The British Journal of Radiology, 81 (2008), 907–915

PICTORIAL REVIEW

Unusual tumours involving the prostate: radiological–pathological findings

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ABSTRACT. The appearance of several unusual tumours in the prostate has resulted in questions being raised concerning their histogenesis; moreover, some of these tumours have prognoses that are quite unlike those of prostatic adenocarcinoma. Unusual neoplasms involving the prostate have been described in recent years, including mucinous cystadenocarcinoma, neuroendocrine cancer, lymphoma, spindle cell neoplasm, squamous cell carcinoma and transitional cell carcinoma. Radiological findings can overlap, and play limited roles in the diagnoses of these entities. However, knowledge of the radiological findings in these conditions can be helpful in making differential diagnoses. Images of prostate lesions using several imaging modalities, including transrectal ultrasound, MRI and CT, as well as available pathological images of such lesions, are presented in this article.

Received 7 May 2006
Revised 22 August 2006
Accepted 16 October 2006

DOI: 10.1259/bjr/68294775

Prostate cancer occurs microscopically in up to 50% of men by the age of 50 years, and almost all men aged 80 years show at least some microscopic evidence of prostate cancer [1]. Serum levels of prostate-specific antigen (PSA) are currently being used to screen for prostate cancer and, although the sensitivity of this test is between 73% and 96%, its specificity is limited; in terms of imaging modalities, transrectal ultrasound (TRUS) is the most commonly used for the diagnosis of prostate cancer [1].

More than 95% of malignant tumours of the prostate are adenocarcinomas [2]. However, numerous rare morphological variants of prostate carcinoma have been identified during the past two decades [2]. These unusual tumours of the prostate may arise from the prostatic epithelium, stroma or ectopically located cells within the prostate. Even though these tumours present with signs and symptoms that resemble those of usual prostate adenocarcinoma, they may have a different prognosis.

The characterization of several unusual prostate tumours has been described during recent years. However, few reports on the imaging findings of these unusual tumours have been published.

Although the roles of radiological imaging modalities are limited owing to much overlap between imaging findings, and biopsies of the tumour are inevitable in most cases, knowledge of the pathological and imaging findings of unusual tumours aids accurate diagnosis and provides important clinical information on treatment and prognosis.

In this article, we discuss and illustrate the TRUS, CT and MRI features of unusual prostate tumours, *i.e.* cystadenoma, leiomyoma, mucinous cystadenocarcinoma, squamous cell carcinoma, transitional cell carcinoma (TCC), leiomyosarcoma, rhabdomyosarcoma, malignant fibrous histiocytoma, synovial sarcoma, small cell carcinoma, carcinoid tumour and lymphoma. In addition, we present the unusual findings of benign prostatic stromal hyperplasia and benign inflammatory conditions mimicking prostate cancer.

Histological classification of prostate tumours

Table 1 shows the World Health Organization (WHO) histological classification of prostatic neoplasm [3]. According to this classification, prostate tumours are subdivided into epithelial, neuroendocrine, prostate stromal, metastatic, mesenchymal, haematolymphoid and miscellaneous tumours.

Unusual benign neoplasms of the prostate

Prostatic cystadenoma

Cystadenoma is a multilocular cyst or giant multilocular prostatic cystadenoma. It often presents with obstructive

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Table 1. Histological classification of tumours of the prostate

Epithelial tumours	Mesenchymal tumours
Glandular neoplasm	Leiomyosarcoma
Adenocarcinoma	Rhabdomyosarcoma
Cardinoma with spindle cell differentiation	Chondrosarcoma
Prostatic intraepithelial neoplasia	Angiosarcoma
Ductal adenocaricnoma	Malignant fibrous histiocytoma
	Malignant peripheral nerve sheath tumour
Uroepithelial tumours	Haemangioma
Urothelial carcinoma	Chondroma
	Leiomyoma
Squamous tumours	Grandular cell tumour
Adenosquamous carcinoma	Haemangioepricytoma
Squamous cell carcinoma	Solitary fibrous tumour
Basal cell tumours	
Basal cell adenoma	
Basal cell carcinoma	
Neuroendocrine tumours	**Miscellaneous tumours**
Endocrine differentiation within adenocarcinoma	Cystadenoma
Carcinoid tumour	Nephroblastoma
Small cell carcinoma	Rhabdoid tumour
Paraganglioma	Germ cell tumour
Neuroblastoma	Yolk sac tumour
	Seminoma
	Embryonal carcinoma and teratoma
	Choriocarcinoma
	Clear cell adenocarcinoma
	Melanoma
Prostatic stromal tumours	**Haematolymphoid tumours**
Stromal tumours of uncertain malignant potential	Lymphoma
Stromal sarcoma	Leukaemia
Metastatic tumours	

urinary symptoms, with or without a palpable abnormal mass. The causes of cystadenoma include obstruction, involutional atrophy of glands and rectovesical ectopic prostatic tissue showing cystic changes [3]. Histologically, this tumour is characterized by glands and cysts lined with cuboidal epithelium in a hypocellular fibrous stroma. Positive immunohistochemical staining of epithelial cells for PSA confirms the prostatic origin of this lesion [4]. Macroscopically, these tumours are well circumscribed, and resemble nodular hyperplasia with multiple cysts [3].

TRUS reveals a large multiseptated cystic mass, and some soft-tissue components may be present (Figure 1). The differential diagnoses include parasitic hyperplasia, a phylloides variant of atypical prostatic hyperplasia, and cystic carcinoma [4]. Cystic degeneration in benign prostatic hyperplasia and retention cysts can be differentiated by size. Cavitary prostatitis and prostatic abscess can be differentiated because they are usually accompanied by clinical symptoms and signs of infection.

