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SHORT COMMUNICATIONS AND CASE REPORTS

Invasive inflammatory pseudotumor of the pelvis: A case report with review of the literature

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Summary

Inflammatory pseudotumor (IPT) is a rare benign lesion of unknown etiology, which mimics malignant neoplasm and may arise from various organs. A 53-year-old woman was submitted to diagnostic evaluation because of bilateral, hydroureteronephrosis and oedema of the left leg after a 3-month history of fever of unknown origin. On bimanual vaginal and rectal examination, a mass was involving the uterus, parametria and mostly left adnexa, while the cervix appeared normal. Computed tomographic (CT) scan revealed a 13×10.5 cm mass in the pelvis, mostly at the place of the left adnexa, uterus and both parametria, also involving the surrounding tissues and producing bilateral hydroureteronephrosis. At laparotomy, a grey solid mass was seen, mainly involving the reproductive system. As no radical operation could be performed, the mass was only biopsied and histology showed an inflammatory pseudotumor. Antibiotic therapy was given for one month. Follow-up CT 4 and 8 months after laparotomy showed local regression of IPT. The last follow-up CT, 20 months after laparotomy, revealed no evidence of tumor.

Key words: computed tomography, inflammatory pseudotumor, spontaneous regression

Introduction

Inflammatory pseudotumor is a lesion of unknown etiology, rare and benign, characterized by a mass which mimics neoplasm. It consists of fibroblasts, lymphocytes, plasma cells, and histiocytes. It is often seen in the lung but it may also arise from various tissues with mesenteric, genitourinary, retroperitoneal, musculoskeletal and cutaneous localizations. The lesion has been reported under several names like pseudotumor (or plasma cell granuloma), inflammatory myofibroblastic tumor (IMT), and inflammatory myofibrohistiocytic proliferation [1]. The rarity of the lesion, its aggressive appearance on imaging and at operation, lead to diagnostic and therapeutic dilemmas. A large amount of specimens is required for accurate histological diagnosis [2]. Surgical resection tends to be the treatment of choice for IPT. In recent years, a few studies have dealt with IPT of the female reproductive system, mostly of the uterus, treated predominantly by surgery [3]. Spontaneous regression has been also described and in case of IPT of the lung, and steroid administration has been reported as efficient [4]. The case we present herein shows an IPT with spontaneous regression which involved the female reproductive system and surrounding tissues recorded by CT imaging.

Case presentation

A 53-year-old, smoking, para 2, female was admitted to our clinic, with a 3-month history of temperature ≥ 39° C, bilateral hydroureteronephrosis and oedema of the left leg.

A previous thorough exploration in another hospital had not revealed the etiology of the fever. Her

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medical, social or family history was not significant for any pelvic inflammatory disease or operations. An intrauterine device which was inserted 20 years ago had been spontaneously expelled 5 months before the fever started. During this period of symptoms the patient had lost 20 kg.

Erythrocyte sedimentation rate was 130 mm/h (normal < 10), white blood cell count 11,900/mm^3 and hemoglobin level 5.2 g/dL. Serum tumor markers (CA-125, CA19.9, and CEA) and liver function test were within normal limits. Results of cultures for bacteria, fungi and mycobacterium tuberculosis were negative. Radiographs of the chest showed no abnormalities. Empirical therapy with broad-spectrum antibiotics was unsuccessful. Around that time, the patient developed severe hydroureteronephrosis, anemia and uremia.

Colposcopy revealed a normal-appearing cervix and cervical cytology showed reactive inflammatory changes without atypical features. On bimanual vaginal and rectal examination, a mass was involving the uterus, parametria and mostly the left adnexa.

CT scan of the abdomen and pelvis (Figure 1) confirmed the presence of a gross pelvic tumor but no evidence of retroperitoneal lymphadenopathy. A 13×10.5 cm homogeneous soft tissue mass in the pelvis, mostly at the place of the left adnexa, was involving both parametria, uterus (Figure 1 A,B) both ureters and producing bilateral hydroureteronephrosis. There was no definite tissue plane among the mass and the intestine, sigmoid colon and bladder, suggesting infiltration into the surrounding tissues (Figure 1 A,B). The presumptive diagnosis based on imaging was an invasive malignancy of the ovary.

