



A Review of the Literature on Primary Rhabdomyosarcoma of the Prostate Gland

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Abstract

Primary rhabdomyosarcoma of the prostate gland (PRMSP) is a rare disease. PRMSP can affect children and adults; it is more commonly encountered in children; it tends to present with lower urinary tract symptoms, retention of urine, haematuria, perineal pain, loin pain or symptoms related to metastatic disease. Diagnosis is established by histological examination of prostate specimens which show: cellular areas, blood vessels alternating with myxoid/edematous areas and areas of necrosis, tumour cells that are small, round or oval or spindly, forms of the tumour may be bizarre with abundant eosinophilic cytoplasm and variable cross striations. The tumour cells on immunohistochemistry stain positively with desmin, MyoD1, myogenin, sarcomeric actin, myoglobin, and cytoplasmic staining with WT1. Ultra-sound/CT/MRI/PET/CT scans are used for staging/assessment. Multi-modality treatment including surgery, combination chemotherapy and radiotherapy have helped improve the prognosis in children and at times chemo-radiation has helped in avoiding surgery or by reducing the tumour mass which has permitted organ preserving surgery. The prognosis is poor in adults. PRMSP is a rare aggressive disease, and its diagnosis requires a high index of suspicion for which early diagnosis and multi-modality treatment would hopefully improve the prognosis.

Key words: Rhabdomyosarcoma of prostate; Desmin; MyoD1, Myogenin; WT1; Sarcomeric Actin; Chemotherapy; Radiotherapy; Prostatectomy; Hemicyectomy.

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Introduction

Primary Rhabdomyosarcoma of the prostate gland is a rare tumour and majority of clinicians would be unfamiliar with the biological behavior of the disease. Furthermore Rhabdomyosarcoma of the prostate in young adults is rare and few cases have been documented in the literature. [1] Various histological sub-types of rhabdomyosarcoma exist some of which include embryonal, alveolar and pleomorphic sub-types. [2] In Rhabdomyosarcoma

immunohistochemistry of the tumour tends to show positivity for desmin, as well as skeletal muscle markers including MyoD1, myogenin, sarcomeric actin, myoglobin. [2] and recently cytoplasmic staining with WT1 has been added as an immunomarker for rhabdomyoblastic differentiation [2] [3] The ensuing review of the literature on primary rhabdomyosarcoma of the prostate gland is divided into two parts: (A) Overview and (B) miscellaneous narrations and discussions from some reported cases of rhabdomyosarcoma of the prostate gland.

Methods

Various internet data bases were searched including Google; Google Scholar; PUBMED and Educus to look for literature on primary rhabdomyosarcoma of the prostate gland. The search words that were used include: Rhabdomyosarcoma of prostate; Embryonal rhabdomyosarcoma of prostate; prostatic rhabdomyosarcoma. Information obtained from 42 references including case reports, case series review papers and other documentations relating to rhabdomyosarcoma of the prostate gland was used to

write the literature review on primary rhabdomyosarcoma of the prostate gland.

Literature Review

(A) Overview

General Comments

- (i) It has been stated that embryonal rhabdomyosarcoma of the prostate gland is the commonest malignant tumour of the prostate gland in children and infants [4]
- (ii) Rhabdomyosarcoma of the prostate gland tends to present as a firm and smooth enlargement of prostate gland on clinical examination. [4]
- (iii) Nodal enlargement in primary rhabdomyosarcoma of the prostate gland tends to be less common in comparison with primary rhabdomyosarcoma of the head and neck region [4]
- (iv) It has been stated that the prognosis of primary rhabdomyosarcoma of the prostate gland affecting children has improved; [5] however, it has also been stated that the prognosis of primary rhabdomyosarcoma of the prostate gland in adults has remained poor [6]
- (v) It been stated that primary rhabdomyosarcoma of the prostate gland tends to present as stage 3 tumour but at times rhabdomyosarcoma of the prostate gland does present with distant metastases. [4]

Definition

Rhabdomyosarcoma is a malignant neoplasm which has pleomorphic cells that exhibit skeletal muscle differentiation [7] and when the prostate gland is affected by such a tumour, it is called rhabdomyosarcoma of the prostate gland. Various types of rhabdomyosarcoma exist which have been defined and clarified by the Stanford Surgical Pathology Criteria which in the first instance has defined rhabdomyosarcoma in general followed by the criteria for diagnosing the various sub-types of rhabdomyosarcomas as follows:

Diagnostic Criteria

General definition

Rhabdomyosarcoma is a primitive malignant tumor of embryonal skeletal muscle progenitor cells (myoblasts)

