



## Research Article

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# Familial polyposis coli: the management of desmoid tumor bleeding

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**Abstract:** Background: There is currently no standard treatment for desmoid tumors (DTs) associated with familial polyposis coli (FAP). Familial adenomatous polyposis in DT patients is sometimes a life-threatening condition.

**Methods:** We enrolled all consecutive patients with FAP treated at Unit of General Surgery and Transplant, University of Naples Federico II and evaluated the incidence of DTs on FAP between 1996 and 2016.

**Results:** We observed 45 consecutive patients with FAP; of these 5 were DT-FAP-associated. All 5 cases with FAP were young women, age 25 to 65 years, previously treated by colectomy. Of these, 4 patients presented a parietal localization and had been treated with a wide surgical exeresis; one patient had an intra-abdominal, mesenteric tumor that was unresectable at laparotomy. We performed CT-guided drainage, ureteral stenting, medical therapy (sulindac+tamoxifene), and chemotherapy (dacarbazine+doxorubicine).

All patients were alive and underwent follow-ups for 5 years post-surgery; only 1 patient with parietal localization showed a local relapse after 2 years.

**Conclusions:** We propose a modulated approach to the single patient with FAP, with surgery as treatment of choice for parietal localization disease and integrating different kinds of therapies (surgery alone or associated with RT, CT) for the intra-abdominal tumor.

**Keywords:** Desmoid tumor; Familial adenomatous polyposis; Radiotherapy; Surgery

## 1 Background

In 1838 Johannes Mueller first described a desmoid tumor (DT) as a neoplasia arising from tendons, bandlike in shape, with local aggressiveness and possibility of recurrence [1]. Patients with familial adenomatous polyposis (FAP) may develop soft-tissue tumors, DTs. These tumors are considered benign but can be life threatening through progressive enlargement and consequently, pressure on gastrointestinal or urinary tracts, nervous or vascular systems.

DTs can arise in the mesentery, abdominal wall, or areas of scars; they are considered a benign entity but can cause severe morbidity and mortality because of their progressive growth that threatens the intra-abdominal organs, nerves, and vessels [2]. They occur in about 10% to 25% of FAP patients, commonly in women, and are one of the most important causes of death after colectomy [3].

FAP is an inherited syndrome that, with other similar neoplasms such as Lynch syndrome, MUTYH-associated polyposis (MAP), and several hamartomatous polyposis conditions, accounts for about 3% to 6% of all colorectal cancers [3-7]. The etiopathogenesis is still unknown, but there are

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different hypotheses, including genetic alterations [8,9] and/or an endocrinological or traumatic genesis [10-12].

However, several doubts about therapy and management of FAP have been reported [13]. The surgical approach is the first therapeutic step, but the unfavorable biologic characteristics of desmoids do not always allow a wide excision; therefore, radiotherapy and chemotherapy have been tested as the primary definitive treatment or as an adjuvant therapy after surgery. Recently, several authors reported a cell-based therapeutic approach. A therapy with progenitors like endothelial progenitor cells (EPCs), using intracellular signals, may impair the adverse tumor vascularization [14-20]. In particular, the role of vascular endothelial growth factor (VEGF) and its calcium-mediated signaling as a possible target site of anti-angiogenetic therapy in EPCs has been addressed [21-30].

## 2 Methods

We enrolled all the consecutive patients with FAP who underwent surgery at the Unit of General Surgery and Transplant, University of Naples Federico II and evaluated the incidence of DTs on FAP between years 1996 and 2016. All procedures applied were in accordance with international guidelines, with the standards of the local ethics committees, and with the Helsinki Declaration of 1975, 1983 revision. At the first appointment, each patient signed informed consent for the surgical procedure and collection and use in clinical research of the data obtained, as established by the Ethics Committee of AOU-University of Naples Federico II.

All patients at admission submitted to blood exams, ultrasound, CT Scan, and fine-needle cytology (FNC) in accordance with good clinical practice. The safety and the efficacy of surgical treatment were assessed. All patients were re-evaluated by periodic follow-ups, including examination by a physician, chest X-ray, and computed tomography abdominopelvic or magnetic resonance imaging every 3 months for the first year, every 6 months for the following 4 years, and subsequently every year.

## 3 Results

During the ten years 1996 to 2016 we observed 45 consecutive patients with FAP; of these 5 presented with both FAP and DT. These 5 patients were all female, aged between 25 and 65 years old, and underwent surgery in the previous 3 to 6 years for FAP: 1 underwent total colectomy combined

with ileo-rectal anastomosis (IRA) and 4 received a proctocolectomy with ileal pouch-anal anastomosis (IPAA). The demographic and clinical characteristics of the 5 patients with FAP and DT are shown in Table 1. The desmoids were located in 2 patients who were members of the same family, at rectus abdominis; in 2 cases at the external oblique muscle, and at the mesentery in 1 patient. (Table 1)

The patients with parietal tumor showed no symptoms; they referred only to the onset of a movable and painless abdominal mass. One of the desmoids found in the external oblique muscle showed bleeding, but without anemia. The patient with the mesenteric desmoid reported abdominal pain, weight loss, and sub-occlusive crises, associated with left hydronephrosis.

