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A case report and literature review

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Desmoid tumor of the abdominal wall. A case report and literature review

BACKGROUND: *Desmoid tumor is a rare soft tissues neoplasia characterized by local invasiveness and by a tendency towards local recurrence although not towards metastasization.*
DISCUSSION: *Etiology is not clear. Desmoid tumors originate from the monoclonal proliferation of one mesenchymal cell and develop in the context of fascial, muscular and aponeurotic tissue. They are free of capsule and do not usually metastatize, although they do present a high risk of local recurrence*
CONCLUSION: *In the absence of a systematic data collection and of a clear distinction, in the existing databases, between primitive and recurrent lesions and between lesions of different sites, there are no standard guidelines for a correct management of desmoids.*

KEY WORDS: Aggressive fibromatos Desmoid tumor, Soft tissue neoplasia

Case Report

A 31 year old woman arrived at our department complaining for a progressively ingraving mass on the right abdomen.
Past medical history no familiarity for cancer or FAP, adenoidectomy and a pregnancy in the two years preceding the onset of neoformation.
An ultrasound examination showed a solid nodular neoformation, with a homogeneous echostructure, which did not infiltrate the muscular profiles with some small vascular components, possible expression of desmoid lesion. A subsequent MRI confirmed the ecotomographic survey.A colonoscopy was negative
At clinical examination we founded a mass with increased consistency,mobile on the surface planes, located in the muscular wall.
At the radical enucleation, the lesion appears as a solid mass in the thickness of the abdominal rectum muscle (Fig. 1).
The post-operative course takes place in a regular manner and on the second day the patient is discharged.
Histological examination confirms desmoid origins.
The follow-up of 1, 3 ,6 months and one year after surgery does not show signs of relapse and any patient disturbance.

Discussion and Literature Review

Desmoid tumor is a rare soft tissues neoplasia .The first description by MacFarlane dates back to 1832 [1] while

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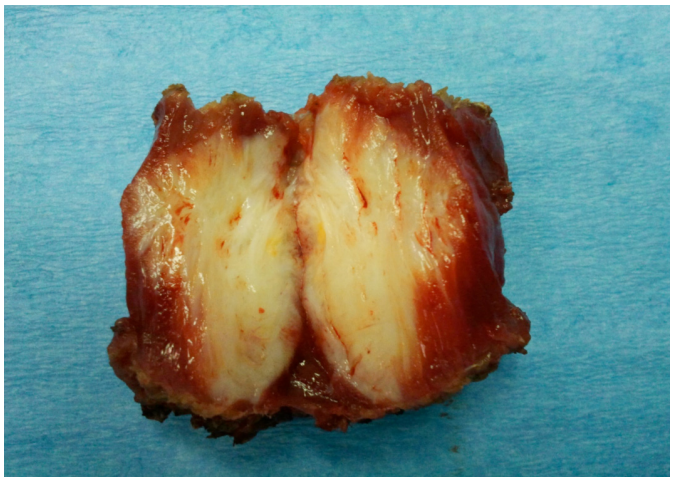

Fig 1: At the radical enucleation, the lesion appears as a solid mass in the thickness of the abdominal rectum muscle.

the term desmoid was introduced only later, in 1838, by Müller [2].

It represents the 3% of all soft tissues tumors. It more commonly interests the female sex (F: M=1.4-1.8), especially women of reproductive age (from 18 to 36 years of age with a range extending between 4 months and 80 years. Up to now, no predisposing factors or racial or ethnical predispositions have been identified. Between 35 and 50% of desmoid tumors are abdominal while the more common extra-abdominal locations include the shoulder girdle, chest wall, inguinal region and limbs . It can be sporadic or present in association with Familiar Adenomatous Polyposis (FAP) and especially with Gardner [3].

The biological behavior of this condition is intermediate between benign lesions and sarcomas. Because of the intense cellularity and local aggressiveness, this lesion is also defined "aggressive fibromatosis" [4].