General Diagnostic Criteria

In view of the various sub-types of rhabdomyosarcoma and in view of the rarity of the disease in the prostate perhaps some urologists and

pathologists may have difficulty in establishing the correct sub-type of the tumour. In order to clarify and stratify the histological diagnosis of rhabdomyosarcoma, Stanford University in the United States of America has developed a Surgical Pathology Criteria which is very helpful. The General Diagnostic Criteria documented by Florette K Gray Hazard, in Rhabdomyosarcoma Stanford Surgical Pathology Criteria is as follows: [7]

- Myogenin expression is essentially diagnostic
- The only exception is rare expression of myogenin by melanotic neuroectodermal tumor of infancy and the composite tumors listed below;
 - Malignant triton tumor (rhabdomyosarcoma plus malignant peripheral nerve sheath tumor)
 - Ectomesenchymoma (rhabdomyosarcoma plus peripheral primitive neuroectodermal tumor)
 - Malignant teratoma
 - Carcinosarcoma
- Rhabdomyosarcoma is predominantly a pediatric neoplasm
 - Most common soft tissue sarcoma of childhood
 - Up to 10% of all childhood malignancies
 - Only sclerosing and pleomorphic types show significant adult incidence
- Histologic types show markedly different clinical features
 - Embryonal (includes botryoid, spindled and NOS)
 - Alveolar
 - Mixed embryonal and alveolar
 - Sclerosing
 - Pleomorphic
- Staging (Staging for IRSG modified TNM, do not use TNM from AJCC) [7]
- Pathologic staging of rhabdomyosarcoma is performed using the Pretreatment TNM Staging System established by the Intergroup Rhabdomyosarcoma Study Group (Note this is not the TNM system described in the AJCC Cancer Manual)

Embryonal Rhabdomyosarcoma [7]

Definition

Primitive myoblastic neoplasm most commonly found in hollow visceral organs, the genitourinary tract and head and neck region

Diagnostic Criteria [7]

- Embryonal rhabdomyosarcoma is the most common type of rhabdomyosarcoma, (68%)
- Embryonal rhabdomyosarcoma is considered a favorable histologic type
- 5 year failure free survival rate, (82%)
- Alternating cellular and myxoid areas
- Foci of immature cartilage or bone are occasionally present
- Hyperchromatic histologically undifferentiated small cell population usually predominates
- May be round or spindled
- Immature cells showing muscle differentiation frequently scattered, rarely predominates

- Round cells with abundant, usually eccentric eosinophilic cytoplasm
- Cross striations not typically present
- Nuclei frequently vesicular with prominent nucleolus

- Spindle cell myoblast with prominent tapered fibrillary eosinophilic cytoplasm
- May form tadpole or strap cells
- Nuclei may be multiple
- Cross striations may be present

- Anaplastic cellular features may be seen in approximately 13% in all subtypes of rhabdomyosarcoma
- Anaplastic is defined as neoplastic nuclei at least 3 times the size of their neoplastic neighbors and/or atypical myotonic figures

- If present, the focal or diffuse nature of the anaplasia should be described
- Focal anaplasia refers to anaplastic cells loosely scattered among non-anaplastic tumor cells
- Diffuse anaplasia refers to anaplastic cells arranged in multiple clusters or diffuse sheets

- The presence of anaplasia confers a worse prognosis
- Three histologic subtypes of embryonal rhabdomyosarcoma:
- Botryoid
- Requires by the presence of a condensed layer of neoplastic cells beneath intact epithelium (cambium layer)
- Typically separated from mucosa by a myxoid, hypo-cellular zone
- Primarily occurs in mucosal lined sites

- Grape like gross appearance is typical but not required
- Spindled
- Spindled morphology
- Primarily found in para-testicular and orbital regions
- Not otherwise specified (NOS) is most common
- No PAX-FOXO1 translocations
- Common sites of involvement:
- Genitourinary system (infants and young children)
- Orbit
- Head and neck
- Population: 42% children < 4 years of age
- May be seen in adults

Alveolar Rhabdomyosarcoma [7]

Definition [7]

Primitive myoblastic neoplasm found most commonly in the extremities, paranasal sinuses and parameningeal region

Diagnostic Criteria [7]

- Second most common type of rhabdomyosarcoma, comprises 31% of rhabdomyosarcomas
- Considered an unfavorable histologic type
- 5-year failure free survival rate: 65%
- Sheets of uniform cells, frequently discohesive, broken up by fibrous septae
- Generally round to oval nuclei
- Hyperchromatic with small nucleoli
- Occasional rhabdomyoblasts seen in 30% of cases
- Fibrillar cytoplasm but only rare cross striations
- Usually round
 - Sheets broken up by fibrous septae
- Vessels contained in septae