Intravenous pyelography (IVU) showed stenosis of both ureters. Cystoscopy and biopsy showed no pa-

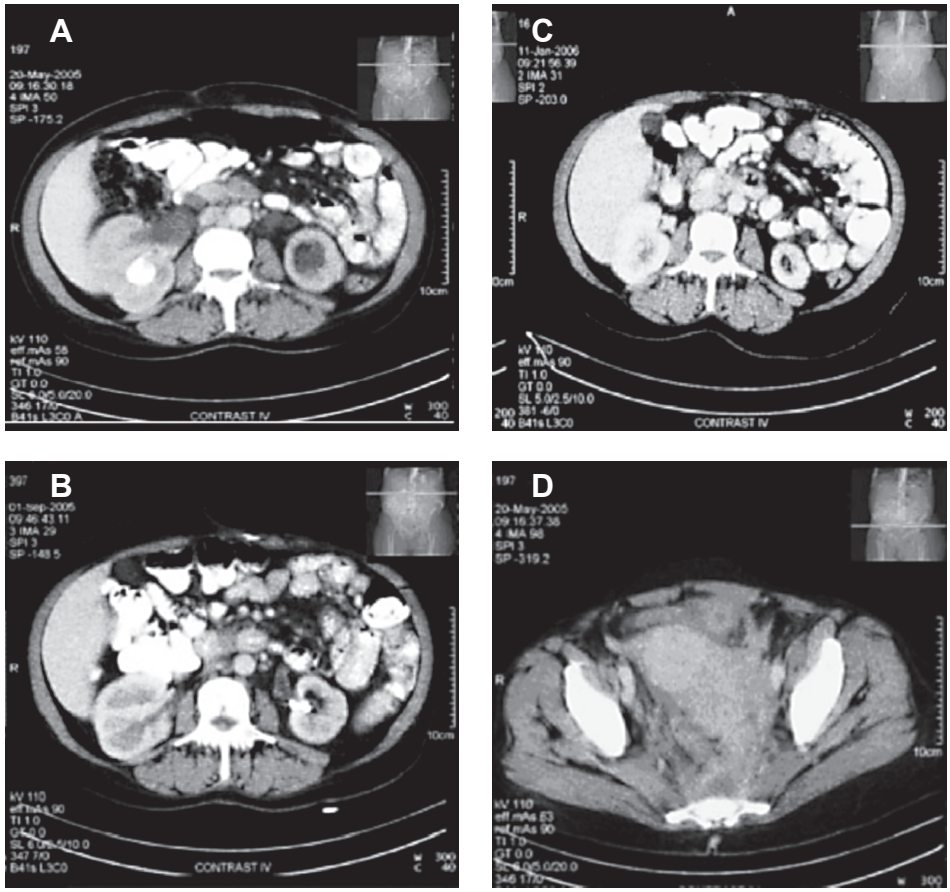


Figure 1. Corresponding CT scan of the pelvis and abdomen: initial (**A,B**), 4 months (**C**) and 8 months (**D**) after laparotomy demonstrates the spontaneous regression of the ITP. Initial axial (contrast) CT scans of the pelvis (**A**) and frontal reconstructed initial CT image (**B**) demonstrate gross heterogeneous soft tissue mass of the pelvis, mostly at the place of the left adnexa, uterus and both parametria. There is no definite tissue plane among the mass and the intestine, sigmoid colon and urinary bladder suggesting infiltration into surrounding tissue (**A,B**). Follow-up CT scans of the pelvis 4 and 8 months after the laparotomy show spontaneous partial regression after 4 months (**C**) and complete regression with normal anatomic structure of female reproductive system (uterus) after 8 months (**D**).

thological findings. After percutaneous nephrostomy had been placed in the left kidney, the renal function tests returned to normal levels compared to elevated serum creatinine level up to 342 μmol/l at presentation.

Barium enema and rectosigmoidoscopy showed narrowing of the lumen due to compression by an extrinsic mass. A biopsy taken showed no pathological findings.

A laparoscopic exploration was done and identified a gross tumor mass the FNA of which revealed no malignancy.