Leiomyoma

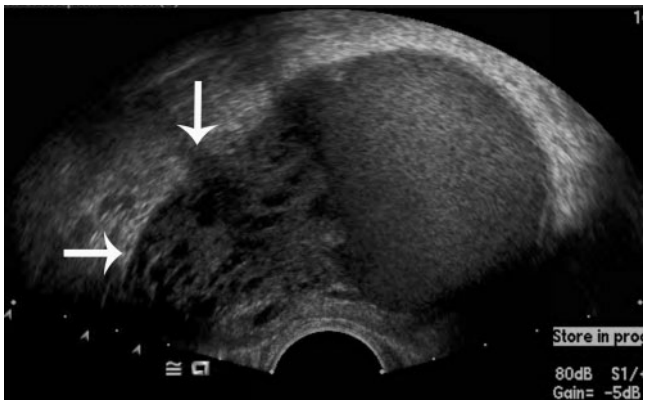
Pure leiomyoma of the prostate is a rare disease, which is believed to originate from smooth muscle elements of periglandular prostatic tissue, the prostatic capsule or the Müllerian duct remnant. It is defined specifically as a circumscribed or encapsulated mass of smooth muscle, 1 cm or more in diameter, containing varying amounts of fibrous tissue (devoid of glandular elements), which is either obviously prostatic or juxtaprostatic in origin and position [5]. Only a few case reports have described radiological findings. TRUS reveals a circumscribed low echoic mass (Figure 2) and, on contrast-enhanced CT images, leiomyoma appears to be a round heterogeneous attenuated mass with central necrosis. MRI reveals it as an isointense signal relative to muscle on T_1 weighted images and as slightly hyperintense on T_2 weighted images [6].

Unusual malignant neoplasms of the prostate

Epithelial tumours

Mucinous adenocarcinoma

Mucinous adenocarcinoma of the prostate is an uncommon variant of prostatic carcinoma, and occurs in 0.1–2.0% of prostatic surgical specimens [2]. Moreover, 60–90% of adenocarcinomas of the prostate secrete some mucoid material, and thus the difference between these common tumours and true mucinous carcinoma is primarily one of degree. The diagnosis of mucinous adenocarcinoma requires that more than 25% of an excised tumour consists of tumour cells and clusters of cells floating in lakes of mucin. In contrast to the more cellular typical glandular tumour, mucinous carcinomas demonstrate an accumulation of large amounts of extracellular mucin during histological examination.



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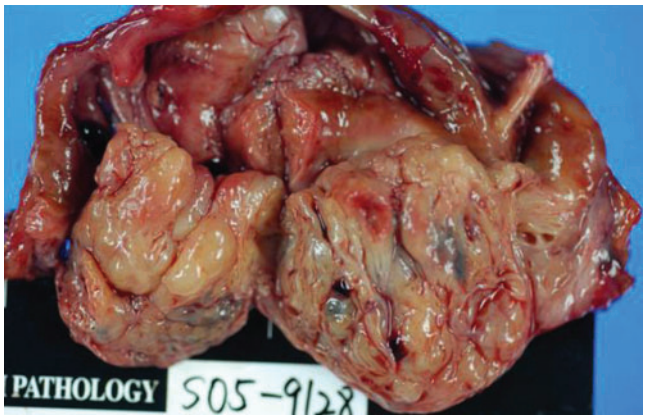

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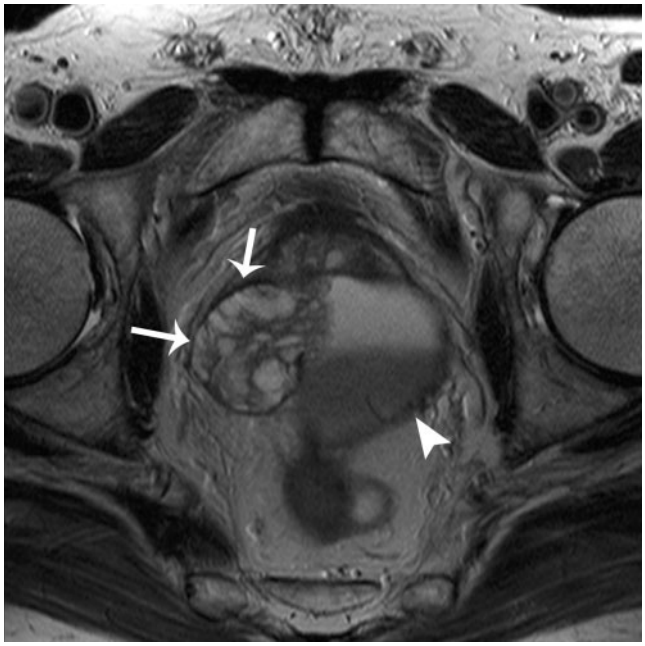
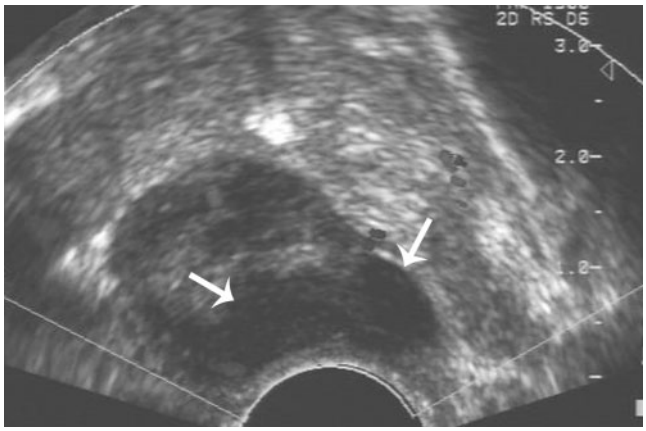


(b)

Figure 1. A 64-year-old man with multilocular cystadenoma. Recurrent haematuria developed 3 years ago and abdominal discomfort developed recently. His prostate-specific antigen level was not checked. (a) Transrectal ultrasound reveals a multilocular variable sized cystic mass of the prostate (arrows). (b) T_2 weighted MRI shows a high signal multiloculated mass with low signal intensity septum (arrows) and fluid–fluid levels in the mass (arrowhead). (c) Gross specimen reveals a mass with variable sized cysts and septa.