- Two histologic sub-types:
- Classical
- Nests of neoplastic cells arranged in alveolar spaces
- Cells adhere to the periphery of the alveoli
 - (a) Hobnail or tombstone appearance
 - (b) May look like a non-cohesive papillary pattern.
- Non-cohesive cells appear to float in the center
- Multinucleated giant cell forms may be seen
- Nuclei usually peripheral, wreath-like
- Normal muscle fibers may be entrapped

- Solid
 - Sheets of neoplastic cells
 - Nests separated by thin fibrovascular septae but alveoli are not seen
- PAX-FOXO1 translocations aid in diagnosis and determination of prognosis

Considered diagnostic if present

- PAX3-FOXO1 t(2;13)(q35;q14) – 60%
- PAX7-FOXO1 t(1;13)(p36;q14) – 20% (better prognosis)
- Fusion negative ~ 15%
- Anaplastic cellular features may be seen in approximately 13% of all sub-types of rhabdomyosarcoma.
 - Anaplastic is defined as as neoplastic nuclei at least 3 times the size of their neoplastic neighbors and/or atypical mitotic figures
 - If present the focal or diffuse nature of the anaplasia should also be described
- (a) Focal anaplasia refers to anaplastic cells loosely scattered among non-anaplastic tumor cells
- (b) Diffuse anaplasia refers to anaplastic cells arranged in multiple clusters or diffuse sheets
- The presence of anaplasia confers a worse prognosis, especially when the anaplasia is diffuse
- *Common sites of involvement:*
 - Extremities
 - Trunk
 - Population: most > 10 years of age
 - May be seen in adults

Mixed Alveolar/ Embryonal Rhabdomyosarcoma [7]

Definition [7]

Rhabdomyosarcoma exhibiting a mixture of alveolar and embryonal patterns

Diagnostic Criteria [7]

- Tumors showing mixed histologic features of embryonal and alveolar sub-types
- These histologically distinct morphologies may be intermixed or distinct from each other
- There is no percentage cutoff that facilitates classification of one tumor subtype over another
- The presence of both alveolar and embryonal morphological features is all that is required for the designation of mixed alveolar/embryonal rhabdomyosarcoma

- Anaplasia should be evaluated and reported as described for embryonal and alveolar subtypes
- Expression of myogenin and PAX-FOXO1 fusion transcripts is variable
- They may be concordant or discordant with histologic pattern, diffuse, focal, or negative
 - Behavior and incidence unknown
 - Common at least sites of involvement
- Extremities
- Trunk
- Population: most < 10 years of age; however all ages have been reported
- Rare case reports in adults (i.e. prostate gland)

Sclerosing Rhabdomyosarcoma [7]

Definition [7]

Rhabdomyosarcoma with densely sclerotic background stroma

Diagnostic Criteria [7]

- Neoplastic cells set in a densely hyalinized eosinophilic background stroma
- Arranged in nests, micro-alveoli or cords
- May produce a pseudo-vascular pattern
- Composed of small undifferentiated cells
- Giant cells or myoblasts are rare
- Anaplastic cellular features may be seen in approximately 13% of all subtypes of rhabdomyosarcoma
- Anaplasia is defined as neoplastic nuclei at least 3 times the size of their neoplastic neighbors and / or atypical mitotic figures
- If present, the focal or diffuse nature of the anaplasia should also be described
 - Focal anaplasia refers to anaplastic cells loosely scattered among non-anaplastic tumor cells
 - Diffuse anaplasia refers to anaplastic cells arranged in multiple clusters or diffuse sheets
- The presence of anaplasia confers a worse prognosis, especially when the anaplasia is diffuse
 - No distinct translocation
 - Common sites of involvement:
 - Extremities
 - Trunk
 - Retroperitoneum
 - Rare, < 1% of rhabdomyosarcoma
- Reported in children and adults of all ages
- Unknown behavior

Pleomorphic Rhabdomyosarcoma [7]

Definition [7]

Malignant neoplasm with large pleomorphic cells exhibiting skeletal muscle differentiation

Diagnostic Criteria [7]

