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Case Report

Spontaneous Regression of an Inflammatory Myofibroblastic Tumor: A Case Report and a Review of the Literature

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Abstract
Introduction: Spontaneous tumor regression is the volumetric reduction or complete disappearance of a primary tumor or metastatic sites (single or multiple) without the administration of treatments. This rare phenomenon occurs most commonly in certain types of neoplasms. ***Case Presentation:*** In this manuscript, we describe a spontaneous tumor regression in an adult patient followed at the Modena Cancer Center and affected by retroperitoneal inflammatory myofibroblastic tumor, an ultra-rare subtype of sarcoma. Finally, we will provide a concise review of the literature and try to explain the mechanisms underlying the tumor regression described in the clinical case. ***Conclusion:*** The etiopathogenetic mechanisms for spontaneous tumor regression are not yet fully understood and likely involve a complex interplay among immunological mechanisms, growth factors, cytokines, and hormonal factors.

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Introduction

Spontaneous tumor regression, which is the volumetric reduction or complete disappearance of a primary tumor or metastatic sites (single or multiple) without the administration of an anticancer treatment, has been rarely described in the literature. This phenomenon occurs most commonly in certain types of neoplasms, namely, renal carcinoma, melanoma, neuroblastoma, testicular germ cell tumors, choriocarcinoma, sarcomas and breast tumors, with an overall incidence of approximately 1 case per 60,000–100,000 tumor cases [1].

The first cases reported in the literature date back to the 19th century. It is supposed that the etiopathogenetic bases for spontaneous tumor regression involve a complex interplay between immunological mechanisms, growth factors, cytokines, and hormonal factors; indeed, activation of the host's immunological response and oncotic apoptotic processes are probably the main driving pathological mechanisms [2]. The role of the immune system in the phenomenon of tumor regression is very likely; for example, cases of tumors regressed after COVID-19 infections and after SARS-CoV-2 vaccinations are reported [3].

However, the exact mechanisms underlying this phenomenon are still not fully understood. In this manuscript, we describe a case of spontaneous tumor regression occurring in an adult patient suffering from a retroperitoneal inflammatory myofibroblastic tumor (or inflammatory pseudotumor [IPT]), a rare tumor of the stroma of the submucosa. IPT, according to WHO (World Health Organization) classification, is defined as a distinctive lesion composed of myofibroblastic spindle cells accompanied by an inflammatory infiltrate of plasma cells, lymphocytes, and eosinophils [4].

This type of tumor usually has a benign behavior and a favorable prognosis. However, when the disease has local recurrence or invasive presentation, the risk of developing metastases is about 5%, with a worse prognosis [5]. The etiology of IMT still has not been elucidated; some triggers such as trauma, inflammation, autoimmune diseases, and human herpesvirus or Epstein-Barr virus infections have been hypothesized [6].

The most affected site is the lung but also the visceral organs and deep soft tissues of the abdomen, pelvis, retroperitoneum. The picture can be insidious and be confused with nodular fasciitis, a fibrous histiocytoma, a leiomyoma, a leiomyosarcoma, a rhabdomyosarcoma, GIST, and other mesenchymal tumors because of histological similarities [7].

The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material at https://doi.org/10.1159/000541337.

Case Presentation

In April 2021, a 77-year-old man presented to the emergency room with a 2-month history of abdominal pain, weight loss, and low-grade fever. His medical history was remarkable for hypertension, dyslipidemia, benign prostatic hyperplasia, and previous inguinal hernioplasty.

The physical examination showed a voluminous, aching, and slightly movable palpable mass on the left hemi-abdomen, with a tough consistency. Bowel sounds were audible and normal. On rectal examination, there was no blood present and prostatomegaly was palpable. Other physical examinations were normal. Laboratory blood test revealed an increase of the white blood cell count (15.590/mmc), a reduced hemoglobin level (8.7 g/dL), an increased C-reactive protein level (16.7 mg/dL), and mild impaired renal function (creatinine 1.35 mg/dL and eGFR 50 mL/min). All tumor markers were within normal limits.

Computed tomography (CT) scan demonstrated a voluminous solid mass with diameters of 14 × 16 × 18 cm, extended from the ribs to the gluteal muscles in the left side of the abdomen, with signs of muscle infiltration. Furthermore, this mass was not dissociable from

the spleen and the left kidney, which appeared dislocated. Despite having a posterior relationship with the L1-L2-L3 vertebrae, no bone erosions were visible. No distant metastases or lymphadenopathy were documented.