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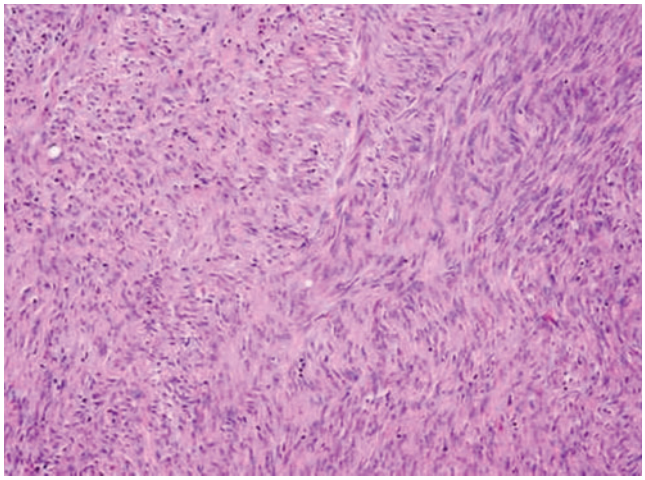
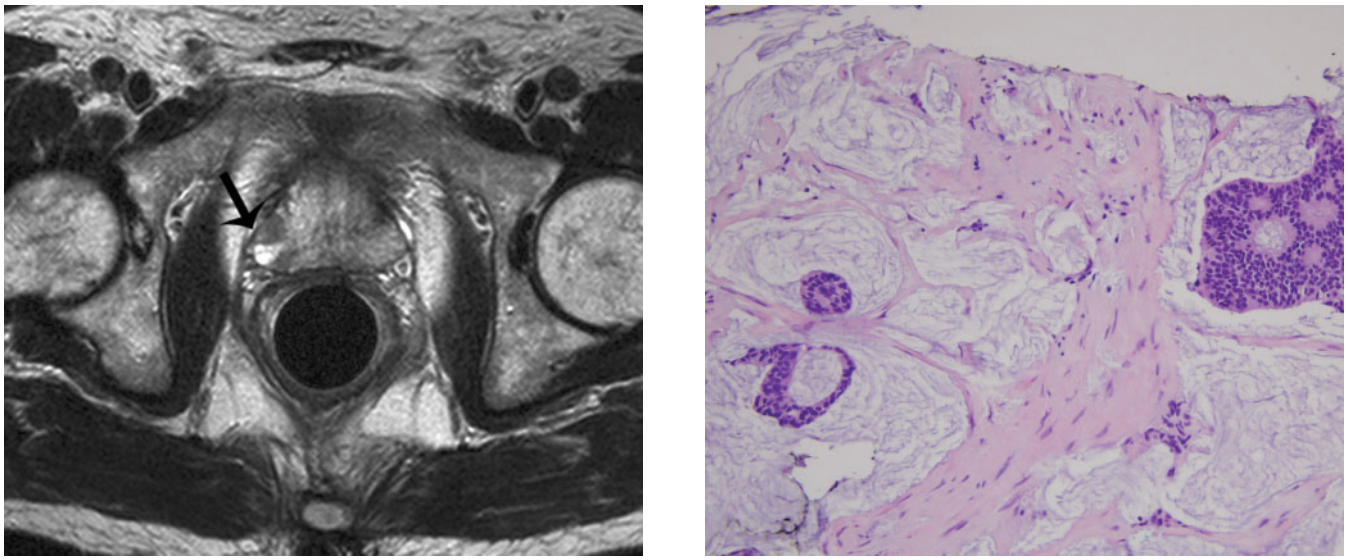


(b)

Figure 2. A 71-year-old man with leiomyoma. He complained of hesitation, frequency and conturia. His prostate-specific antigen level was 2.1 ng ml^{-1} (within the normal range). (a) Transrectal ultrasound reveals a low echoic mass located between the prostate (arrows) and the rectum. (b) Microscopic examination reveals connective tissue containing spindle cells arranged in a fascicular and whorled manner (haematoxylin and eosin, $\times 200$).



(a) (b)

Figure 3. A 70-year -old man with mucinous adenocarcinoma. He presented with a prostate-specific antigen (PSA) abnormality; his PSA level was 16.27 ng ml^{-1}. (a) T_2 weighted MRI shows a high signal cystic lesion in the right lobe of the prostate. Note the fluid–fluid level (arrow) in the cystic mass. (b) Pathological specimen reveals abundant extracellular mucin lakes (haematoxylin and eosin, $\times 400$).

Moreover, the mucin within these tumours differs in chemical composition from that of normal prostatic tissue [2].

On MRI, tumours appear as high signal intensity lesions on T_1 and T_2 weighted images owing to the mucin component (Figure 3). However, in some cases, variable T_2 weighted signal intensities may be observed owing to a smaller mucin amount or a different chemical composition, which both induce T_2 relaxation time shortening [2]. Some articles have reported that mucinous adenocarcinoma signal intensity is similar to that reported for rhabdomyosarcoma of the prostate, although the clinical, morphological and histopathological features of this tumour are distinctly different [7]. The differential diagnosis includes cystic prostatic hyperplasia, abscesses and cystadenomas.

