



A Review on Inflammatory Myofibroblastic Tumour of the Prostate Gland: An Update

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Abstract

Inflammatory myofibroblastic tumour of the prostate gland (IMFTP) is uncommon. IMFTP is a rare disease which mimics other types of prostatic lesions. Microscopic examinations of IMFTPs tend to show: myxoid lesions, slightly atypical-looking spindle fibroblastic cells within a background of granulation-tissue, vascularity and inflammatory cells, rare mitoses and no evidence of atypical mitosis. The tumours exhibit positive staining for vimentin, smooth muscle actin, as well as CD68 which is exhibited in histiocytes. IMFTPs have been treated by TURP, open prostatectomy, and total cystectomy with prostatectomy. Most IMFTPs have not recurred after surgical treatment but a case of recurrence with distant metastasis and subsequent death has been reported which would indicate that IMFTPs represent a spectrum of neoplasms that exhibit most commonly a benign behaviour but some of them are malignant hence IMFTPs must be carefully followed. The recent illustration of anaplastic lymphoma kinase (ALK) by means of immunohistochemistry in most cases of IMFTs and a report of the development of metastasis and subsequent death from metastatic IMFTP would support a postulate that inflammatory myofibroblastic tumour is a neoplastic process. Through reports of more cases of IMFTPs, eventually a consensus opinion would be formed regarding the best treatment option(s) and the pathological features that would predict aggressive biological behavior.

Key words: Inflammatory myofibroblastic tumour of prostate; pseudo-sarcomatous fibromyxoid tumour of prostate; inflammatory pseudo-tumour of prostate; spindle fibroblastic cells; atypical mitosis; vimentin; smooth muscle actin; CD68.

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Introduction

1.1 Inflammatory myofibroblastic tumours (IMFTs) are lesions which have been sporadically reported in various organs including the lungs, heart, liver,

vagina, kidneys, as well as other organs. [1] [2] [3] The terminology of “inflammatory pseudotumor” was first coined by Umiker and Ivensen in 1954 in the description and report of 4 cases involving the lung. [1] [2] Roth [4] in 1980 described “reactive pseudosarcomatous response” in the urinary tract which has been stated to be the first case of inflammatory fibromyoblastic tumour involving the genitourinary tract to be reported [1]. Hafiz et al. [5] described the first case of inflammatory myofibroblastic tumour of the prostate gland in 1984. In view of the rarity of inflammatory myofibroblastic tumour of the prostate gland, it would be envisaged that most clinicians would be unfamiliar with the biological behaviour of the disease. The ensuing literature review on inflammatory myofibroblastic tumour of the prostate gland (IMFTP) which also discusses few other diseases that may mimic IMFTPs is divided into two parts: (A) overview and (B)

Miscellaneous narrations and discussions from some reported cases of IMFTs.

Aim: 2.1 To Review the literature on IMFTs and some of the differential diagnoses

Method

Google, PUB MED and Google scholar data bases were searched. The key words used included: inflammatory myofibroblastic tumour of prostate; inflammatory myofibroblastic tumour of prostate; pseudo-sarcomatous fibromyxoid tumour of prostate; inflammatory pseudo-tumour of prostate. All in all 48 references were identified which were used for the review.

Results/ Literature review

4.1 [A] Overview

4.1.1 General Statements

A number of terminologies have been used for Inflammatory Myofibroblastic Tumour (IMFT) including: pseudo-sarcomatous fibromyxoid tumour, inflammatory pseudo-tumour [6].

Inflammatory myofibroblastic tumour of the prostate gland (IMFT) mimics post-operative spindle cell nodule but in IMFT there tends to be no history of previous trans-urethral resection of the prostate gland. [6].

It has been stated that IMFT is a rare lesion which mimics sarcoma or sarcomatoid carcinoma [6] [7].

Flow cytometry studies of IMFTs tend to exhibit DNA diploidy features and low S phase fraction [6] [7].

Even though IMFT of prostate gland (IMFT) may be localized to the prostate gland at times the mass lesion may be seen as a mass involving the urinary bladder and the prostate gland and in such situations it could be difficult in establishing whether the tumour is an IMFT of the prostate gland (IMFT) that had invaded the urinary bladder or the tumour mass is an inflammatory myofibroblastic tumour of the urinary bladder (IMFTUB) which had invaded the prostate gland. [8]

On the whole IMFTs tend to portend a benign biological behaviour [6] [7].

Roth [4] in 1980 described a spindle cell lesion which was located in the urinary bladder and used the terminology “reactive pseudosarcomatous response”.

[3] [4] Hafiz and associates [5] described a lesion in the prostate gland which was similar to the one described by Roth. Similar types of tumorous lesions have also been reported in the genito-urinary tract including the prostate gland. [3]

Other cases of lesions that could be called IMFTs involving other organs of the genitourinary tract have been reported sporadically in the literature (see bladder for bladder [9] [7] [10] [11]); ureter, [12]; vagina [13]; and urethra [14]; for examples)

Tsuzuki and associates [11] reported an expression of anaplastic lymphoma kinase (ALK-1) in inflammatory myofibroblastic tumours of the urinary bladder. [3]. Morris et al. [15] had earlier on identified the ALK gene in anaplastic large-cell lymphoma carrying the t (2:5) (p23;q35) translocation [3]

4.2 Pathogenesis

It has been stated that the pathogenesis of pseudosarcomatous fibromyxoid tumours (inflammatory myofibroblastic tumours) is not known and that in majority of cases that had been reported the frequent associations had been smoking, previous instrumentations, and previous surgery. [3]

4.3 Epidemiology

IMFTs of the prostate gland have been reported in men whose ages have ranged from 42 years to 80 years [8] [16] [17] [18]

4.4 Presentation

IMFTs may present with lower urinary tract symptoms or retention of urine

4.5 Clinical Examination Findings

Digital rectal examination may reveal any of the following which are not specific to IMFT:

- A small benign feeling prostate without any palpable nodule
- An enlarged benign feeling prostate
- An enlarged rubbery prostate
- An enlarged prostate which may be associated with a nodule or nodules which may be firm
- An enlarged elastic feeling prostate

4.6 Laboratory Investigation findings

4.6.1 Microbiology Investigation

- Urinalysis, as well as urine microscopy and culture are basic tests that are done as part of the initial assessment of the patient so that if there is any evidence of urinary tract infection it is treated before any invasive procedure is undertaken on the patient including cystoscopy, trans-urethral resection of prostate, prostate biopsies or open prostatectomy.
- MRSA screening of specimens obtained from the groin and axillar is undertaken pre-operatively as part of the initial assessment.