Following these results an exploratory laparotomy was performed through a midline incision. At operation, the tumor mass was seen in the pelvic and abdominal cavities. The reproductive system including uterus, adnexa and both parametria was completely involved by a tumor of rubbery consistency. The corpus uteri was enlarged and the tumor mass was tightly adherent to the adjacent structures (bladder, sigmoid, sacrum, and parts of small intestine. Relief of intestine and omental adhesions was performed. Both ureters were entrapped into the tumor mass. As no radical operation could be performed, only biopsy of the tumor close to small intestine and omentum was taken. Routine H&E stain showed spindle cells proliferation accompanied by a prominent lymphoplasmacytic and histiocytic infiltration embedded in hyalinized stroma (Figure 2 A,B). No cell mitoses and atypia were observed. Immunohistochemistry (IHC) for cytokeratin HMW and MNF116, smooth muscle actin, desmin, vimentin, S-100, CD68, CD34 and LCA using the streptavidin-biotin method (all DAKO antibodies) was positive for actin and vimentin (Figures 3 and 4); negative for desmin, S-100, cytokeratin HMW; and focally positive for cytokeratin MNF116. Inflammatory cells were positive for LCA and CD68. Anti-CD34 antibody was positive in the walls of blood vessels. The pathological diagnosis was IPT.

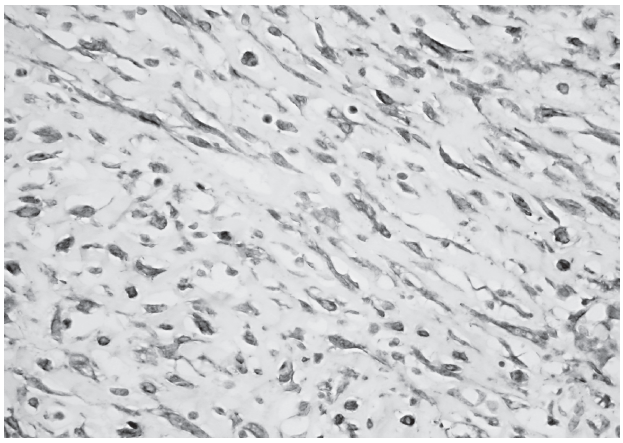


Figure 3. Cells show positivity for actin (×200).

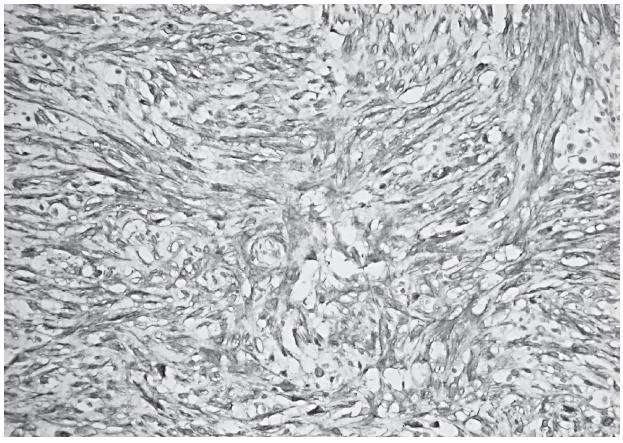
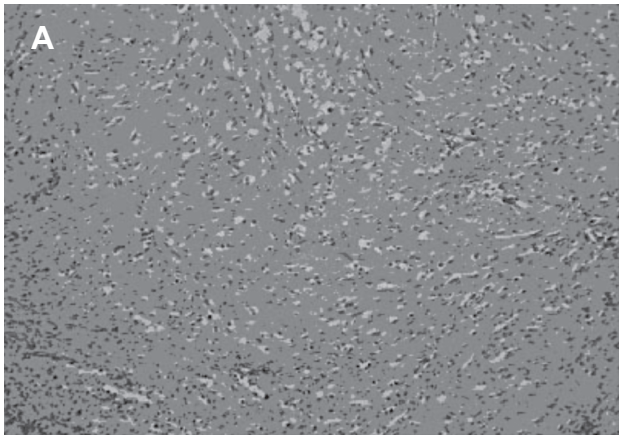


Figure 4. Cells show positivity for vimentin (×200).