Squamous cell carcinoma

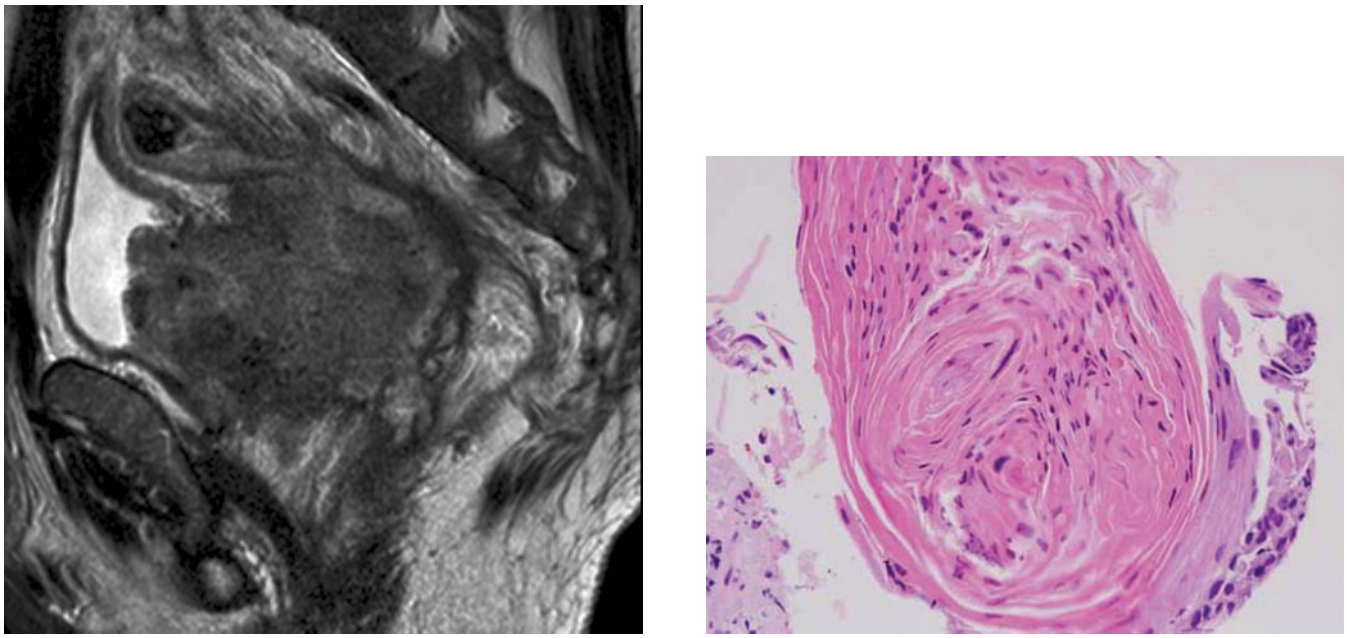
Primary squamous cell carcinoma of the prostate is rare and accounts for approximately 0.5–1.0% of all prostate cancers [2]. Before a diagnosis of primary squamous cell carcinoma of the prostate can be made, primary vesical and urethral carcinomas must be excluded. The presentation of prostatic urethral obstruction, haematuria or symptoms of metastatic bone disease in elderly men can help in the differentiation from usual adenocarcinoma. However, even in cases of squamous cell carcinoma with metastatic disease, serum acid phosphatase levels are usually not elevated [2]. Squamous cell carcinomas often arise in the setting of previous hormone or radiation therapy, and the prognosis of this tumour is poor [2]. Pathologically squamous features of keratinization, squamous pearls and intercellular bridges are characteristic (Figure 4) [8]. Radiography usually visualizes osteolytic bony metastases from prostatic squamous cell carcinomas, whereas adenocarcinoma shows osteoblastic metastasis [8]. TRUS shows low echoic hypervascular lesions and MRI shows low lesion signal intensities in the prostate on T_2 weighted images, as for adenocarcinoma (Figure 4), but no characteristic imaging findings of the prostate mass have been reported. Lymph node metastasis has also been noted in (i) iliac, inguinal, obturator and paraaortic lymph nodes, (ii) adjacent nerves, (iii) bladder, (iv) seminal vesicles, (v) rectum, (vi) liver and (vii) lung [2].

Transitional cell carcinoma

TCC of the prostate can occur as a primary lesion within prostatic ducts or acini, or may result from synchronous or metachronous spread from carcinoma of the bladder or urethra. The primary form is rare and accounts for only 2–4% of all prostate cancers, whereas secondary involvement of the prostate is much more common. Whether primary or secondary, TCC of the prostate is believed to have a poor prognosis [2]. On TRUS, discrete hypoechoic lesions involving the prostatic stroma, ejaculatory ducts and periprostatic tissues may be noted [9]. On CT, a low attenuating lesion in the central portion of the prostate is noted (Figure 5). Pathologically, with extensive tumour involvement, a urothelial carcinoma fills and expands ducts and often develops central comedonecrosis. Stromal invasion is associated with a prominent desmoplastic stromal response, with tumour cells arranged in small irregular nests, cords and single cells [3].

Neuroendocrine neoplasm

Prostatic tumours with neuroendocrine differentiation are increasingly being reported [10]. Neuroendocrine differentiation in prostatic carcinoma has three forms: (i) focal neuroendocrine differentiation in conventional prostatic adenocarcinoma; (ii) carcinoid tumour (WHO well-differentiated neuroendocrine tumour); and (iii) small cell



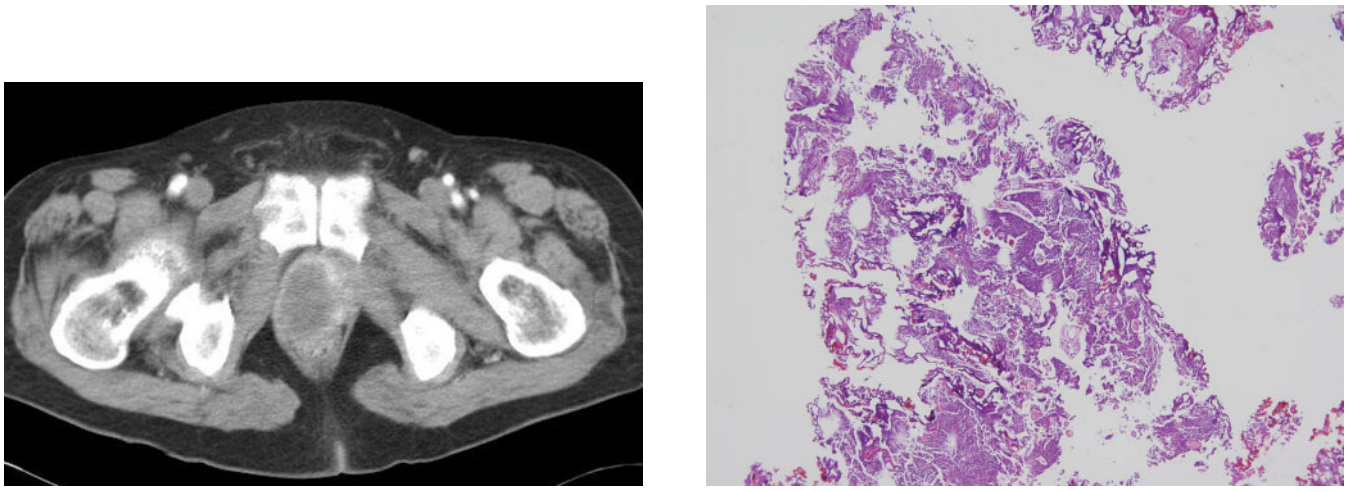
(a) (b)