4.6.2 Haematological Investigations

Full blood count and coagulation screen are basic haematological tests that are undertaken as part of the assessment of the patient but these are not specific for the diagnosis of IMFT but if any anaemia or haematological abnormality is detected it can be corrected as part of the general management of the patient.

4.6.3 Biochemistry Investigations

- Serum urea and electrolytes, serum glucose, and liver function tests are basic laboratory investigations that are carried out as part of the basic assessment of the patient. Any biochemical derangements found can be corrected prior to the treatment of the patient. If there is retention of urine and kidney injury, insertion of a urethral catheter may result in improvement of renal function but on the whole the initial renal function may be normal.
- Serum prostate specific antigen (PSA) level assessment is a routine assessment in the investigation of patients with lower urinary tract symptoms and enlarged prostate glands. The PSA level may be normal in most cases of IMFT but the serum PSA level may be raised in cases of associated benign of the prostate gland or associated adenocarcinoma of prostate or prostatitis or urinary tract infection or following urethral catheterization for retention of urine.

4.7 Radiological imaging findings

4.7.1 Ultra-sound scan (see [3] for example)

- Ultrasound scan of renal tract and pelvis is a useful radiological assessment which is undertaken and this would show whether the

upper renal tract is normal or there is hydronephrosis; it would also show whether or not there is trabeculation or protrusion of the prostate into the urinary bladder or an additional lesion in the urinary bladder. The ultrasound characteristics and size of the prostate gland can be assessed to see if the prostatic lesion or lesions are iso-echoic, hypo-echoic, hyper-echoic or of mixed echogenicity.

- Trans-rectal ultrasound scan of the prostate gland is useful for the assessment of the prostate gland for taking biopsies of prostate including obtaining specimens from a prostatic nodule for histological examination. Histological examination in cases of IMFT may show features characteristics of IMFT or the features of the specimen obtained may be interpreted as non-specific inflammation.

4.7.2 Computed Tomography (CT) Scan (see [3] for example)

- CT Scan of renal tract / Abdomen and pelvis is a useful investigation for the assessment of the prostate gland to determine the size and imaging characteristics of the prostate, the urinary bladder, the upper renal tracts as well as presence or absence of enlarged regional nodes or any abnormality or metastasis in any organ within the abdomen and pelvis. When a diagnosis of IMFTP is made CT scan of thorax, abdomen and pelvis would be a useful imaging modality for the follow-up assessment of the patient to exclude any local recurrence or distant metastasis.

4.7.3 Magnetic Resonance Imaging (MRI) Scan (see [3] for example)

MRI Scan of renal tract / Abdomen and pelvis is a useful investigation for the assessment of the prostate gland to determine the size and imaging characteristics of the prostate, the urinary bladder, the upper renal tracts as well as presence or absence of enlarged regional nodes or any abnormality or metastasis in any organ within the abdomen and pelvis. When a diagnosis of IMFTP is made MRI scan of thorax, abdomen and pelvis would be a useful imaging modality for the follow-up assessment of the patient to exclude any local recurrence or distant metastasis.

4.8 Macroscopic Features

Gross examination of IMFTPs may show fleshy and somewhat gelatinous mass of the prostate gland which has a white tan surface and no evidence of necrosis or haemorrhage. [18] Macroscopic

examination of IMFTs may show a solid looking prostate with fibromuscular capsule with a grey-tan colour [44]

4.9 Microscopic Features

Microscopic examinations of IMFTs tend to show:

- Myxoid lesions [6]
- Proliferation of spindle fibroblastic cells, with slightly atypical look, within a background of granulation-tissue vascularity and inflammatory cells [6]
- Rare evidence of mitoses [6] and no evidence of atypical mitosis [6]

4.10 Immunohistochemistry

4.10.1 Positive Staining

Immunohistochemistry of IMFT tends to show positive staining of the tumour with:

Vimentin [6] [7]

Smooth muscle actin [6] [7]

CD68 which is exhibited in histiocytes [6]

4.10.2 Negative Staining

Immunohistochemistry of IMFT tends to show negative staining of the tumour with:

S100 [6] [7]

Desmin [6] [7]

Myoglobin [6] [7]

Keratin [6] [7]

4.11 Electron Microscopic Features

Electron microscopic examination of IMFTs, tend to show fibroblastic and myofibroblastic cell features. [6] [7]

4.12 Flow-Cytometry Studies

Flow cytometry DNA content studies may show tumours that had uniform DNA diploidy and a low S phase fraction as observed by Roy and associates. [7]

4.13 Differential Diagnoses

Differential diagnoses of IMFT include: Sarcomatoid urothelial carcinoma, leiomyosarcoma, and rhabdomyosarcoma, in view of the mesenchymal proliferation in the tumour. [3] [16] Post-operative spindle cell nodule which was first described by Proppe and associates, [3] [19].

It has been documented that sarcomas tend to exhibit marked cytological atypia, atypical mitotic figures, as well as non-myxoid areas that have marked increased cellularity in the spindled cell areas. The aforementioned findings would allow for a diagnosis

of sarcomatoid carcinoma. [3] Very few cases of pseudosarcomatous tumours have been reported to be active mitotically. [3] [20]

It has been stated that positive immunohistochemistry study reactivity for cytokeratin, is regarded as a definitive feature for the diagnosis of sarcomatoid carcinoma; nevertheless, majority of pseudosarcomatous fibromyxoid tumours could exhibit pan-cytokeratin reactivity. [21]

4.14 Treatment (see section B for various examples of treatment)

There is no consensus opinion on the management of IMFTs but they have been treated by:

(a) Trans-urethral resection of the lesion / trans-urethral resection of prostate

(b) Open supra-pubic prostatectomy

(c) Trans-urethral resection of prostate plus urinary bladder lesion, as well as cystectomy and ileal conduit construction with pelvic lymphadenectomy

(d) Total cystectomy and prostatectomy plus construction of ileal conduit

4.15 Outcome

In majority of cases of IMFTs the prognosis has been good without any recurrence of the disease following treatment of the disease by means of trans-urethral resection of the lesion in the form of trans-urethral resection of the prostate or by means of suprapubic prostatectomy or total cystectomy and prostatectomy. However, Liu et al. [18] reported a patient who died as a result of metastatic pulmonary disease 30 months after undergoing suprapubic prostatectomy. There is no consensus opinion on which types of IMFTs would be associated with disease recurrence or death following treatment. Furthermore there is no consensus opinion regarding how to decide on the indications for deciding which patients should be treated by the various treatment options including: trans-urethral resection of prostate alone, suprapubic prostatectomy alone, total prostatectomy and cystectomy. There is also no opinion of the characteristic features of IMFTs which would indicate the need for adjuvant therapy.