- Unfavorable histologic type
 - 5-year failure free survival rate: ~ 40%
 - Markedly enlarged pleomorphic cells
 - Abundant deeply eosinophilic cytoplasm
 - Cross striations rare
 - Multinucleated forms may be seen
 - Spindled to epithelioid neoplastic cells admixed
 - Lacks background of uniform immature cells
 - Presence of immature cells suggests instead anaplasia in embryonal or alveolar subtypes
 - Requires demonstration of skeletal muscle differentiation
 - MyoD1 or myogenin
 - Anaplastic cellular features may be seen in approximately 13% of all subtypes of rhabdomyosarcoma
 - Anaplasia is defined as neoplastic nuclei at least 3 times the size of their neoplastic neighbors and / or atypical mitotic figures
 - If present, the focal or diffuse nature of the anaplasia should also be described
 - Focal anaplasia refers to anaplastic cells loosely scattered among non-anaplastic tumor cells
 - Diffuse anaplasia refers to anaplastic cells arranged in multiple clusters or diffuse sheets
 - The presence of anaplasia confers a worse prognosis, especially when the anaplasia is diffuse
 - Anaplasia can be very difficult to assess in pleomorphic subtype
 - No distinct translocation
 - Common sites of involvement:
 - Deep extremities
 - Retroperitoneum
 - Most often seen in adults
 - Rare cases reported in children
- Supplemental Studies [7]
Immunohistochemistry [7]
- Desmin is an effective screening stain as nearly all cases of all types are positive
 - Smooth muscle neoplasms are also desmin positive
 - More specific and virtually diagnostic are myogenin and myoD1

- The only sensitivity exception is the sclerosing type, which may show only dot like desmin and may be only variably positive for myogenin
- The only specificity exception is rare expression by melanotic neuroectodermal tumor of infancy
- Composite tumors must be ruled out
- MyoD1 reagents may produce nonspecific cytoplasmic staining
- Myogenin is preferred by many for this reason

Genetic Study [7]

- PAX-FOXO1 fusion transcripts are specific for alveolar rhabdomyosarcoma
 - PAX3-FOXO1 t(2;13)(q35;q14) – 60%
 - PAX7-FOXO1 t(1;13)(p36;q14) – 20% (better prognosis)
- Nonspecific minor translocations and fusion negative cases may occur
 - Fusion negative
 - Amplifications of genes: MYCN, MDM2, CDK4, IGF-R1
 - FGFR1-FOXO1 t(8;13;9)(p11.2;q14;9q32)
 - PAX3-NCOA1 t(2;2)(p23;q53)
 - PAX3-NCOA2 t(2;8)(q35;q13)
 - There is no specific genetic abnormality specific for embryonal or other subtypes of rhabdomyosarcoma
- A number of nonspecific genetic abnormalities have been described
 - LOH at 11p15.5
 - Gains of chromosomes 2,7,8,11,12,13,17,19, and 20
 - Amplifications of genes: MYCN, MDM2, CDK4, IGF-R1
- Stanford University test all cases of pediatric rhabdomyosarcoma for FOXO1 abnormalities with FISH on paraffin sections
- Classical cytogenetic study is then necessary in positive cases to determine the specific fusion partner
- All pediatric specimens considered suspicious for soft tissue sarcoma should have a portion of unfixed tissue set aside for cytogenetic study
- No specific genetic abnormalities associated with anaplasia

Epidemiology

Rhabdomyosarcoma of the prostate gland commonly occurs in male children and infants and it is a highly malignant tumour [1] [2] [6].

Presentation

Rhabdomyosarcoma of the prostate tends to present predominantly with lower urinary tract symptoms [8] [9] which may include urinary frequency, dysuria and this may culminate in the development of retention of urine. RMSP may also present with haematuria [10]. RMSP is characterized by rapid growth and the ensuing development of local invasion tends to lead to the development of bladder outflow obstruction and rectal compression. [2] The main sites for the development of metastasis include: the lungs for which the patient may present with breathlessness, the liver, the skeleton. RMSP may also present as subcutaneous nodules over different sites of the body including forehead, scalp, face, and upper trunk [11]. Occasionally PRMSP may present with rare symptoms like worsening dyspnea skin nodules poly-arthritis and fever and scattered crackles in chest on examination of the chest. [11]

Findings on clinical examination

Clinical examination of patients with PRMSP may reveal smooth and / or firm enlarged prostate gland on rectal examination, occasional supra-pubic mass, regional lymph node enlargement, respiratory symptoms and abnormal findings on examination of the respiratory tract due to presence of lung metastases, associated with normal serum PSA levels and normal serum prostatic acid phosphatase levels as well as evidence of osteoclastic bone metastases [8] [9] [12].

Investigations

Laboratory Investigations

Full blood count and coagulation screen are carried out as part of the general screening of the patient and any anemia or coagulation pathologies found are corrected before treating the patient (see [2] for example when full blood count was normal).