Etiology is not clear. Predisposing factors include traumas, estrogens, and genetic alterations. One of the most important causes of trauma appears to be laparotomy surgery in the previous five years with cases of desmoid tumor in FAP patients developing both intra-abdominally and on the abdominal wall after total colectomies with ileal rectal anastomoses and proctocolectomies with sphincter sparing and pouch creation. A few cases of desmoid developing after laparoscopic surgery are also described. For what concerns the role of estrogens, evidence shows a higher incidence of these lesions in women of reproductive age and a more rapid growth in female patients when compared to males. In 1995 genetic studies showed an association between distal (3') germline APC mutations and desmoid tumor.

Desmoid tumors originate from the monoclonal proliferation of one mesenchymal cell and develop in the context of fascial, muscular and aponeurotic tissue. They are free of capsule and do not usually metastatize, although they do present a high risk of local recurrence.

Prove of the fundamental benign nature of this neoplasia are the normal length and activity of telomerases, the small size and regular shape of the nuclei and the low mitotic activity at microscopic examination.

It is believed that desmoids may derivate from a single precursor undergoing a pattern of genetic alterations leading to the development of the mature neoplasia, in analogy with the adenoma-carcinoma sequence in colorectal tumor. In FAP, a plaque-like lesion has been described and identified as a possible precursor which might evolve in mesenteric thickening (fibrosis) and finally in desmoid tumor [5,6]. In contrast with colorectal adenoma, in desmoids loss of expression of APC is a delayed event. It leads to a β-catenin over-expression with augmented transcription of genes that have a key role in the cell cycle. β-catenin levels have been suggested has possible markers to discriminate desmoids from other histologically similar neoplasia. Cytogenetic anomalies (like 8 trisomy or 1q21 chromosome band gain) have also been described but only in some sporadic forms of extra abdominal desmoids.

Desmoid tumors are classified in extra-abdominal, abdominal and intra- abdominal, with a further distinction between mesenteric and pelvic fibromatosis. FAP-associated forms are mostly localized at the abdomen (80-95% of cases), especially at intra-abdominal level (70% of cases) and therefore have a higher morbidity and mortality and require a more complex surgical approach. The condition tends also to be more aggressive in FAP patients where natural history of the disease follows four different patterns: spontaneous resolution (10%), cyclic growth and regression (29%), stability (47%) and rapid progression (10%). Sporadic forms arise more often from the anterior abdominal wall (50%of cases) and develop at intra-abdominal level only in 10% of cases. In sporadic lesions, natural history depends mostly on age and sex with a slow progression in male patients and in pediatric or elderly female patients and a rapid growth in women of reproductive age.

Vandevenne et [7] first described the three phases of desmoid tumor development: the first is characterized by a high cellularity and reduction of hyaline collagen areas, the second by an enhanced collagen deposition and the third by the increment of the fibrous component in association with a reduction in cellularity and liquid mass. Treatment can be medical or surgical [8,9].

In FAP patients, Non Steroid Ant inflammatory Drugs (NSAIDs) (mostly Sulindac) and anti-estrogens (Tamoxifen, Toremifene) represent the first line of treatment, alone or in combination. The rationale behind NSAID employment comes from studies on desmoid lesions in mice evidencing high levels of cyclooxygenase-2 (Cox-2) and a reduction in size after treatment. The use of anti-estrogens is based on the observation of the close relation between desmoid tumors growth and estro-

gen levels. These drugs are employed both in sporadic and in FAP-associated forms, with a posology equivalent or even superior to the one employed in breast cancer. Cyclic-AMP inhibitors and -interferon are employed in extra-abdominal FAP-associated forms. Some trials also evaluated the effectiveness of pirfenidone and mesylate Imatinib .