4.16 [B] Miscellaneous narrations and

discussions from some reported cases.

Roy et al. [7] undertook a retrospective study which included nine pseudo-sarcomatous fibromyxoid

tumours which had involved the urinary bladder and the prostate gland in order to determine the characteristic peculiarities of the tumours that would enable correct and accurate diagnosis of the disease. The patients whose mean age was 48.7 years included for men and five women. Microscopic examination of the tumours showed myxoid lesions which had a proliferation of spindled fibroblastic cells within a background of granulation tissue-vascularity and inflammatory cells. Microscopic examination of the tumours also showed that mitosis was infrequent and there was evidence of any atypical forms of mitosis. Roy et al. [7] also reported that immunohistochemistry studies of the tumours had exhibited positive immunohistochemical staining with vimentin and smooth muscle actin and that the tumours exhibited negative immunohistochemical staining S-100 protein, desmin, myoglobin, and keratin. Roy et al. [7] additionally reported that ultrastructurally, the tumours exhibited myoblastic and fibromyoblastic cell features and that flow cytometry DNA content studies had shown that the tumours had uniform DNA diploidy and a low S phase fraction. With regard to outcome, Roy et al. [7] reported that pursuant to a mean follow-up of 4.8 years after treatment, all the patients were alive and well with no evidence of disease. In comparison with the control group of sarcomatoid carcinomas and sarcomas of the urinary bladder and prostate gland, the tumours occurred in older patients, and the tumours had more frequent mitoses with atypical forms, tumour type necrosis, and immunostaining profiles that were different from the immunostaining profiles of the nine pseudo-sarcomatoid fibromyxoid tumours; the sarcomatoid carcinomas and the sarcomas of the bladder and prostate were predominantly aneuploid, or diploid with high S-phase fraction. Roy et al. [7] concluded that awareness of the clininopathological and the biological characteristics of these lesions is necessary to ensure that accurate diagnosis of the disease and to ensure that unnecessary radical treatment of these lesions are prevented.

Cespedes et al. [22] reported a 42-year-old white man, who presented with urinary obstruction. His radiological imaging showed a 4 cm mass in the prostate gland which had extended into the urinary bladder. He had trans-rectal biopsies of the prostatic mass and pathological examination of the specimen showed features sarcomatoid histology with atypical spindled cells which were adjudged to be suspicious for sarcoma. He underwent trans-urethral resection of

the prostate gland and histological examination of the resected specimen showed features which was adjudged to be consisted with a benign fibromyxoid lesion with spindle cell proliferation. At his one-year follow-up he had been voiding well with no evidence of recurrence. Cespedes et al. [22] concluded that the clinical manifestation and histological features of the lesion were consistent with pseudosarcomatous fibromyxoid tumour which is a rare benign disease which had previously been mistaken for a malignant sarcoma of the prostate gland and that it is important for the pathologist to recognize this benign disease entity in order not to perform a radical treatment procedure.

Jensen et al. [23] in 2003, reported a man who presented with lower urinary tract symptoms who underwent another trans-urethral resection of his prostate gland. Pathological examination of the resected prostate, revealed features, adjudged to be consistent with the diagnosis of pseudosarcomatous fibromyxoid tumour of the prostate.

Bencheckroun et al. [24] in 2003 reported a case of pseudosarcomatous fibromyxoid tumour of the prostate gland. They stated at that time that to their knowledge, the disease was benign and that the differential diagnosis, include sarcoma of the prostate gland. They also stated that diagnosis of the disease is based upon histological examination of the specimen and its treatment is surgical.

Perez Garcia et al. [25] in 2004 reported a 67-year old man who was catheterized for retention of urine and who subsequently failed trial without catheter. His rectal examination revealed a small benign feeling prostate without any evidence of a palpable nodule. His serum prostate specific antigen (PSA) level was 1.01 ng / ml. He underwent trans-urethral resection of prostate and pathological examination of the specimen showed a hyper-cellular stroma which had inflammatory infiltrate and myxoid stromal background with slightly atypical fusiform cells that were distributed peri-vascularly. Immunohistochemistry studies of the resected specimen showed that the fusiform cells had stained positively with vimentin and the histiocytes in the lesion had also stained positively with CD68; nevertheless, the immunohistochemistry study showed negative staining with cytokeratin. Based upon the pathological examination findings, a diagnosis of prostatic inflammatory pseudotumor was made. Perez Garcia et al. [25] concluded that even

though IMFT is rare, it is important that IMFT which tends to be a benign lesion should be considered in order to avoid unnecessary aggressive radical complementary treatments.

Kuramoto et al. [26] in 2003 reported a man with a history of hematospermia and chronic prostatitis who was presented with voiding difficulties. He had urethroscopy which revealed a large non-papillary tumour in the prostatic urethra and two calculi in the urinary bladder. He had magnetic resonance imaging (MRI) scan which showed a 7-cm mass in the prostate gland which was protruding towards the urinary bladder and the rectum. He underwent trans-urethral resection of the prostatic lesion and cystolithotripsy. Pathological examination of the resected prostatic lesion, showed a benign looking fibromuscular lesion which had spindle cell proliferation adjudged to be consistent with a diagnosis of inflammatory pseudo-tumour. He was voiding well at his five-month follow-up. Kuramoto et al. [26] stated prior to the publication of their paper in 2005, only 10 cases of IMFT had previously been reported in the English and Japanese literature and that the presentation of IMFT may be similar to the presentation of malignant sarcoma of the prostate gland. Kuramoto et al. [26] further stated that accurate diagnosis of IMFT which tends to be a benign process should be accurately diagnosed in order to avoid radical prostatic surgery.

Zhang et al. [27] reported a 62-year-old man who was referred twice to their hospital because of recurrence of dysuria. He had been diagnosed as having benign prostatic hyperplasia (BPH) and he had on two previous occasions, undergone trans-urethral resection of the prostate gland (TURP). Pursuant to his TURP, he had developed frequent recurrence of dysuria for which he was referred and upon admission he underwent cystoscopy and trans-urethral resection of prostate (TURP) and trans-urethral resection of urinary bladder tumour (TURBT). Pathological examination of the specimen showed chronic inflammation of the bladder, papillary hyperplasia with mild dysplasia in the regional urothelium and inflammatory myofibroblastic tumour of the prostate gland. Six months subsequently, he re-presented with recurrence of dysuria. He had a computed tomography scan which showed a large mass in the urinary bladder. He underwent laparoscopic radical cystectomy and construction of ileal conduit urinary diversion and pelvic lymph adenectomy. Pathological examination

of the specimen showed features which were adjudged to be confirmatory of inflammatory myofibroblastic tumour of the prostate gland with involvement of the urinary bladder but the regional lymph nodes were not involved. At his 11-month follow-up, there was no evidence of local recurrence or distant metastasis. Zhang et al. [27] concluded that inflammatory myofibroblastic tumour of the prostate gland is liable to recur and even invade the urinary bladder and that they would recommend radical resection for patients with large and recurrent tumours furthermore close follow-up is warranted in such cases.