Biochemistry tests including serum urea and electrolytes, bone profile and liver function tests and serum glucose are carried out as part of the general assessment of the patient and any abnormalities detected are corrected as part of the general management of the patient (see [2] for example when the renal function tests and liver function tests were normal).

Serum prostate-specific antigen (PSA) and serum prostatic specific acid phosphatase tend to be carried out. Generally the serum PSA tends to be normal (see [2] for example when the serum PSA was normal) but in some cases where there may be inflammation of the prostate, the serum PSA level may be elevated.

Urinalysis and Urine Culture and Sensitivity

Urinalysis as well as urine culture and sensitivity are carried out as part of the general assessment of the patient and if urinary tract infection is diagnosed the infection is treated appropriately (see [2] for example when urine microscopy was normal).

Radiological investigations

Ultra-sound scan of abdomen and pelvis

Ultrasound scan of abdomen and pelvis undertaken would tend to reveal the prostatic lesion in the prostate gland and the extent of the lesion. The scan would also indicate presence or absence of hydronephrosis, enlarged or non-enlarged lymph nodes in the abdomen and pelvis as well as if there is any liver involvement by the lesion. [14]

Ultrasound scan-guided biopsy of the prostatic lesion

Ultrasound scan-guided biopsy of prostate is a means by which specimens of the prostatic lesion are obtained for histological diagnosis of rhabdomyosarcoma of the prostate gland (see [8] for example when trans-rectal ultrasound guided biopsy was undertaken in a case).

Ultra-sound guided insertion of nephrostomy

In cases of hydronephrosis and impaired renal function, ultrasound scan of the renal tract can be performed as a guide to insertion of nephrostomy as may be required in the management of the patient.

Computed tomography (CT) scan of abdomen, pelvis and thorax (see for example [2] [8] [13] [14] [15] in which CT scan was undertaken)

CT scan of the abdomen and pelvis may be undertaken in the initial assessment of the patient to study the prostatic lesion and the extent of lesion as well as presence or absence of enlarged involved lymph nodes in the abdomen and pelvis as well as presence or absence of any metastasis in the abdomen and pelvis. The CT scan of abdomen and pelvis may reveal a heterogeneously enhancing mass in the prostate gland and it would show whether or not the mass is invading or infiltrating the urinary bladder, seminal vesicle or not, and whether or not the mass had extended beyond the capsule of the prostate and involved other nearby organs. This CT scan of abdomen and pelvis would form part of the staging assessment of the tumour. Furthermore CT scan of abdomen and pelvis can be undertaken as part of the follow-up assessment for response to treatment or progress of the disease.

CT scan of the thorax tends to be undertaken as part of the initial staging assessment to determine

whether or not there is any metastasis in the lung or thorax. CT scan of thorax can also be done in the follow-up of the patient to determine whether or not the patient has developed metastasis in the thorax (for example CT scan of the thorax was undertaken in e cancer [2]).

Magnetic Resonance Imaging (MRI) Scan of abdomen, pelvis and thorax (see [14] and [15] in which MRI scan was used)

MRI scan of the abdomen, pelvis and thorax may be undertaken in the initial assessment / staging of the tumour and it can also be undertaken in the follow-up assessment of the patient to confirm absence of or progress of disease

PET/CT scan (see [15] in which MRI scan was used)
PET/CT scan can be used to identify metastatic lesions in the body

Isotope Bone Scan

Isotope bone scan can be undertaken to confirm absence or presence of bone metastasis in the initial assessment of follow-up of the patient

Diagnosis by histological examination of trans-urethral resection of prostatic specimens

Diagnosis of RMSMP may sometimes be made by histological examination of trans-urethral resection of prostate specimens [2] [6].

Biopsy of subcutaneous nodules

If there is any subcutaneous nodule in a patient, then histological examination of biopsy specimen of the nodule or lump would help establish the diagnosis.

Macroscopic features

There is no specific macroscopic feature of the enlarged prostatic tissue that could be described as definitely diagnostic of rhabdomyosarcoma of prostate.