Figure 4. Squamous cell carcinoma in a 44-year-old man. He presented with haematuria of 6 months' duration. He had a history of hypospadias, and corrective surgery was performed when he was 6 years old. His prostate-specific antigen level was less than 0.3 ng ml^{-1}. (a) A T_2 weighted sagittal MRI shows a low signal intensity contour bulging mass from prostate. (b) A pathological specimen reveals that keratin pearl formation is a characteristic finding of squamous cell carcinoma (haematoxylin and eosin, $\times 400$).

neuroendocrine carcinoma (new WHO classification: poorly differentiated neuroendocrine carcinoma) [3]. The most common type of neuroendocrine differentiation observed in prostate malignancy is focal individual cell neuroendocrine differentiation in conventional adenocarcinoma. Small cell carcinomas and carcinoid tumours constitute a small percentage of prostatic malignancies, and represent less than 5% of all prostatic malignancies [2]. The presence of a neuroendocrine component can also affect clinical management, because treatment and prognosis may differ from that of typical adenocarcinoma.

Carcinoid tumour

True carcinoid tumours of the prostate are exceedingly rare and show classic cytological features of carcinoid tumours and diffuse neuroendocrine differentiation (chromogranin A and synaptophysin immunoreactivity) [3]. They should be essentially negative for PSA. No



(a) (b)

Figure 5. Transitional cell carcinoma (TCC) in a 83-year-old man. He had a history of prostate cancer 4 years ago, and bilateral orchiectomy was performed. Haematuria developed and his prostate-specific antigen level was only 0.2 ng ml^{-1}. Transurethral biopsy of the prostate revealed prostate involvement of TCC. (a) Post-contrast CT shows a peripheral enhancing, low attenuating mass in the prostate central portion. (b) Microscopic specimen reveals TCC extensively involving the prostatic ducts (haematoxylin and eosin, $\times 40$).

image findings have been reported for carcinoid tumours of the prostate. In our case, TRUS showed a low echoic irregularly shaped mass with increased vascularity, and CT a low attenuating mass with peripheral enhancement (Figure 6).

Small cell tumour

Schwartz et al [10] reported that 44% of patients with a clinically anaplastic clinical variant of prostate cancer show a small cell carcinoma component in the mass. The anaplastic clinical variant is defined clinically by one or more of the following: (i) a rapid progression of clinical symptoms; (ii) the presence of visceral metastasis; (iii) poor response to androgen ablation therapy; and (iv) relatively low serum PSA levels. Small cell cancer has an aggressive clinical course characterized by widespread metastatic disease and a lack of response to hormone therapy [10].

The rapid onset of bladder outlet obstructive symptoms is a common presentation. Distant metastases are generally observed at the time of diagnosis and paraneoplastic syndromes are occasionally observed [2]. These tumours are morphologically identical to carcinoid tumours and small cell carcinomas of the lung and other sites [10]. Currently, neuroendocrine tumour cells are thought to arise from a common stem cell or multipotent cell that can differentiate into multiple tissues [2]. This theory explains the heterogeneous cell population present in many prostate cancers, and the observation that diagnosis of small cell cancer is often preceded by a diagnosis of adenocarcinoma of the prostate.

Imaging findings have rarely been reported for small cell carcinoma of the prostate, but extensive bone metastasis and abdominal and pelvic lymphadenopathy are noted at CT [10]. In our case, CT showed a well-enhanced lobulated contoured soft-tissue mass (Figure 7)

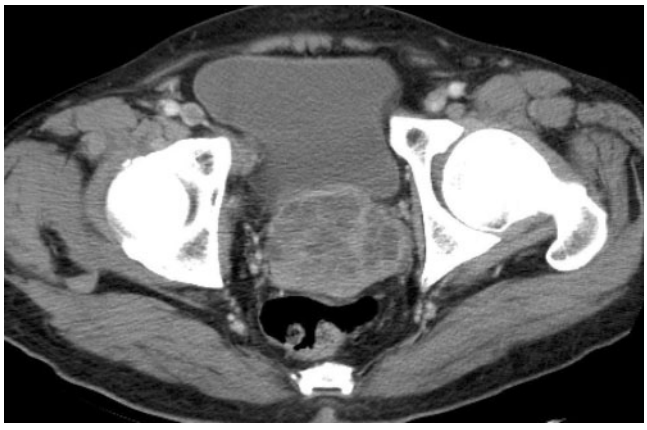


Figure 6. A 39-year-old man with a carcinoid tumour. He presented with abdominal distension. There were multiple cystic masses in the liver, and biopsy of the liver revealed metastatic, poorly differentiated carcinoma. He underwent colonoscopy for primary site work-up, and mass compression rectal mucosa was detected. His prostate-specific antigen level was not checked. Contrast-enhanced CT shows a heterogeneous enhancing pattern of the mass. Transrectal ultrasound biopsy identified a carcinoid tumour.