Zhang et al. [27] in 2011 reported another case of inflammatory myofibroblastic tumour of the prostate gland of which the details are not available to the author.

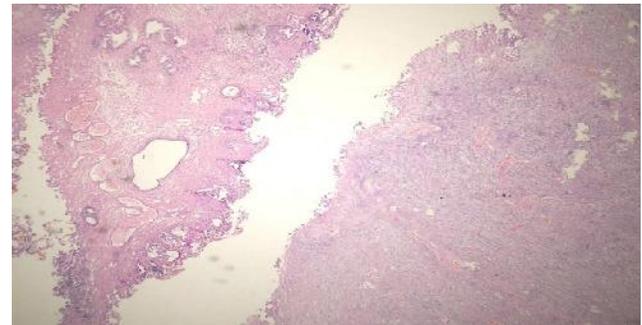


Figure 1: Overview of the dominating structures (haematoxylin-eosin staining original magnification x 100) Reproduced from Atis G, Gurbuz C, Kiremit M C, Guner B, Zemheri E, Caskurlu T. (2011) Pseudosarcomatous Fibromyxoid Tumour of the Prostate. The ScientificWorldJOURNAL TSW Urology 11; 1027 – 1030 ISSN 1537-744X DOI: 10.1100/tsw.2011.87 with Permission from Atis G on behalf of the authors. The copyright to the figures is retained by the original authors and any further use or reproduction of the figure would require a fresh copyright permission from the original authors.

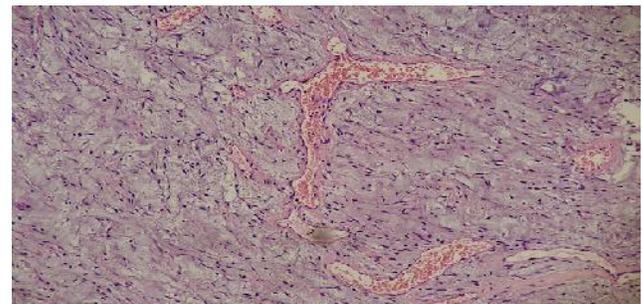


Figure 2: An image of spindle cells in a myxoid stroma (haematoxylin - eosin staining; original magnification x 100) Reproduced from Atis G, Gurbuz C, Kiremit M C, Guner B, Zemheri E, Caskurlu T. (2011)

Pseudosarcomatous Fibromyxoid Tumour of the Prostate. The ScientificWorldJOURNAL TSW Urology 11; 1027 – 1030 ISSN 1537-744X DOI: 10.1100/tsw.2011.87 with Permission from Atis G on behalf of the authors. The copyright to the figures is retained by the original authors and any further use or reproduction of the figure would require a fresh copyright permission from the original authors.

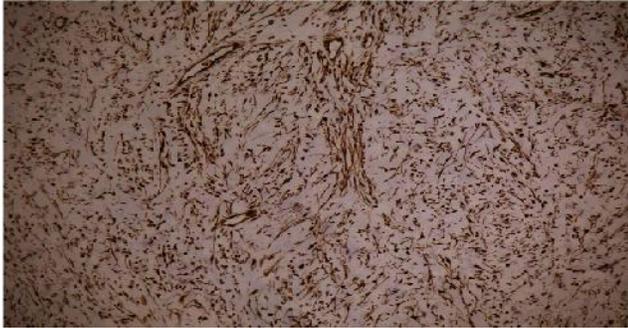


Figure 3: Staining for vimentin (original magnification x 100) Reproduced from Atis G, Gurbuz C, Kiremit M C, Guner B, Zemheri E, Caskurlu T. (2011) Pseudosarcomatous Fibromyxoid Tumour of the Prostate. The ScientificWorldJOURNAL TSW Urology 11; 1027 – 1030 ISSN 1537-744X DOI: 10.1100/tsw.2011.87 with Permission from Atis G on behalf of the authors. The copyright to the figures is retained by the original authors and any further use or reproduction of the figure would require a fresh copyright permission from the original authors.

Atis et al. [3] reported a 61-year-old man who presented with acute retention of urine for which he was catheterized. He subsequently failed trial without catheter. He did not have any history of instrumentation, radiotherapy of the pelvis or previous malignancy. He had smoked for a period of 40 years. He had rectal examination which revealed an enlarged prostate gland without any evidence of nodularity. His serum prostate specific antigen (PSA) level was 1.73 ng / ml. He had ultrasound scan of renal tract which revealed normal upper renal tracts and normal urinary bladder. He underwent trans-urethral resection of prostate (TURP). Gross examination of the resected prostate revealed a 20 gram resected prostate which had gross nodular characteristics. Microscopic examination of the specimen revealed a tumour which consisted of spindled cells arranged in a myxoid background with many inflammatory cells (see figures 1 and 2). The microscopic examination also showed rare mitotic figures which did not have any significant atypia. Immunohistochemistry studies of the tumour revealed positive staining for vimentin (see figure 3),

and negative staining for cytokeratin and CD34. The proliferation activity of the tumour using Ki-67 was low with Ki-67 level lower than 1%. Post-operative the patient voided normally after removal of his urethral catheter and he had remained well with no evidence of disease over a period of one year-follow-up.

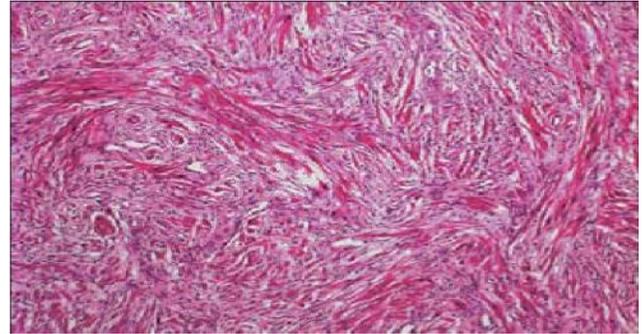


Figure 4: Overview of the stromal structures (H&E staining, original magnification x 10). Reproduced from Toksoz S, Kervancioglu E, Atilgan A O, Güvel S. Pseudosarcomatous fibromyxoid tumor of the prostate revealed on suprapubic prostatectomy Cent European J. Urol. 2012; 65(2): 98 – 99. DOI: 10.5173/ceju.2012.02.art12. Epub 2012 Jun 12 with copy right permission under the Creative Commons Attribution License Copy Right: Polish Urological Association This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-commercial 3.0 Unported License, permitting all non- commercial use, distribution, and reproduction, in any medium, provided the original work is properly cited.