Microscopic features

Microscopic examination of the prostate gland in primary rhabdomyosarcoma of the prostate gland tends to show:

- (a) Cellular areas, particularly surrounding blood vessels which alternate with myxoid/ edematous areas and areas of necrosis [4]
- (b) Tumour cells which tend to be small, round or oval or spindly [4].
- (c) At times forms of the tumour may be bizzare with abundant, eosinophilic cytoplasm and cross striations that vary. [4]

- (d) Evidence of extension beyond the prostate gland [4]

Immunohistochemistry findings

Positive staining

In Rhabdomyosarcoma immunohistochemistry of the tumour tends to show positivity for [2] [3]

- (a) Desmin
- (b) Skeletal muscle markers including MyoD1, myogenin, sarcomeric actin, myoglobin.
- (c) recently Cytoplasmic staining with WT1

Negative staining

In rhabdomyosarcoma immunohistochemistry of the tumour would tend to be negative for:

Cytokeratin [2]

Leucocyte common antigen (CD45) [2]

Differential diagnosis

With regard to large tumours that invade the urinary bladder difficulties may arise in deciding whether or not the tumour is primary rhabdomyosarcoma of the urinary bladder invading the prostate gland or primary rhabdomyosarcoma of the prostate gland invading the urinary bladder. [4]

Treatment

- (i) Primary rhabdomyosarcoma of the prostate gland has been treated by means of multi-agent chemotherapy, surgery and chemotherapy. [4]
- (ii) Ashlock and Johnstone. [16] stated that: remarkable strides had occurred in the treatment of rhabdomyosarcoma of the prostate with a resultant decrease in the duration of chemotherapy, less cumulative doses of radiotherapy, and improving survival documentation; a focus on preservation of the urinary bladder had not been documented to adversely affected the survival of patients majority of studies undertaken; even in cases when it is not possible to achieve preservation of organ, improvements in the techniques of urinary diversion do offer improvement of quality of life; it is clear that the use of multi-modality treatment has improved survival; the necessary duration of therapy has decreased by 50%
- (iii) It has also been stated that (a) preservation of the urinary bladder is the main goal of treatment of primary rhabdomyosarcoma arising in the urinary bladder and/or the prostate gland; (b) patients who have a primary rhabdomyosarcoma of the urinary bladder/

prostate gland causing bladder obstruction tend to be treated with radiotherapy following an initial chemotherapy treatment to relieve bladder outlet obstruction; (c) Currently, a more effective chemotherapy and radiotherapy have increased the frequency of salvage of the urinary bladder; (d) With regard to patients who have residual tumour pursuant to chemotherapy and radiation treatment, the appropriate surgical treatment may entail partial cystectomy or prostatectomy [2] [5] [17].

Outcome

The outcome of primary rhabdomyosarcoma of the prostate gland tends to be better if the tumour exhibits leiomyosarcoma-like histological appearance [4].

(B) Miscellaneous narrations and discussions from some reported cases

In 1989, McLone et al. [18] reported six boys who had been treated in their institution since 1978. They reported that three of the boys had localized disease and they were treated by means of initial biopsy for histological confirmation of diagnosis followed by vincristine, actinomycin-D, and cyclophosphamide (VAC) chemotherapy, and urinary bladder sparing surgery with or without radiotherapy. Additional combination chemotherapy (“pulse” VAC, Adriamycin, VP-16, cisplatin, and ifosfamide) was continued for 20 months to 22 months after the induction course of treatment. Two of the boys did have microscopic residual disease which was undetected by frozen section examination and which was unresponsive to radiotherapy. Cystectomy undertaken subsequently 4 months and 7 months later was ensued by eradication of the disease. In one of the patients, preservation of urinary bladder was achieved from the age of 3 months for a period of 8 years. Artificial sphincter which was inserted as an attempt to treat his urinary incontinence failed due to ischemia secondary to scar tissue and cuff compression. He was alive at the time of publication of the paper with a constructed Koch pouch urinary diversion. With regard to the 50% of the patients (3 patients) who had metastases at the time of their presentation, two had died within 12 months irrespective of aggressive chemotherapy and radiotherapy they had received. The third patient was at the time of publication of the paper on treatment. McLone et al. [18] iterated that even though chemotherapy had markedly improved the prognosis of rhabdomyosarcoma of the prostate gland, in

majority of cases surgery is still necessary; salvage of the urinary bladder is a desirable goal; nevertheless, residual microscopic disease, difficulty with regard to frozen-section detection of disease, and poor vascularization of tissue for subsequent insertion of sphincter replacement had remained significant obstacles.

In 1994 Ruzkiewicz and Vernon-Roberts [19] reported an incidental rhabdomyosarcoma of the prostate gland in a sudden infant death syndrome (SIDS) and they highlighted the value of histological examination of all organs in autopsy cases and the possible significance of the co-existence of malignant tumors in death that are attributable to SIDS.

In 1968, Bapna et al. [20] reported the case of rhabdomyosarcoma of the prostate in a boy who was only 11 months old. Bapna et al. [20] stressed the utmost value of diagnosing cases of rhabdomyosarcoma of the prostate as early as possible.