The postoperative course was uneventful. Further



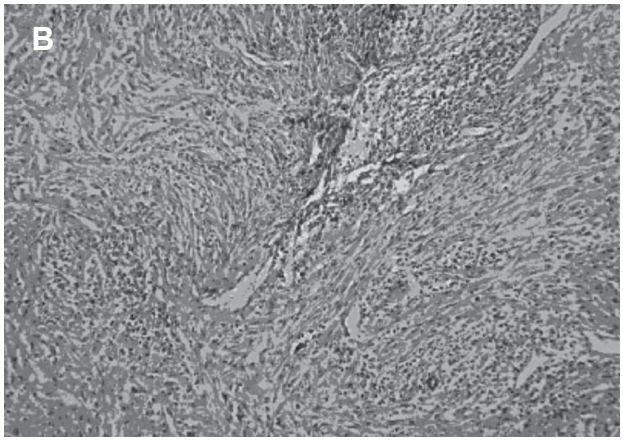


Figure 2. A: Myofibroblastic proliferation with dense hyalinization and with inflammatory infiltrate (H&E ×100). **B:** Myofibroblastic proliferation with dense lymphoplasmacytic infiltration (H&E ×100).

antibiotic therapy with tetracycline was given for one month. Control exams were performed monthly during the first 3 months with bimanual pelvic and laboratory examinations. The patient's inflammatory constitutional symptoms and laboratory abnormalities resolved completely within 3 months. IVP and follow-up CT obtained 4 months postoperatively showed normal ureters and renal pelvis and percutaneous nephrostomy was removed. Follow-up CT showed partial regression of IPT (Figure 1 C) 4 months after surgery and local complete regression 8 months after surgery (Figure 1 D). Last follow-up CT 20 months after laparotomy revealed no evidence of local recurrence or metastatic disease.

Discussion

IPT, now frequently reported as inflammatory myofibroblastic tumor (IMT), is an aggressive invasive mass which is histologically benign and may appear in various tissues and organs with a great variability of histological and clinical appearances [3,5-7].

There is no apparent tissue or organ predilection for IPT. Generally, most etiologic hypotheses have been based on immunologic response to an inflammatory or infectious insult. A few case reports describe IPT secondary to Epstein-Barr virus, cytomegalovirus (CMV) and mycobacterium avium-intracellulare (MAI) infection [8,9]. Other etiologic factors such as previous surgery, chemotherapy and radiation can also result in activation of tissue reaction, and immunomodulation occurs resulting in proliferation of spindle cells and plasma cell infiltration [7,9]. In our patient the previous spontaneous expulsion of intrauterine device after a long period of permanent implantation might be the etiologic factor.

Commonly, the clinical presentation of IPT reflects mass effect and can be accompanied by symptoms and signs of inflammation such as fever, weight loss, and a variety of laboratory abnormalities such as leukocytosis, increase in erythrocyte sedimentation rate and anemia (in 15-30% of the cases) [10,11]. The laboratory and imaging findings are not specific to IPT, creating a diagnostic dilemma. Frequently, CT demonstrates an invasive aggressive mass with no findings specific to IPT [2]. After preoperative diagnostic work up, surgical excision of the mass and histopathological study are necessary to exclude malignancy.

The clinical presentation, laboratory and imaging findings in our case were consistent with those reported from other authors.

Histopathological identification can often be very difficult. Frozen section may be inconclusive. FNA is difficult to confirm a pathological diagnosis because of an inadequate specimen.

The histological appearance of IPT of any origin is similar [11]. Typical findings include myofibroblastic proliferation and lymphoplasmacytic infiltration with variable degree which is distributed among the tumor cells in myxoid or hyalinized stroma. Three architectural patterns have been described: hypocellular, fascicular and sclerotic. No nuclear atypia or necrosis is present [11-14].

AFIP reviewed a significant number of these tumors located in the abdomen and pelvis and concluded that actually they might be fibrosarcomas with a prominent inflammatory component, simulating pseudotumor [1]. They were prevalent in the retroperitoneum, mesentery, mediastinum and peritoneal surfaces of the abdomen. In the study of 38 cases, 37% had at least one local recurrence, and 11% had histologically proven metastases, commonly of the lungs and brain. The histopathological diagnosis of IPT does not entirely exclude the possibility that some of these tumors may harbor occult fibrosarcomas [5,13]. Montgomery et al. [7] in a study with 46 cases of IMT of the urinary tract reported that a separate IMT was found incidentally in a cystectomy specimen performed for urothelial carcinoma. In 2 cases of IMT a specimen showed sarcomatoid carcinoma with high grade urothelial carcinoma accompanied with separate fragments of IMT.