Toksoz et al. [28] reported a 70-year-old man who presented with lower urinary tract symptoms of two years duration. He had rectal examination which revealed an enlarged soft benign feeling prostate gland. His post-void residual urine volume was 220 ml. His serum PSA level was 5.02 ng / ml. He had a prostate biopsy elsewhere and histological examination of the specimen was adjudged to be consistent with benign hypertrophy of the prostate. His prostate gland was found on pelvic ultra-sound scan to be 200 grams. He had cystoscopy which revealed a normal anterior urethra, a large protruding prostate and a normal urinary bladder. He underwent suprapubic prostatectomy and had remained well and voiding well at his 2-year follow-up. Microscopic examination of the prostatectomy specimen showed that the prostatic tissue consisted of hyoid tissue which contained spindle cell proliferations. There was evidence of inflammatory cells and hyalinization of vascular walls. Within the limited periphery of the gland small gland proliferations were observed which

were immuno-reactive with HMWCK and p63 antibodies in the basal cells (see figures 4 to 7). Immunohistochemistry study of the specimen showed positive staining for smooth muscle actin by the spindle cells (see figure 3). Immunohistochemistry of the spindle cells showed negative staining for CD34. The characteristics of prostate, was adjudged to be consistent with the diagnosis of pseudosarcomatous fibromyxoid tumour of the prostate gland (IMFTP).

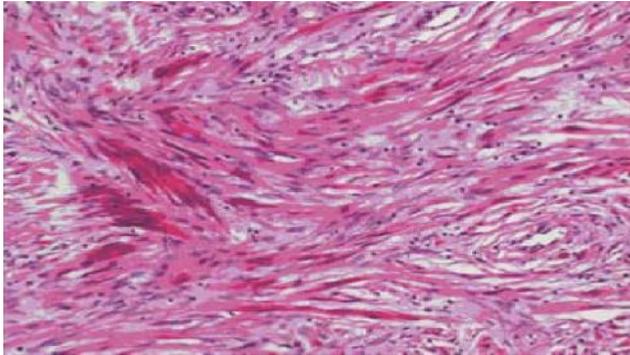


Figure 5: Myxoid stroma with spindle cell proliferation, H&E staining (original magnification x 20). Reproduced from Toksoz S, Kervancioglu E, Atilgan A O, Güvel S. Pseudosarcomatous fibromyxoid tumor of the prostate revealed on suprapubic prostatectomy Cent European J. Urol. 2012; 65(2): 98 – 99. DOI: 10.5173/ceju.2012.02.art12. Epub 2012 Jun 12 with copy right permission under the Creative Commons Attribution License Copy Right: Polish Urological Association This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-commercial 3.0 Unported License, permitting all non- commercial use, distribution, and reproduction, in any medium, provided the original work is properly cited.

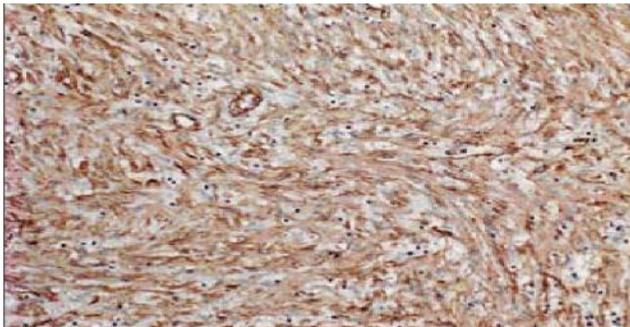


Figure 6: Staining for smooth muscle actin (original magnification x 10). Reproduced from Toksoz S, Kervancioglu E, Atilgan A O, Güvel S. Pseudosarcomatous fibromyxoid tumor of the prostate revealed on suprapubic prostatectomy Cent European J. Urol. 2012; 65(2): 98 – 99. DOI: 10.5173/ceju.2012.02.art12. Epub 2012 Jun 12 with copy right permission under the Creative Commons Attribution

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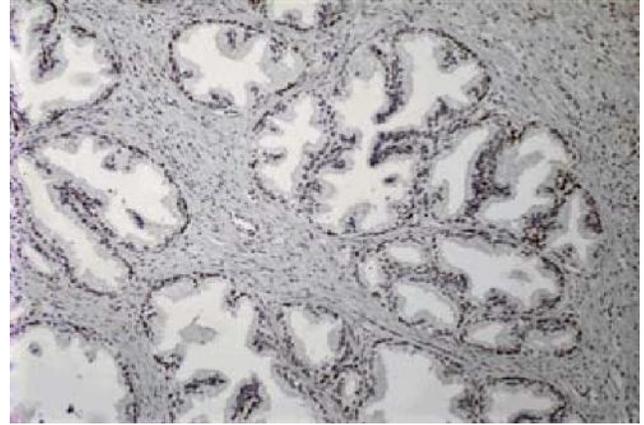


Figure 7: Staining for p63 (original magnification x 10). Reproduced from Toksoz S, Kervancioglu E, Atilgan A O, Güvel S. Pseudosarcomatous fibromyxoid tumor of the prostate revealed on suprapubic prostatectomy Cent European J. Urol. 2012; 65(2): 98 – 99. DOI: 10.5173/ceju.2012.02.art12. Epub 2012 Jun 12 with copy right permission under the Creative Commons Attribution License Copy Right: Polish Urological Association This is an Open Access article distributed under the terms of the Creative Commons Attribution Non-commercial 3.0 Unported License, permitting all non- commercial use, distribution, and reproduction, in any medium, provided the original work is properly cited.