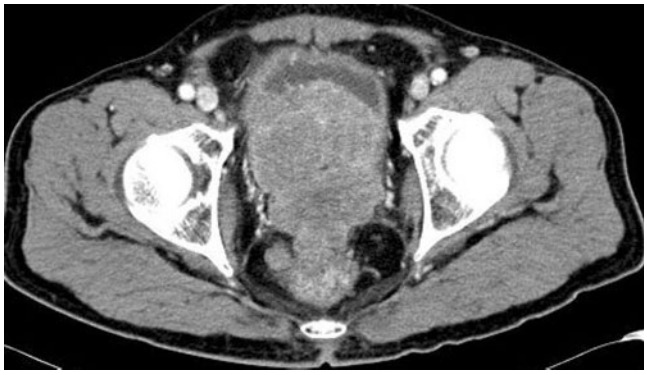


Figure 7. A 68-year-old man with small cell carcinoma. He visited our hospital because of voiding difficulty, and transrectal ultrasound (TRUS) biopsy revealed prostate adenocarcinoma. At that time, his prostate-specific antigen (PSA) level was 378 ng ml^{-1}. After a year of chemotherapy, voiding difficulty redeveloped. His PSA level was 0.7 ng ml^{-1}. TRUS biopsy revealed small cell carcinoma of the prostate. Contrast-enhanced CT shows a hyperdense multilobular mass in the prostate invading the bladder. Multiple liver and bone metastases were also revealed.

Mesenchymal tumours

Leiomyosarcoma

Leiomyosarcoma is the second most common sarcoma involving the prostate following rhabdomyosarcoma, and constitutes ~25% of all prostatic sarcomas. It usually occurs between 40 years and 70 years of age and presents as a bulky tumour with diffuse infiltration of the surrounding tissues (Figure 8) [1]. This histological subtype tends to be somewhat slower growing than

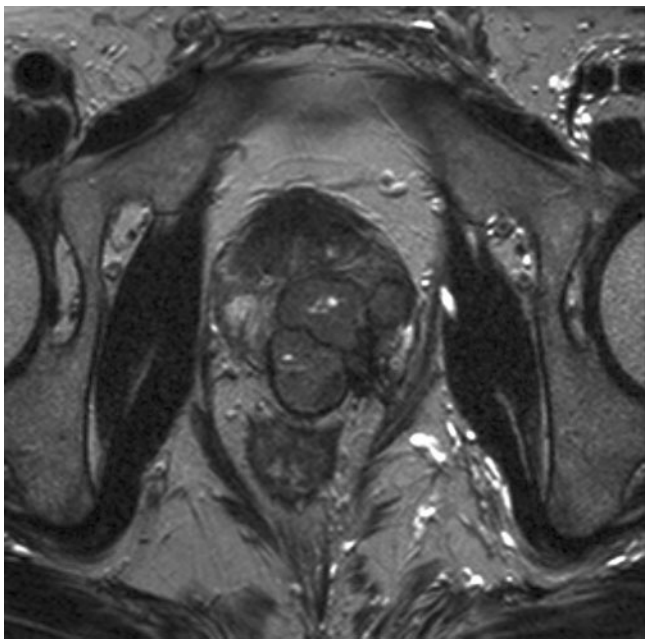


Figure 8. A 45-year-old man with leiomyosarcoma. He presented with urinary retention. His prostate-specific antigen level was 0.3 ng ml^{-1}. A T_2 weighted MR image shows a multilobular low signal intensity mass originating from the prostate. Focal high signal intensity suggesting cystic or necrotic change is also seen.

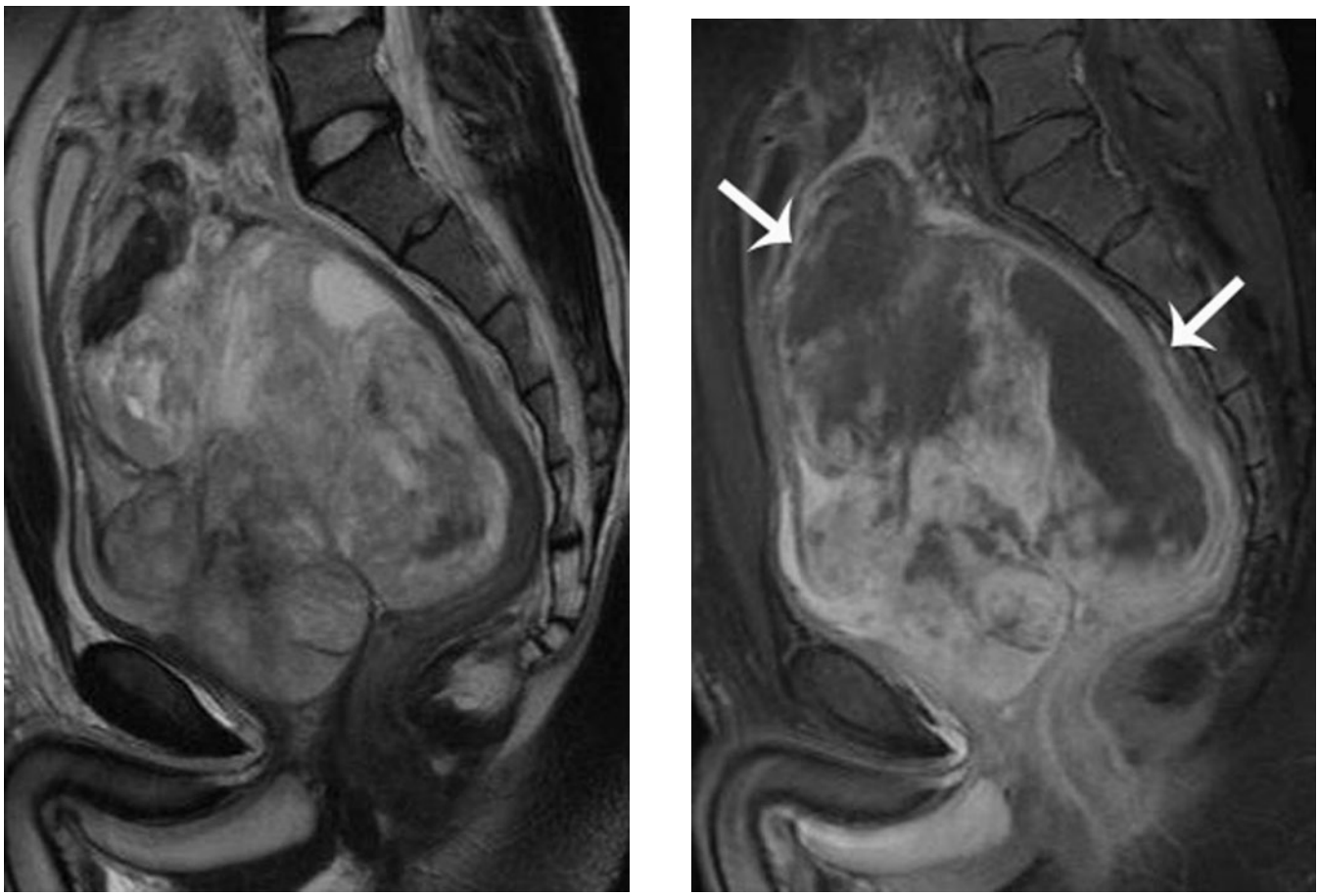
childhood rhabdomyosarcomas. Pathologically, leiomyosarcoma consists of interlaced bundles of spindle cells with blunt-ended nuclei and eosinophilic cytoplasm on light microscopy [2]. Necrosis and haemorrhage frequently accompany these neoplasms [11].