The patient was admitted to the general surgery department, where he underwent ultrasound-guided biopsy of the mass in the left side of the abdomen, with discharge of a purulent and bloody material. The microbiological examination showed identified *Escherichia coli*, and the cytological analysis identified an inflammatory necrotic material. The patient underwent antibiotic therapy. Furthermore, a transfusion support was required. A CT scan was repeated a week later revealing a notable reduction in size of the mass to diameters of 11 × 4.4 × 12.4 cm. It also showed the appearance of two lymphadenopathies in the retroperitoneal area near the left kidney, with diameters of 16 × 27 mm and 28 × 23 mm, respectively. A second biopsy of the mass confirmed the inflammatory nature of the mass. Ten days later, the CT scan was repeated with the finding once again of an increase of the diameters of the mass (12 × 7 × 12.4 cm) and of the lymphadenopathies (30 × 20 mm and 35 × 25 mm). Therefore, a third biopsy was performed and gave the same result as the previous ones. Finally, the patient underwent exploratory laparoscopy with a biopsy of both the left retroperitoneal lesion and the solid formation on the wall of the descending colon.

The histological examination, after further revision by an experienced pathologist, made the diagnosis of inflammatory myofibroblastic tumor with a rich histiocytic component, infiltrating the colic muscle layer and the soft tissues. The immunophenotype was as follows: CD1a−, CD31−, CD34−, CD68+, CD117−, CD163+, S100−, MNF116−, actinML+/−, caldesmon+, desmin−, podoplanin−, Ki-67: 10–15%. ALK rearrangement was detected by FISH technique and was present in 20% of the cells analyzed. The fusion partner was unknown.

Based on the histological diagnosis, the patient continued only with a clinical-radiological follow-up with regular CT scan of the chest and abdomen. Initially, the first CT scan after laparoscopic biopsy revealed stability in the size of the mass and lymphadenopathies. Subsequently, a progressive reduction in the diameters was found, despite the patient did not undergo specific treatments. After a first observation period of approximately 1 year with quarterly CT scans, the diameters of the retroperitoneal lesion were reduced up to 6 × 15 × 34 mm, and the lymphadenopathies near the left kidney shrank to a size of 17 × 11 mm and 13 × 7 mm, respectively. Afterward, the follow-up continued with six-monthly CT scans, with the confirmation of stability of the radiological framework until today, 3 years after diagnosis (Fig. 1, 2).

Conclusion

We reported here a case of a patient experiencing spontaneous tumor regression of a retroperitoneal inflammatory myofibroblastic tumor in the absence of any oncological treatment. Tumor regression is a rare phenomenon that remains not fully understood. In the literature, cases of tumor regression are described after infections, administration of antibiotics, corticosteroids, anti-inflammatories, after blood transfusions and hormonal changes (cases of melanoma regressed during pregnancy or ovarian tumors regressed after ovariectomy are reported) [8].

Sarcoma, a rare type of neoplasm that affects connective tissue and can be classified into several different subtypes, is one of the cancer types most commonly associated with tumor regression. Table 1 summarizes published cases of spontaneous sarcoma regression.

The patient in our clinical case was affected by IPT, a sarcoma with an aggressive behavior and a tendency to give hematogenous metastases. This cancer may have aggressive behavior

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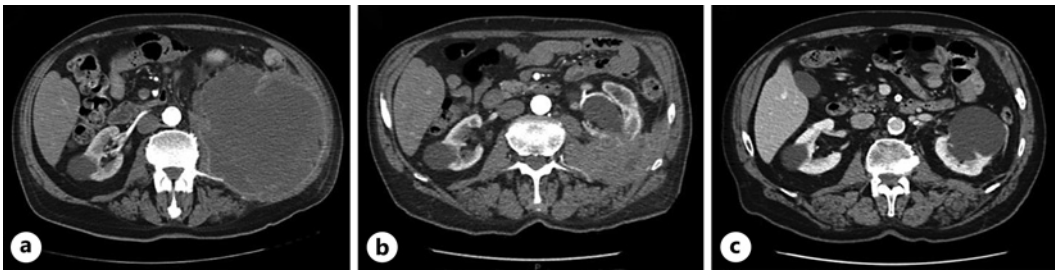

Fig. 1. CT scan images of the retroperitoneal mass in size reduction: at diagnosis (**a**); 4 months from diagnosis (**b**); approximately 3 years after diagnosis (**c**).