Kocer et al. [1] reported a 63-year-old man who presented with lower urinary tract symptoms and pollakiuria of 2 years duration. Despite being on tamsulosin and finasteride his urinary tract symptoms persisted. He did not have any previous history of an operation or instrumentation. His serum PSA level was 1.22 ng / ml. He had ultrasound scan which showed the size of the prostate gland to be 186 cc. He had a rectal examination which showed an enlarged prostate which felt clinically benign. He had urethroscopy which showed he had a longer than usual prostatic urethra and enlargements of the median lobe and lateral lobes of the prostate gland. He had urodynamic assessment which showed a high pressure low flow diagnostic of bladder outflow obstruction. He underwent suprapubic prostatectomy with a provisional diagnosis of a very large benign prostatic hyperplasia. Macroscopic examination of the prostate which was separated into two because of its size revealed that the prostate gland had a smooth surface and was grey-white in colour. The prostate

gland weighed 141 grams. The cut surfaces of the prostate gland were solid grey-white with a fibrillary appearance. Microscopic examination of the specimen showed a well demarcated lesion which consisted of spindle cells that formed long, transecting bundles, which was pushing but not invading the normal tissue of the prostate gland. There was evidence of focal nuclear hyperchromasia and pleomorphism. Mitosis was rare. There was no evidence of necrosis or atypical mitotic figures. The microscopic examination also showed foci of mononuclear inflammatory response which included plasma cells and myxoid degeneration. Immunohistochemistry studies of the prostate showed positive staining for vimentin and smooth muscle actin; as well as focal positive staining for anaplastic lymphoma kinase – 1 (ALK-1). However, immunohistochemistry studies showed negative staining for S-100 and pancytokeratin. ALK positivity was confirmed by means of fluorescent in-situ hybridization (FISH) with DAKO split signal (FISH) probe. Based upon the aforementioned pathology findings a diagnosis of inflammatory myofibroblastic tumour of the prostate gland was made. The patient at the time publication of the case report has been followed-up for five years with no evidence of recurrence.

Liu et al. [18] in 2013 reported an 80-year-old man with a 3-months history of chronic retention of urine which was treated by means of oral medication who presented with acute retention of urine which required urethral catheterization. He did not have any history of haematuria, urinary trauma or infection. His investigations including full blood count, serum biochemistry urinalysis and urine culture were normal. His serum PSA level was 5.8 ng/ml. He had a rectal examination which revealed an enlarged prostate gland with elastic consistency and firm nodules. He had ultra-sound scan of the renal tract which revealed a hypo-echoic enlarged mass within the prostate gland which measured 6.3 cm x 5.5 cm. He had computed tomography (CT) scan of abdomen and pelvis which showed a 6.5 cm x 5 cm x 5.6 cm irregular iso-dense mass of 35 Hounsfield units which had extended into the urinary bladder. He also had magnetic resonance imaging (MRI) scan which showed a mass in the prostate gland that measured 6 cm x 5.5 cm with low-signal and mixed-signal intensity on an axial T1-weighted image. On the sagittal section scan, the MRI signal within the T2-weighted sequence was observed to be lower in the peripheral zone with evidence of localized mixed-

signal, but on the other hand, the central zone of the prostate gland had a slightly higher signal. There was no evidence of involvement of any local or distant organ on the MRI scan. He had trans-rectal ultrasound-guided biopsy of the prostate and histological examination of the biopsy specimens showed a fibrous lesion which contained inflammatory cells without any evidence of malignancy. Based upon the aforementioned histological findings a pre-operative diagnosis of benign prostatic hyperplasia (BPH) was made. He failed trial without catheter and underwent suprapubic prostatectomy. During the operation, a large and rubbery prostate gland which had extended partly into the urinary bladder was observed. Macroscopic examination of the prostatectomy specimen showed a fleshy and somewhat gelatinous prostatic mass which had a white and tan cut surface with no evidence of necrosis or haemorrhage. Microscopic examination of the specimen showed tumour cells that were mainly arranged in a fusiform pattern with inflammatory infiltrate which consisted of lymphocytes and eosinophils. There was no evidence of nuclear pleomorphism or mitotic figures; however, occasional atypical cells which had large nuclei were observed. Immunohistochemistry studies of the tumour showed positive staining for smooth muscle actin, desmin, and vimentin; however the tumour stained negatively for CD117, CD34, and S100. Based upon the aforementioned pathological findings a diagnosis of inflammatory myofibroblastic tumour of the prostate gland was made. He did not receive any adjuvant treatment. He remained well with no evidence of disease for 12 months. At his 24-months follow-up, he was found to have multiple enlarged lymph nodes within his left groin and he had a chest X-ray which showed multiple lung metastatic tumours. He had lymph node biopsy and histological examination of the biopsy specimen confirmed metastatic inflammatory myofibroblastic tumour (IMFT). The patient refused to have any further treatment and he died 6 months subsequently. Liu et al. [18] stated the following:

- The pathogenesis of IMFT is controversial but some cases of IMFT had been related to an infectious or autoimmune process [29]
- IMFT has been considered to be a benign lesion with classical features like spindle cell proliferation intermingled with inflammatory process. [30]
- Subsequent studies had indicated that the true nature of IMFT is a neoplasm with frequent clonal

alterations in chromosome 2p23, [31] with the potential for local aggressiveness, recurrence, metastasis, as well as malignant transformation. [32] [33]

- In order to avoid designation ambiguity in the terminology of the disease, the current World Health Organization (WHO) classification IMFT is recognized as a neoplasm with the morphological character of proliferating spindle cells admixed with variable amounts of a lymphoplasmacytic infiltrate. [34]

- The differential diagnosis of IMFT includes benign and malignant spindled-cell tumours such as fibrous histiocytoma, fibroblastic/myofibroblastic tumour, and solitary fibrous tumour. Its spindle-cell morphology could be misdiagnosed as both benign reactive processes as well as malignant spindle-cell neoplasm because of their similar morphology.

- With regard to immunohistochemistry features, majority of IMFTs stain positively for smooth muscle actin (SMA), desmin, and cytokeratin. ALK immunohistochemistry study is positive in 40% to 60% of cases.

- There are potential risks of IMFTs to develop metastasis and the potential for malignant transformation, which quite often has been correlative with minimal atypia, prominent nucleoli, increased mitotic figures, and DNA aneuploidy. [35] However, the histological characteristics of IMFT have not correlated well with clinical behaviour. A study by Meis and Enzinger, [36] found that 37% of IMFTs had local recurrence and 11% had developed metastases.