The local extent of these sarcomas can be determined by CT or MRI, but findings of leiomyosarcoma are indistinguishable from those of rhabdomyosarcoma [1]. Both of these modalities can clearly delineate tumours from surrounding normal tissues. In addition, they allow the assessment of kidney status and are important when planning surgical resection. Local recurrence is frequent and the most common metastatic site is the lung, followed by the bone and liver. Regional lymph nodal metastases occur infrequently [2].

Rhabdomyosarcoma

Rhabdomyosarcoma is a solid neoplasm of unknown aetiology that may arise from a primitive cell in any organ system. Rhabdomyosarcoma is the most common tumour of the lower genitourinary tract in the first two decades of life and it represents 5–10% of malignant solid tumours of childhood, ranking it fourth in frequency after central nervous system neoplasms, neuroblastoma and Wilms' tumour [12]. Genitourinary rhabdomyosarcoma accounts for 15–30% of rhabdomyosarcoma cases in children; more than 65% of cases are embryonal rhabdomyosarcomas and the remainder are of the alveolar subtype.

Rhabdomyosarcoma may be small and apparently limited to the prostate at the time of diagnosis; however, it can grow rapidly and invade adjacent soft tissues and the bladder. The majority of patients with bladder or prostate rhabdomyosarcoma present because of a bladder outlet obstruction that produces abdominal pain and distension, dysuria or signs of urinary tract infection [12]. The gross appearance of rhabdomyosarcoma is variable. The margins of the tumour may be infiltrative or well defined by a compressible pseudocapsule. Cut sections of rhabdomyosarcoma typically appear firm, fleshy and lobulated, and may display gelatinous myxoid areas or regions of secondary haemorrhage or necrosis [12]. TRUS reveals a hyperechoic or hypoechoic solid lesion, which may contain sonolucent foci representing haemorrhage or necrosis [12]. On CT, rhabdomyosarcoma of the prostate appears as a bulky pelvic mass with heterogeneous attenuation (Figure 9). The mass may invade periurethral and perivesical tissues or it may extend into the ischiorectal fossa. Calcification is rare. The precise origin of the tumour is often difficult to determine because primary prostate lesions may invade the bladder base, or



(a) (b)

Figure 9. A 27-year-old man with rhabdomyosarcoma. He presented with abdominal pain, dysuria and urinary and faecal retention. His prostate-specific antigen level was 0.9 ng ml^{-1}. (a) A T_2 weighted sagittal image shows a bulky mass with heterogeneous signals in the prostate. (b) Gadolinium-enhanced T_1 weighted sagittal image reveals strong enhancement of solid portions. Note the low signal intensity lesions suggesting massive necrosis (arrows).

the prostate may have been invaded by a tumour arising in the bladder [12]. MRI clearly shows the site of origin as the central prostate area, with compression of the clearly recognizable peripheral portion. The tumour may display a well-defined low signal intensity pseudocapsule on T_2 weighted images. Gadolinium-enhanced T_1 weighted MR images show heterogeneous mass enhancement (Figure 9), and the multiplanar capability of MRI permits accurate assessment of the extent of local tumour [7].

Malignant fibrous histiocytoma

Malignant fibrous histiocytoma (MFH) is a pleomorphic sarcoma than can occur in bone or soft tissue, and contains both fibroblast-like and histiocyte-like elements in varying proportions. MFH arising from the prostate is very rare, and few case reports have been published. A microscopic examination disclosed a mesenchymal proliferation of spindle cells with abundant eosinophilic cytoplasm [13]. No specific findings have been reported for MFH in the prostate; the differential diagnosis includes rhabdomyosarcoma and other soft-tissue sarcomas. Our case showed a low echoic, contour-bulging mass on TRUS. In addition, strong peripheral contrast enhancement of the soft-tissue mass was noted on contrast-enhanced CT (Figure 10).

Synovial sarcoma

Synovial sarcoma is a mesenchymal neoplasm that typically arises in para-articular soft tissues of the lower extremities in young adults [14]. In most patients with this disease, distant pulmonary metastases develop after primary tumour surgery. Primary synovial sarcomas can occur unusually in a variety of locations, including the middle ear, orofacial or oropharyngeal regions, oesophagus, larynx, lung, pleura, heart, blood vessels, abdominal wall and retroperitoneum, although involvement of the genitourinary tract is exceedingly rare [14]. Prostatic synovial sarcoma image findings are not well reported. In one case report by Shirakawa et al [14], T_2 weighted MR revealed a high signal mass originating in the prostatic fascia (Figure 11).