In 2002, Nabi et al. [8] stated that embryonal rhabdomyosarcoma of the prostate gland is commonly found in children and the tumour is rarely found in adults. Nabi et al. [8] reported two cases of rhabdomyosarcoma of the prostate gland in adults as follows:

Case 1

A 56 year-old man presented with a 3-month history of dysuria and obstructive voiding symptoms. His general and systematic examinations on the whole were normal. His rectal examination revealed an enlarged prostate gland which was smooth. His full blood count and serum biochemistry examination results were normal. His serum prostate specific antigen level was 7.5 ng / ml. He had trans-rectal ultrasound guided biopsy of the prostate gland and histological examination of the specimen revealed an embryonal rhabdomyosarcoma of the prostate gland. He had computed tomography (CT scan) of the pelvis which revealed a large soft tissue mass which had replaced the prostate gland and which had infiltrated the base of the urinary bladder. He was treated by means of radiotherapy and chemotherapy. He received 6500 rads of radiotherapy treatment and doxorubicin based chemotherapy over a 2 month period. He had a subsequent CT scan which did show significant decrease in the size of prostatic tumour mass. At 3 months pursuant to the completion of his treatment, he developed generalized weakness and body pain. His general condition worsened and he developed skeletal metastases and pancytopenia and he died at 5 months following his initial presentation.

Case 2

A 47-year-old man with a one month history of difficulty in voiding developed acute retention of urine. On examination his prostate gland was found to be enlarged. His serum PSA was 2 ng / ml. The results of his full blood count and his serum biochemistry tests were within normal limits. He underwent trans-urethral resection of prostate and histological examination of the specimen revealed embryonal rhabdomyosarcoma of the prostate gland. He had magnetic resonance imaging scan in another hospital which showed a large soft tissue mass in the prostate gland which had infiltrated the base of the urinary bladder. The fat planes between the prostate gland and the wall of the rectum were noted on the MRI scan to be obliterated. He was offered surgical operative treatment but he refused to undergo surgery. He was treated by means of a combination of doxorubicin based combination chemotherapy and external beam radiotherapy which consisted of 65 Rads and he received his treatment over a period of 2 months. One month pursuant to his treatment he developed hemoptysis and his investigations did reveal that he had developed metastases in the bones, liver and in the lung. He developed septicemia and multi-organ failure. He died 4 months after his initial diagnosis.

Bisceglia et al. [6] in 2011 reported a 49-year-old man with advanced stage primary rhabdomyosarcoma of the prostate gland who initially underwent trans-urethral resection of prostatic tumour and who after a diagnosis of primary embryonal rhabdomyosarcoma of the prostate gland was established received courses of chemotherapy prior to undergoing radical cystoprostatectomy including removal of the seminal vesicles. Diagnosis was established after histological examination and immunohistochemistry studies of the tumour. He developed a huge pelvic recurrence and died of his tumour/disease one year after the initial diagnosis. Bisceglia et al. [6] also reported that they had searched the PUB Med literature and all literature on primary embryonal rhabdomyosarcoma of the prostate gland and found that at the time of the publication of their case report only 24 cases of primary rhabdomyosarcoma of the prostate gland had been reported in men who were eighteen years old or older than eighteen years. Bisceglia et al. [6] stated the following:

(iv) Embryonal primary rhabdomyosarcoma in adults is a very rare and aggressive disease.

- (v) The long-term disease-specific survival rate of primary rhabdomyosarcoma of the prostate gland is poor.
- (vi) The stage of the tumour influences the prognosis of the disease.
- (vii) Early diagnosis and complete surgical resection of the disease would offer patients the best chance of improved survival.

Munoz Velez et al. [21] reported two patients who were aged 27 years and 34 years who had embryonal rhabdomyosarcoma of prostate gland. They reported that both patients had dissemination of the tumour at the time of initial diagnosis and both patients received chemotherapy. They further reported that there was a 60% reduction in tumour volume in one patient who subsequently underwent rescue surgical operation and that he developed recurrence of his tumour but he was alive he was alive, 3 years after the initial diagnosis of his tumour. With regard to the second patient, there was no tumour response to his chemotherapy treatment and he refused to undergo rescue surgical operation and furthermore he was lost to follow-up. Munoz Vélez et al. [21] made the ensuing conclusion and recommendation:

- Embryonal rhabdomyosarcoma of the prostate gland in the adult is an unusual and aggressive tumour which is associated with rapid growth and progression.
- Early diagnosis of primary embryonal primary rhabdomyosarcoma of the prostate gland and prompt treatment by radical surgery would be essential to achieve improvement of the outcome of the disease.