Surgical treatment was possible in all parietal locations, in the form of wide exeresis. (Table 1, Figure 1). The patients were discharged 6 to 8 days after surgery without complications. The mesenteric desmoid was unresectable at laparotomy because of its connections with the great



**Figure 1. A:** Desmoid tumor that arose after total colectomy in the anterior abdominal wall in a young FAP-affected female patient: CT scan.

**B:** Surgical specimen of desmoid tumor that arose after total colectomy in the anterior abdominal wall in a young FAP-affected female patient.

**Table 1:** Demographic and clinical presentation of the 5 patients with FAP and desmoid tumor

PATIENTS' CHARACTERISTICS	N°
AGE (years)	25-65
GENDER	
Female	5
Male	0
PREVIOUS SURGERY	
Total colectomy with ileo-rectal anastomosis (IRA)	1
Proctocolectomy with ileo-anal anastomosis (IPAA)	4
CLINICAL PRESENTATION	
Rectus Abdominis	2
Palpable mass	2
Subocclusion and abdominal pain	0
Bleeding	0
Hydronephrosis	0
External Oblique Muscle	2
Palpable mass	2
Subocclusion and abdominal pain	0
Bleeding	1
Hydronephrosis	0
Mesentery	1
Palpable mass	0
Subocclusion and abdominal pain	1
Bleeding	0
Hydronephrosis	1

abdominal vessels and small bowel loops. Therefore, the patient underwent TC-guided drainage and ureteral stenting to treat the left hydronephrosis and was treated with tamoxifen and sulindac.

One patient received post-operative radiotherapy, whereas the others followed an adjuvant therapy with sulindac and tamoxifen in the year after the operation. After 1 year of follow-up, the patient was alive and in good health, but the tumor had not regressed. Therefore, chemotherapy with doxorubicin plus dacarbazine was performed; she showed a partial response. At 3 years after the initial diagnosis, she is alive with a tumoral regression shown on CT scan and DMSA scintigraphy. (Table 2)

The incidence of desmoid tumors developed in patients with FAP in our series is 11.1%.

All patients were alive and underwent follow-up for 5 years; only 1 patient with an external oblique muscle localization showed a local relapse after 2 years.

**Table 2:** Therapeutic choices

PARIETAL LOCALIZATION, N:	
Surgery (wide excision)	4
Radiotherapy after surgery	1
Adjuvant Chemotherapy (sulindac and tamoxifene)	1
MESENTERIC LOCALIZATION, N:	
Chemotherapy (sulindac and tamoxifene)	1
Chemotherapy (with doxorubicine and dacarbazine)	1

## 4 Conclusion

The DT represents an unfortunate event for patient with FAP and is the third most frequent cause of death in this patient setting. The management of DT is not yet standardized, and it can be different in case of parietal or intra-abdominal locations. Our experience shows how the treatment of these tumors might be particularly challenging. In patients with FAP, the risk of desmoid fibromatosis is increased up to 800-fold compared with the general population; cumulative risk of onset fibromatosis is 16% in the 10 years after colectomy (peak incidence in 1 to 3 years following colorectal surgery) [31]. A surgical approach can be justified for the parietal locations followed by drugs or radiotherapy with a low recurrence rate [32].

In patients with intrabdominal tumors, a modulated therapeutic approach (surgery alone or associated with RT, CT), or also an abstensionist behavior can be justified for the unpredictable natural history of this disease, characterized sometimes by spontaneous regressions and absence of growth of tumor for a long period; even though it has been reported that these lesions have a higher rate of recurrence when associated with FAP [33].

The role of radiotherapy (RT) is yet not clear. Several studies reported the RT efficacy (partial or complete tumoral regression), using 50–60 Gy, with a local control in 89% and recurrences in 20% to 30% [34-35]. Successes could depend on menopausal induction and the consequential estrogenic decrease in women. This hypothesis is also supported by the low radiosensitivity observed in men.

In our study, we observed only 5 patients with FAP and DT among the 45 FAP patients enrolled. In all parietal tumors, a wide exeresis was possible with safe margins and a minimal rate of recurrence. The surgical treatment of desmoids offers some considerations about the possibility of aggressive procedures and the extension of exeresis, when feasible (Figure 1). The biological characteristics of desmoids do not always allow a perfect exeresis because the nearest structures can be strongly infiltrated at the

time of surgery. Thus, it can be necessary to perform a palliative procedure (gastrointestinal bypasses, transuretero-ureterostomy) [36-39].

In conclusion, our experience supports a modulated approach to the single patient, with surgery as treatment of choice for parietal localization and integrating different kinds of therapies for the intra-abdominal ones. We indicate early identification of high-risk subjects, such as young women, who are candidates for a restrictive follow-up and an early colectomy. We urge cooperation with National FAP Registers [40].

## Abbreviations

**FAP:** familial adenomatous polyposis

**DT:** desmoid tumor

**MAP:** MUTYH-associated polyposis

**FNC:** Fine-Needle Cytology

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