- There is currently no consensus opinion on optimal and efficient of IMFTs. Occasionally IMFTs can undergo spontaneous regression. A variety of medical treatment strategies including chemotherapy, radiotherapy, nonsteroidal anti-inflammatory medications or corticosteroids as well as anti-tumour necrosis factor had been given in order to eradicate IMFTs or to shrink them to a resectable size and configuration. [37] [38] However, complete surgical resection would appear to be the preferred mainstay therapeutic option. The outcomes are controversial hence further studies related to the management of IMFTs would be required. Particularly, incomplete resection of the tumour at times leads to recurrence or progression of IMTs. The development of distant metastasis is uncommon and this occurs in 5% of cases of IMFTs. Additionally, half of the cases that had metastasized had shown atypical features and

especially, ALK-negative IMFTs had been reported to be associated with metastases. [39]

- It has been stated that combination therapeutic modality which comprise of surgery and chemotherapy in the treatment of IMFT may result in a patient being disease free for quite some time. [40]

- With regard to genito-urinary tract IMFTs, it has been reported that treatment which had consisted of steroid and conservative resection therapy had offered an apparent resolution of IMFT. [41] On the other hand, it has been stated that aggressive radiotherapy and chemotherapy are not warranted taking into consideration the indolent and often benign clinical biological behaviour course of most of the cases of IMFTs. [42] Gwynn and Clark had stated that even though recurrence of the disease and malignancy with IMFT in the urogenital tract had been reported, metastases had not been previously reported at the time of publication of their paper.

- In view of the indeterminate biological behaviour of IMFTs, they would recommend continued monitoring of the clinical course of the disease.

Grigorian et al. [43] reported a 66-year-old man who was asymptomatic six months pursuant to robotic radical prostatectomy for prostatic carcinoma and synchronous left radical nephrectomy for renal cell carcinoma. He had surveillance computed tomography scan of abdomen and pelvis which showed a mass in his pelvis. He had a serum PSA test done and PSA was undetectable in his serum. He had MRI scan of abdomen and pelvis which showed a contrast-enhanced heterogeneous mass with central necrosis in his prostatic bed. The mass which measured 4.8 cm x 5.5 cm x 5.0 cm was contiguous with the obturator internus but there was no evidence of lymph adenopathy. He had CT-guided biopsy of the pelvic mass and pathological examination of the specimen showed spindle cells with low mitotic index. The patient's son has a history of neurofibromatosis. Immunohistochemistry studies of the biopsy specimen showed diffuse positive staining for desmin and smooth muscle actin as well as focal positive staining for pan-keratin and S100. The immunohistochemistry study was negative for CD34 and CDK4. Fluorescent in situ hybridization test of the specimen did not demonstrate MDM2 (OMIM 164785) gene amplification. Taking into consideration the fact that it had been noted that inflammatory myofibroxyoid tumour/

pseudosarcomatous fibromyxoid tumour could develop after instrumentation / surgery the findings of such a tumour should not be surprising to clinicians who would usually be expecting and wanting to quickly and urgently exclude recurrence of a malignant tumour when a mass is found after aggressive surgical excision of a malignant lesion. Confirmation of recurrence of the previously excised tumour or the development of a de novo lesion would only be established after biopsy and pathological examination of the recurrent lesion including microscopic and immunohistochemistry studies are undertaken like in the aforementioned case.

Young and Scully [14] in 1987, reported three cases of pseudo-sarcomatous lesions of the genito-urinary tract. The first case was that of a 59-year-old man whose lesion was in his urinary bladder. The lesion consisted of atypical spindle cells that were admixed with inflammatory cells in an oedematous stroma. The second case was that of a lesion was found in the stroma of a hyperplastic prostate gland of a 51-year-old man which was characterized by the presence of atypical mesenchymal cells with large, hyperchromatic nuclei. The third case was that of a 57-year-old woman who had a urethral caruncle which contained many atypical cells in its stroma. The three patients were treated conservatively and they were followed up for periods that ranged between 18 months and 8 years with no evidence of recurrence. Young and Scully [14] stated that knowledge of the various atypical mesenchymal cell proliferations which are encountered in the genito-urinary may prevent the misdiagnosis of a malignant tumour.

Takehima et al. [44] in 1997 reported a 42-year-old man who presented with voiding symptoms and constipation of 8-years duration. His clinical examination and radiological imaging had showed an enlarged mass of the prostate gland for which he underwent total cystectomy and prostatectomy. Gross examination of the specimen revealed that the tumour which measured 14 cm x 13 cm x 11 cm, was solid with a fibromuscular capsule and grey-tan in colour. Microscopic examination of the specimen revealed that the tumour consisted of short spindle-shaped and polygonal cells which had mild to moderate nuclear atypia which were predominantly in the so called 'pattern-less pattern' in a fibrocartilaginous background. The microscopic examination also showed occasional mitoses and furthermore there was evidence of vascular invasion.

Immunohistochemistry studies of the specimen showed that the cells were strongly positive for CD34 and vimentin, and occasionally positive for desmin. The maximum Ki-67 labelling index of the tumour cells was reported to be 4.5% and based upon the pathology examination findings, a diagnosis of solitary fibrous tumour of the prostate gland was made. Takehima et al. [44] stated that to their knowledge their case was the first case of solitary fibrous nodule of the prostate gland to be reported in the English medical literature. It would be argued that in view of the fact that microscopic examination of the specimen showed spindle-shaped cells and immunohistochemistry study for vimentin a differential diagnosis of IMFTP would need to be considered and further immunohistochemistry studies using other immune-staining antibodies to confidently establish the diagnosis of solitary fibrous nodule and that the lesion which mimicked IMFTP on macroscopic and microscopic examination was indeed not an IMFTP.

Pins et al. [45] in 2001 reported 2 cases of solitary fibrous nodule of the prostate gland as follows:

Case 1

The first patient was a 57-years-old man who was found to have a hard prostate gland on digital rectal examination. His serum PSA was 1.2 ng / ml which was within normal range. He had a CT scan which showed a large circumscribed tumour within the prostate gland which appeared to be focally intimate with the bladder neck and filled the pelvis. He underwent urethroscopy which revealed prostatic urethral stenosis which prevented advancement of the cystoscope into the urinary bladder. He had prostate biopsies and microscopic and immunohistochemistry studies of the specimen revealed features adjudged to be diagnostic of solitary fibrous tumour of prostate. He underwent radical prostatectomy with excision of a well delineated prostatic was which had invaded the bladder neck, trigone and pelvic side wall. He was well with no evidence of tumour at his 15-month follow-up.

Case 2

A 73-year-old presented with symptoms of bladder spasms, urinary frequency, urinary urgency and incontinence as well as dysuria. He had rectal examination and intravenous urography which revealed a large contoured mass in the left side of the

prostate which had displaced the urinary bladder. His serum PSA was 3.5 ng / ml. He underwent suprapubic prostatectomy. He presented 19 months post-operatively with erectile dysfunction and urinary frequency. His examination and computed tomography scan which he had 21 months post-operatively did not reveal any evidence of recurrence.