Cytotoxic chemotherapy is reserved to unresectable lesion that expand despite combined treatment with NSAID and anti-estrogens. Combinations of doxorubicin and dacarbazine or of cyclophosphamide and vincristine continued for six months for treatment are usually preferred. In rare cases, Doxorubicine was employed as a single agent. Doxorubicin based treatments have a rate of response of 50% but lead to adverse effects such as nausea, vomiting and cardiac toxicity. Alternative therapies with low dosage antiblastic drugs such as combinations of vincristine and methotrexate continued for approximately one year have been employed in slowly progressing FAP associated desmoids . These formulations present with fewer adverse effects but may sometimes cause myelotoxicity.

Recently a treatment with PF-03084014, an Oral Gamma Secretase Inhibitor, is proposed [10].

Radiant therapy is employed as adjuvant and in combination to surgery and reserved to sporadic forms of desmoid tumors located at the limbs. Treatment usually lasts for 6-8 weeks and allows the local control of the lesion in 75-80% of patients.This kind of treatment is never employed in intra-abdominal desmoid for the risk to damage the surrounding organs.

During surgical resection of intra-abdominal desmoid tumors it can be hard to obtain free margins while trying to preserve the surrounding anatomic structures. Indications are limited to cases where CT scan excludes the involvement of surrounding structures and pharmacological treatment is ineffective of in rapidly expanding forms where the survival of the patient is at stake.

In the case of desmoid lesions of the abdominal wall, instead, surgery represents the first choice of treatment. The main problem is local recurrence, which happens in 20-30% of cases, usually within six months after surgery or during later pregnancies . During resection the safety margin should be at least 1 cm [11,12].

The risk of local recurrence depends on many different factors including age, sex, presence of disease-free margins, genetic alterations, size, site, multiple localizations, and previous treatments [13]. It is more common between 18 and 30 years of age. The importance to obtain free margins is debated but, at a wide literature analysis, they seem associated with a lower risk of recurrence and with a longer disease-free interval after treatment .

In recurrent lesions of the abdominal wall or extra-abdominal sites it is advised to do a second surgery ; when this is not possible the alternative is medical treatment [13].

Conclusions

There is no standard guideline for the diagnosis and treatment of desmoid tumors because of their rare nature and variable presentation. A further impediment is the lack of a clear distinction, in most case series present in literature, between primitive and recurrent lesions and between lesions of different sites.

For abdominal wall lesions, surgery should be considered the treatment of choice. The best approach to intra-abdominal lesions is probably a combination between chemo-radio therapy and surgery.

Certainly the creation of a unified register and a multidisciplinary approach would help with the management of the most complex cases.

Future progress in treatment, including the introduction of genetic therapies, may certainly help in the management and allow for a better prognosis for these patients.

Riassunto

INTRODUZIONE: Il tumore desmoide è una rara neoplasia dei tessuti molli caratterizzata da tendenza all'invasività locale, da un elevato rischio di recidiva locale dopo asportazione.

Colpisce maggiormente il sesso femminile, soprattutto in età fertile.

CASE REPORT: Donna caucasica di 31 anni, unipara, con una tumefazione al terzo medio del muscolo retto sinistro dell'addome non dolente, insorta da circa un mese. Un'ecografia e una RMN dell'addome pongono il sospetto di un tumore desmoide della parete addominale. Si pone indicazione al trattamento chirurgico di enucleazione della lesione e ricostruzione dei piani muscolari senza ausilio di reti protesiche. Il follow-up eseguito a 1 anno non ha evidenziato alcuna recidiva.

CONCLUSIONI: La mancata raccolta dei dati e la mancanza di un registro che differenzi tumori desmoidi localizzati in sedi diverse e l'accorpamento di lesioni primitive e secondarie presente in letteratura non hanno standardizzato un corretto iter terapeutico. Sicuramente di fronte a desmoidi della parete addominale il trattamento chirurgico può essere ritenuto il trattamento di scelta. Il prossimo futuro sviluppo di terapie geniche potrà contribuire a migliorare il trattamento e la prognosi dei pazienti.

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