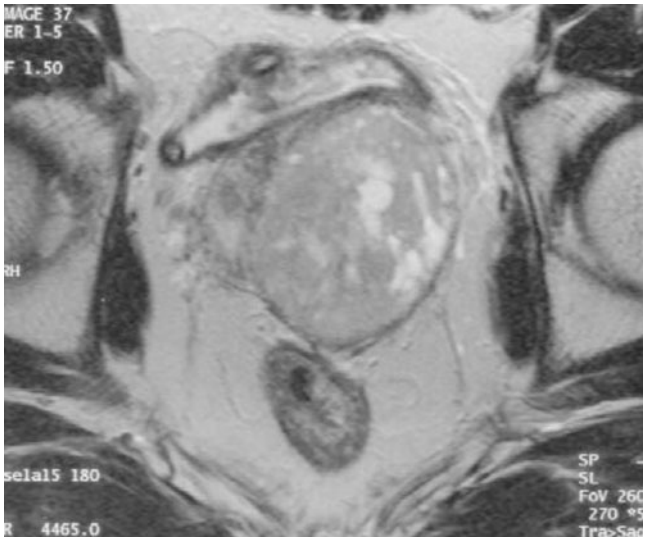
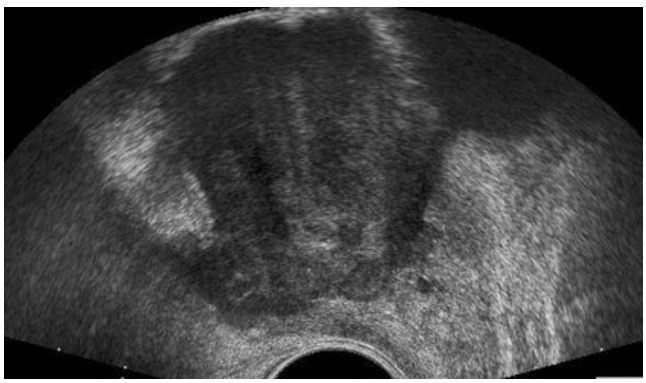


Figure 11. A 36-year-old presented with voiding difficulty. His prostate-specific antigen level was 5.9 ng ml^{-1}. A heterogeneous signial intensity mass compressing the bladder is noted on T_2 weighted axial image. Transrectal ultrasound biopsy revealed synovial sarcoma.

Haematopoietic malignancy

Lymphoma

Malignant lymphoma involving the prostate is rare, whether presenting as a primary extranodal lymphoma or as secondary spread to the prostate from other sites. Lymphoma of the prostate must be considered when a large prostatic mass is palpated in a young man. Systemic symptoms associated with lymphomas, such as fever, chills, night sweats and weight loss, are rarely observed and only in patients with widespread lymphoma. The prostate is usually diffusely enlarged and soft with a rubbery consistency [2]. Primary prostatic lymphomas are much less common than secondary lymphomas, and can be diagnosed when the lesions are exclusively located in the prostate and there is no evidence of systemic lymph node involvement by lymphoma cells [2]. TRUS reveals large hypoechoic



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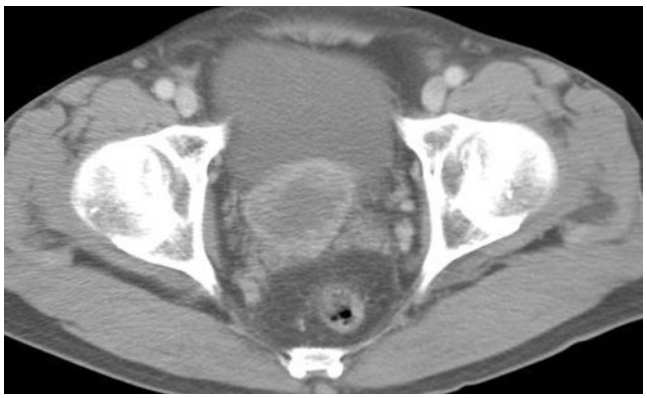

(b)

Figure 10. A 71-year-old man presented with urinary frequency. His prostate-specific antigen level was 0.7 ng ml^{-1}. Transrectal ultrasound (TRUS) biopsy revealed malignant fibrous histiocytoma. (a) TRUS reveals a low echoic, and contour-bulging mass. (b) Strong, peripheral contrast enhancement of the soft-tissue mass is noted on contrast-enhanced CT.

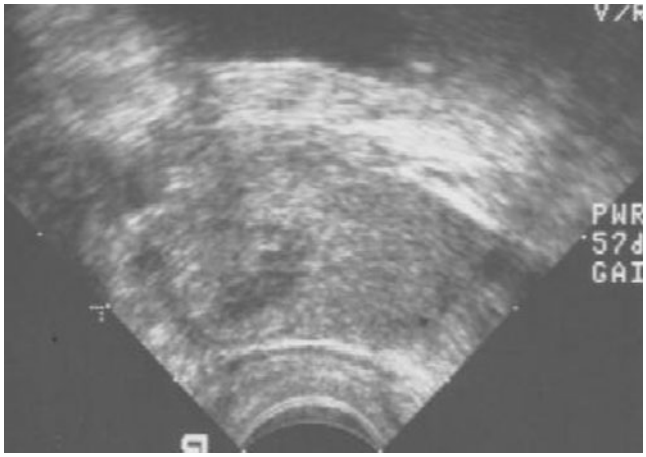

Figure 12. A 17-year-old man with prostatic lymphoma. He presented with terminal haematuria. His prostate-specific antigen level was not checked. Transrectal ultrasound reveals a 3 cm low echoic lesion in the right lobe of the prostate, resembling prostate adenocarcinoma. Biopsy revealed prostatic lymphoma. There was no evidence of bone marrow involvement.

masses within both the central and peripheral zones and beyond the confines of the prostate gland in young men. CT findings of lymphomas are homogeneous soft-tissue masses in the vast majority of cases. MRI additionally provides information about the involvement of the bone marrow in patients with high-grade non-Hodgkin's lymphoma (Figure 12). Both CT and MRI can assess the extent of the primary disease and associated lymph node enlargement [2].

Summary

Many benign and malignant prostate tumours present as subtle low echoic focal lesions or masses on TRUS, and show different signal intensities/attenuations with enhancement patterns on MR/CT according to their histological content. Specific radiological findings indicating the identities of the disease entities involved are rare, and biopsy of the lesion may be essential in most of cases. However, knowledge of their radiological and pathological findings can help to make an accurate radiological diagnosis.

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