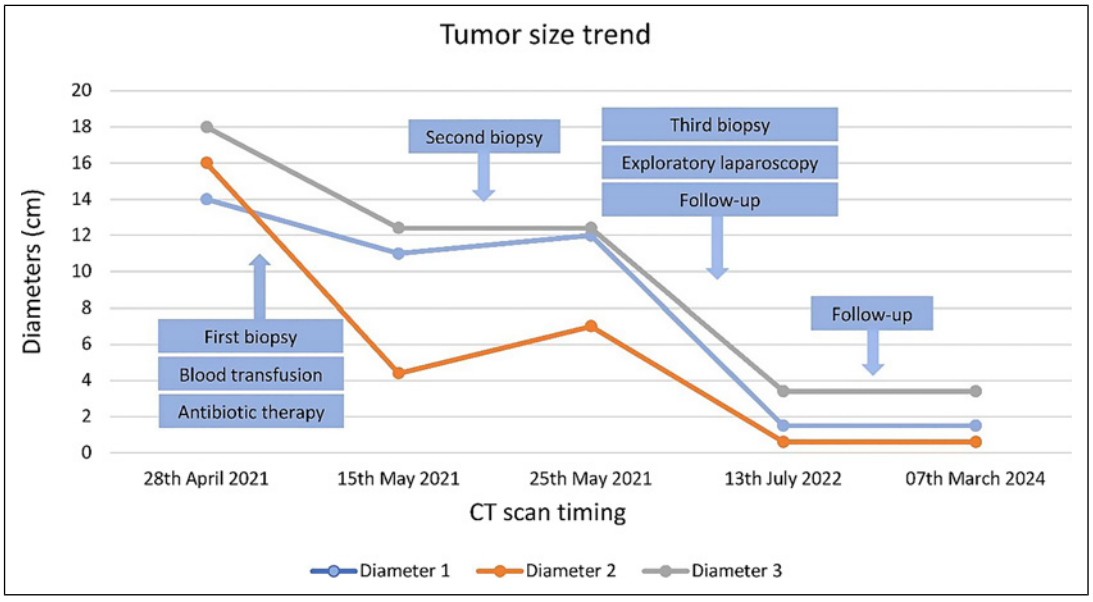

Fig. 2. Tumor size trend over the course of the 3 years covered by the follow-up. Diameters 1, 2, and 3 represent the three dimensions of the tumor mass. The main episodes of care are indicated in the interval between a CT scan and the next one.

and the clinical presentation depends on the affected organ, with many patients presenting with nonspecific clinical picture (fever, malaise, weight loss, anemia, or clinical signs secondary to compression of adjacent organs). The prognosis of this sarcoma varies according to location: usually, those with abdominal onset (which is the most frequent location) have unfavorable course [10]. Surgical treatment remains the mainstay of IPT therapy; on the other hand, adjuvant chemotherapy usually has no indication in this setting [8]. Moreover, cases of spontaneous regression of IPT are most frequently described in middle-aged or elderly patients [10].

Mattei et al. [12] described a case IPT of the proximal duodenum regressing in a 13-year-old boy in only 14 days after administration of intravenous ketorolac post biopsy of the lesion. Germanidis et al. [13] instead reported regression of intestinal tract IPT after infusion of infliximab (5 mg/kg body weight). There are few other described cases of spontaneous regression of IPT in the literature, partly related to the rarity of this disease.

In the clinical case described here, regression did not occur after the administration of anti-inflammatory drugs; we could speculate that there was an underlying infectious event at

Table 1. Published cases of spontaneous sarcoma regression

Author	Year	Type of sarcoma	Site
Coley and Stewart [9]	1945	Bone sarcoma	Bone
Rosenman et al. [14]	1946	Osteogenic chondrosarcoma	Bone
Ota et al. [1]	2001	Endometrial stroma sarcoma	Endometrium
Germanidis et al. [13]	2005	Inflammatory myofibroblastic tumor	Gastrointestinal tract
Mattei et al. [12]	2007	Inflammatory myofibroblastic tumor	Proximal duodenum
Kim and Wylie [15]	2008	Breast angiosarcoma	Breast
BaniHani and Al Manasra [16]	2009	Alveolar soft part sarcoma	Lung
Bonvalot et al. [17]	2013	Desmoid tumor	Abdominal wall
Zhao et al. [10]	2014	Inflammatory myofibroblastic tumor	Retroperitoneum
Tsunezuka et al. [18]	2018	Primary pulmonary synovial sarcoma	Lung

the tumor site, as purulent material was drained early in the history of the disease. This probably initiated a major immune response against IPT, thus leading to a progressive decrease in the size of the tumor mass. In addition, the patient was treated with antibiotic therapy and had transfusion support; as previously reported, cases of tumor regression following such treatment are described in the literature. However, further research is needed to better clarify the molecular underpinnings that underlie this rare phenomenon.

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

Fabio Gelsomino received honoraria for speaker/advisory roles from Servier, Eli Lilly, IQVIA, Merck Serono, Amgen, and Bristol Myers Squibb outside the present work. The other authors declare no conflict of interest.

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Author Contributions

Conceptualization: Eugenia Caffari, Bianca Medici, Massimiliano Salati, Andrea Spallanzani, Ingrid Garajova, Federico Piacentini, Massimo Dominici, and Fabio Gelsomino; writing – review and editing and visualization: Bianca Medici and Eugenia Caffari; and supervision: Fabio Gelsomino. All authors have read and agreed to the published version of the manuscript.

Data Availability Statement

All data generated or analyzed during this study are included in this article and its supplementary material files. Further inquiries can be directed to the corresponding author.

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