Several authors reported IPT originating from the uterus and treated by surgery. In 6 cases the IPT was located in corpus uteri [3] and in 2 cases IPT was identified in the cervix [15,16]. IPT of the uterus grew as polypoid masses in the lower part of uterine corpus and prolapsed through the cervical os or as bulky myometrial mass with focally irregular borders and infiltrated the endometrium, parametrium or cervical stroma. Gucer et al. reported IPT of the uterine cervix with bilateral parametrial involvement causing hydroureteronephrosis [16].

In our case, IPT was located in the pelvis, in the region of the reproductive system, involving adjacent structures, causing hydroureteronephrosis, while mutilating radical resection was not preferable, though complete resection of the tumor is the treatment of choice.

IPT of the uterus can easily be confused with various other mesenchymal tumors, particularly smooth muscle neoplasms [5,6]. Previous reports analyzed histological and immunohistochemical features that distinguish IPT from neoplasms. Rabban et al. [3] in a clinicopathologic study of 6 cases analyzed the features of uterine inflammatory myofibroblastic tumors to distinguish them from aggressive mesenchymal tumors. Immunohistochemical expression of ALK (anaplastic

lymphoma kinase) was present in the cytoplasm of IMT cells, while no ALK expression was identified in uterine leiomyoma, leiomyosarcoma, carcinosarcoma and endometrial stromal sarcoma [12]. Various expression of ALK can be seen depending on the anatomic site of IMT. Less than 10% of IMT involving extremities express ALK, whereas pulmonary, gastrointestinal, peritoneal and urinary bladder IMT express ALK in 45, 60, 100 and 71%, respectively [12,14,17].

Immunoreactivity to anti-actin antibody can show the nature of the spindle cells and can be a helpful marker. Gucer et al. [16] showed no reactivity for actin, but Rabban et al. [3] showed moderate, strong and diffuse actin immunoreactivity in 2 of 6 cases. Also Montgomery et al. [7] revealed focal actin reactivity in 92% of the cases. Desmin expression was absent, or focal and weak, in most reports of various authors [3,7]. S-100 expression, CD34 and LCA were negative in spindle cells in most of the tested cases in previously reported studies.

In our case IPT cells were positive for smooth muscle actin and vimentin, focal positivity was found for cytokeratin MNF116, negative staining was found for S-100 and desmin, while inflammatory cells were positive for LCA and CD68. In the vessel walls the anti-CD34 was positive. We strongly supposed that, owing to the localization of the lesion, clinical data and diagnostic imaging, the origin of IPT was the uterus, but histological examination couldn't confirm it since radical resection was not carried out.

Studies of chromosomal abnormalities and monoclonality of the cells have shown the biological heterogeneity of ITP. Limited studies in pediatric patients suggest that cytological atypia and DNA aneuploidy may be associated with poor prognosis [6,18,19]. Patients with aneuploid lesions may have local recurrences or distant metastases, while diploid lesions are less aggressive without potential of recurrence or metastasis [5,20].

Azuno et al. [10] found an overproduction of interleukin (IL)-6 in an inflammatory myoblastic tumor of the uterus. The serum concentrations of several inflammatory cytokines were estimated; only IL-6 was high and dropped to normal 2 weeks after surgery. The disappearance of symptoms and fall of serum IL-6 concentration after treatment suggest that IL-6 plays an important role in the mechanism of evoking symptoms.

In all cases, complete removal of the tumor remains the optimal treatment. If ITP is histologically proven, a policy of "wait and see" can be recommended only for patients who may not tolerate radical resection for any reason.

Close clinical follow-up is recommended for early identification of local recurrence, as some of these benign tumors may harbor occult fibrosarcomas. Clinical and laboratory parameters such as erythrocyte sedimentation rate, hematocrit, serum immunoglobulins, and body temperature can be valuable in monitoring. Periodic imaging, with quarterly to semiannual CT or MRI, is recommended.

In conclusion, we presented a case with locally advanced IPT of the pelvis and reproductive system treated with medical management without surgery. For IPT, surgical resection and appropriate imaging follow-up is the recommended strategy, as some of these lesions may harbor occult sarcomas. Immunohistochemical features including positive immunoreactivity for actin and negative for desmin and presence of ALK can be of diagnostic value in distinguishing IPT from malignant conditions.

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