Pins et al. [45] stated that histological examination revealed that both tumours had demonstrated a multi-patterned architecture with various degrees of collagenisation and hemangiopericytoma-like foci, and both of the tumours were shown on immunohistochemistry studies to be composed of CD34 immuno-positive spindled-cells which insinuated themselves between strips of collagen. The tumours with regard to the first case of the 57-year-old man were well circumscribed, and had minimal mitotic activity or pleomorphism; on the other hand, the tumour of the second case of the 73-year-old man was more cellular, less collagenous, as well as it had a more diffuse growth pattern. This tumour also exhibited cytological atypia and high mitotic activity. Pins et al. [44 new 45] stated that solitary fibrous tumour of the prostate gland should be distinguished from other spindle cell tumours that are reported in the prostate gland and that their two reported cases represent the fifth and sixth reported cases of solitary fibrous tissue of the prostate gland to be reported in the literature. It would be argued that solitary fibrous tumour of the prostate gland is a distinct and different disease and should not be included in a review of the literature on IMFTP; nevertheless, because of the rarity of both IMFTP and solitary fibrous tumour of the prostate, there is the need to include a few cases of solitary tumour of the prostate in order to illustrate some of the similarities between the pathological characteristics of both diseases and the need to use careful immunohistochemistry studies to differentiate between both diseases.

Ishii et al. [46] in 2004 reported a 36-year-old man who presented with voiding symptoms. He had retrograde urethrogram and urethroscopy which showed intra-urethral protrusion of the left lobe of the prostate gland which had completely obstructed the prostatic urethra. He had magnetic resonance imaging (MRI) scan which showed the prostatic tumour with intra-vesical protrusion. He had trans-rectal ultra-sound scan-guided biopsy of the prostatic lesion with a provisional clinical diagnosis of leiomyosarcoma of the prostate. Pathological examination of the biopsy specimen showed features

which were consistent with a benign fibrous tumour. He underwent trans-urethral resection of the protruding left lobe of the prostate gland only in order to improve his voiding but to avoid retrograde ejaculation. Pathological examination of the resected specimen showed a dense proliferation of dense spindle cells which did not have any nuclear atypia and that there was no evidence of any mitotic figure. Immunohistochemistry study of the specimen showed positive staining for CD34 and negative staining for alpha-smooth muscle actin and desmin. Based upon the pathology findings, a diagnosis of benign fibrous tumour of the prostate gland was made. The patient was alive and voiding well at his six-year follow-up. Ishii et al. [45 new 46] stated that at the time of publication of their paper only five cases of solitary fibrous tumour of the prostate gland had been reported. Whilst it is known that solitary fibrous tumour is a lesion that is different from IMFTP, because of the rarity of both lesions difficulties may be encountered in differentiating IMFTPs from solitary fibrous tumours of the prostate. However, the immunohistochemistry features can be used to differentiate IMFTP from solitary fibrous tumour of the prostate gland.

Scholtmeijer et al. [47] in 1988 reported an 11-month-old boy who had retention of urine due to fibromatosis. He had cystoscopy which revealed a normal urinary bladder but an impression of enlarged lobes of the prostate gland. He had repeated trans-urethral and trans-perineal biopsies of the prostate and pathological examinations of the specimens showed proliferation of randomly arranged spindle cells in a loose collagenous matrix. Mitotic figures were scarce in the specimens. Scholtmeijer et al. [47] stated the following: Fibrous proliferations of the prostate and urinary bladder are rare. The fibromatoses constitute a group of non-metastasizing fibrous growths that tend to invade the surrounding tissues. The fibromatoses show a wide range of range of histological appearance and biological behaviour, which range from spontaneous regression to aggressive and destructive local growth. They also stated that the histopathological diagnosis of the case was fibromatosis without any further specification and that it was impossible to predict the behaviour of the process. Scholtmeijer et al. [47] stated that they had adopted a wait and see approach in the management of the patient and after a short period of time the tumour had regressed. To the knowledge of the author, inflammatory myofibroblastic tumour of the prostate has not been reported in an infant;

however, the pathological features of the spindle cell lesion in this child had not been described in detail or the detailed features of the lesion in this child are not available to the author. It would be argued that any spindled-cell lesion of the prostate gland should be thoroughly examined in order to establish an accurate diagnosis and that inflammatory myofibroblastic tumour of the prostate should be a differential diagnosis in this case.

Baydar and Aki [48] in 2011 reported a 44-year-old man who presented with abdominal pain which had been progressing. He had CT scan which revealed a large retroperitoneal mass for which he underwent surgical resection. During the operation, a second smaller mass was found in the pelvis which was left untouched. He subsequently had trans-rectal ultrasound scan of the prostate. Pathological examination of the resected retroperitoneal mass and the prostate biopsy specimen both showed the same mesenchymal tumour. He next underwent radical cystoprostatectomy and metastatic tumour which had involved the prostate gland, both seminal vesicles, and the base of the urinary bladder was found. Microscopic examination of the specimen showed typical histomorphological features of low-grade fibromyxoid sarcoma. At his 3-year-follow-up he was alive with no evidence of metastatic disease. Baydar and Aki, [48] reported that their case was the first documented case of metastatic sarcoma metastasizing to the prostate gland and this case expands the list of malignant mesenchymal neoplasms that may involve the prostate gland. Whilst this spindle cell tumour was diagnosed correctly as a mesenchymal sarcoma, because of its rarity and the fact that it was a spindle cell tumour it would be argued that the features of the lesion mimic that of an inflammatory myofibroblastic tumour of the prostate and hence low-grade fibromyxoid sarcoma should be considered as a differential diagnosis of IFMTP. In this particular case because it was a metastatic disease of the prostate the diagnosis was established. Nevertheless, perhaps when a case of primary low-grade fibromyxoid sarcoma of the prostate gland is encountered its diagnosis may require careful microscopic examination and immunohistochemistry studies to differentiate such a lesion from IFMTP.

Conclusions

IMFTPs are rare tumours that are sporadically reported which may mimic other pathologies affecting the prostate gland. IMFTPs

most commonly tend to exhibit a benign biological behaviour. The recent illustration of anaplastic lymphoma kinase (ALK) by means of immunohistochemistry in most cases of IMFTPs and a report of the development of metastasis and subsequent death from metastatic IMFTP would support a postulate that inflammatory myofibroblastic tumour is a neoplastic process. There is no clear cut way of predicting which IMFTPs would exhibit benign biological behaviour and which IMFTPs would be associated with the development of local recurrence / metastases / death. Clinicians should report cases of IMFTPs they encounter including their treatment and outcome so that eventually a consensus opinion would be formed from lessons learnt from the management of IMFTPs on pathological features of IMFTPs that would predict outcome and the best treatment option(s) for IMFTPs in relation to their characteristic features.

Conflict of Interest: – None

Ethical approval: – Not required in Literature Review

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