (%)
Females	238 (87)	37 (13.5)	275
Males	139 (73.8)	33 (19.2)	172
Total	377 (84.3)	70 (15.6)	447

Table 2. Frequency of site of desmoid tumor development in non-FAP and FAP patients stratified by site and gender.

	Abdominal (%)	Limb (%)	Trunk (%)	Total (%)
Female non-FAP	24 (10.1)	88 (37)	126 (53)	238
Male non-FAP	17 (12.2)	43 (30.9)	79 (56.8)	139
Total non-FAP	*41 (10.9)*	*131 (34.7)*	*205 (54.4)*	*377*
Female FAP	24 (64.9)	1 (2.7)	12 (32.4)	37
Male FAP	23 (69.7)	0 (0)	10 (30.3)	33
Total FAP	*47 (67.1)*	*1 (1.4)*	*22 (31.4)*	*70*

Table 3. Average age of diagnosis of desmoid tumors in non-FAP and FAP patients stratified by site and gender.

	Abdominal	Limb	Trunk	Average
Female non-FAP	35.8	31	30.4	33.8
Male non-FAP	38.4	30.9	39.4	36.6
Female FAP	42	34	39.4	37.6
Male FAP	39.4	na	40.3	40.3

of affected individuals have a family history of colorectal cancer and polyposis, thereby assisting in the diagnosis of FAP in a family. However, it has estimated that up to 33% of affected individuals have *de novo* mutations within the *APC* gene and thus, no family history. A positive genetic test can resolve the question of whether or not a person presenting with a desmoid tumor has a causative *APC* gene mutation but a negative test alone is not reassuring. Similarly, a colon exam showing multiple adenomas can resolve this question, but because of the variable age of development of adenomas, a negative exam, especially at younger ages, is also not reassuring.

The cases of the attenuated form of FAP (AFAP), which is associated with mutations in the 3′ and 5′ ends of the *APC* gene, are especially challenging to diagnosis. Caspari et al. [16] found an association between desmoid tumor formation and mutations in the 3′ end of the *APC* gene, suggesting that individuals who develop desmoids may have less than the classical presentation of the disease. Given that individuals with FAP have up to a 100% risk of colorectal cancer and significant increased risk for additional malignancies throughout their lifetimes, making an accurate diagnosis in this population is essential.

Although age, gender and site do not individually provide much discrimination between FAP and non-FAP, we found the results of our study can be combined and using Bayesian calculation can be used to estimate institution-specific probabilities that a person presenting with desmoid tumor does or does not have FAP. Examples of Bayesian calculations using our findings are shown in Tables 4 and 5. Using this data, we now have a much more useful tool for counseling patients on the likelihood that they do or do not have FAP. This type of risk assessment can help determine the need for genetic testing and colonoscopic screening in individuals presenting with an apparently isolated desmoid tumor.

These calculations assume that the desmoid cases presenting to Mayo Clinic between 1976 and 1999 are similar to those presenting currently. We have not proven that this is true, so this fact needs to be considered if results are being used for clinical purposes.

In addition, we cannot rule out the possibility that some of the individuals categorized as having sporadic desmoid tumors actually had undiagnosed FAP. Long-term follow up was not available on all patients included in this chart review-based study. Additional prospective studies will be needed to validate these findings through other centers.

Conclusions

We conducted a chart review of all patients who presented to Mayo Clinic between 1975 and 1999 with

Table 4. Bayesian calculation using desmoid data to calculate the likelihood that a man presenting with an abdominal desmoid tumor would have FAP.

	Has FAP	Does not have FAP
Prior probability (of all desmoids seen at Mayo Clinic)	16%	84%
Conditional probabilities		
Male	33/70 = 47%	139/377 = 37%
Abdominal site	47/70 = 67%	41/377 = 11%
Joint probability		
Prior × Conditionals	~0.05	~0.03
Posterior Probability	*63%*	*37%*

Table 5. Bayesian calculation using desmoid data to calculate the likelihood that a woman presenting with a desmoid tumor of the limb would have FAP.

	Has FAP	Does not have FAP
Prior Probability (of all desmoids seen at Mayo Clinic)	16%	84%
Conditional probabilities		
Female	37/70 = 53%	238/377 = 63%
Limb	1/70 = 1.4%	131/377 = 35%
Joint probability		
(Prior×conditionals)	0.001	0.185
Posterior Probability	*0.5%*	*99.5%*

a diagnosis of desmoid tumor to obtain information to inform our counseling of patients presenting for genetic risk assessment because of a diagnosis of a desmoid tumor. Of the 447 patients on whom all study information was obtained, 15.6% had FAP and in 84.6% of cases, the desmoids were apparently sporadic. There were more females than males in both categories, although the sex distribution was more equal among the FAP-related cases. FAP-associated desmoids were much more likely to be abdominal in location than non-FAP desmoids. The mean ages at consultation, tumor site and gender were not individually useful in distinguishing FAP-associated desmoids from non-FAP desmoids. However, using a Bayesian approach, conditioning on gender and tumor site was useful in estimating the probability that a given individual may have FAP based on the specific experience of our institution. This has the potential to enable geneticists and genetic counselors to provide a more appropriate risk assessment regarding the likelihood of FAP, and therefore may impact the recommendation for FAP screening for those with the highest risks.

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