In 1992, Waring and Newland [1] reported three cases of embryonal rhabdomyosarcoma of the prostate gland in adults. They stated that their literature review had revealed six cases of primary embryonal rhabdomyosarcoma of the prostate which had been reported in the literature prior to their report of three cases and that from their literature review they had made the following observations:

- The natural history of primary rhabdomyosarcoma of the prostate gland is characterized by rapid growth, with the typical development of large abdominal or pelvic masses, quite often resulting in renal failure which had been caused by bilateral ureteric obstruction.
- The rhabdomyosarcoma of the prostate gland eventually disseminates widely, mostly to the lungs, bone, liver, and serosal surfaces, and

unlike, majority of other sarcomas, regional lymph node metastases tend to be common in primary rhabdomyosarcoma of the prostate.

- Combination modality treatment has resulted in marked improvement in the survival rates and reduction in surgical morbidity of children who have developed primary embryonal rhabdomyosarcoma of the prostate gland. Nevertheless, with regards to adults the outcome has remained poor, with all of the patients dying of disseminated disease within 16 months of the histological diagnosis and the mean survival of adults was 8 months.

In 2000, Dalal et al. [9] reported a case of primary embryonal rhabdomyosarcoma of the prostate gland in a man who was more than 60 years old. They stated that embryonal rhabdomyosarcoma of the prostate gland is rare and the median age of occurrence of the tumour was 5 years; nevertheless, sporadic cases of primary embryonal sarcoma of the prostate gland have been reported in adults. They further stated that to their knowledge, up to the time of the report of their case in 2000, less than ten cases of primary embryonal rhabdomyosarcoma of the prostate gland had been reported in the literature and of these and only two cases had previously been reported in men older than sixty years.

In 1972, Timmons et al. [22] reported that of 30 children who had undergone treatment for primary embryonal rhabdomyosarcoma, the primary site of the tumour was the urinary bladder in 14 cases of which 9 were in boys and 5 were in girls, and the prostate gland in 16 cases. They also reported that with regard to the rhabdomyosarcomas of the urinary bladder the mean age at diagnosis was 3 years but on the other hand the mean age at diagnosis of rhabdomyosarcomas of the prostate in the children was 6.5 years. They further reported that with regard to outcome, the overall survival rate was 23%; and 5 children who had embryonal rhabdomyosarcoma of the urinary bladder as well as 2 children who had rhabdomyosarcoma of the prostate gland were alive from one and half years to twenty three years post-operatively. Timmons et al. [22] stated that with regard to treatment, they would recommend aggressive coordinated treatment with surgery, radiotherapy, and cyclic combination chemotherapy.

Levin et al. [14] in 1992 stated that invasive embryonal rhabdomyosarcomas of the prostate gland tend to extend superiorly into the base of the urinary bladder which requires partial cystectomy as part of

the primary tumour excision. Levin et al. [14] studied three patients by means of ultra-sound Scan, computed tomography (CT) scan and magnetic resonance imaging (MRI) scan and demonstrated the extension of the tumour superiorly and anteriorly to the urinary bladder in the pre-vesical space of Retzius. Levin et al. [14] reported that complete excision of the tumour with sparing of the urinary bladder was successful in two of the patients. Levin et al. [14] also stated that the radiological imaging of pelvic tumours in children (even though well studied with ultrasound scan and CT scan) is helped by MRI scan in the sagittal plane and / or in the lateral films of intravenous pyelograms and cystograms in order to determine the relation of the tumour to the urinary bladder.

Nagata et al. [23] in 1985 reported a six-year-old boy who had rhabdomyosarcoma of the prostate gland who presented with pain on voiding. His investigations revealed lung metastasis and involvement of lymph nodes by the tumour. He was treated by means of vincristine, actinomycin-D, and cyclophosphamide; however, the combination chemotherapy was not effective. He died as a result of respiratory failure due to diffuse lung and pleural tumour metastases, 41 days following his admission. Nagata et al. [23] stated that rhabdomyosarcoma of the prostate gland in children is rare and that their case was the 9th case of rhabdomyosarcoma of the prostate gland in a child to be reported in Japan.

In 1994, Carvarjal Busslinger and Plaschkes [24] reported two children, both of whom had rhabdomyosarcoma of the urinary bladder and prostate gland. One of the children who presented in 1983 was operated and he received chemotherapy as well as he underwent cystoprostatectomy, and the second child who presented in 1991 received chemotherapy which eradicated the tumour without him undergoing cystectomy. They also reported that both children were alive and free of tumour after ten years and two years respectively.

Almeida et al. [15] in 2007 reported a 27-year-old man who presented with recurring episodes of left flank pain which was provisionally diagnosed as left sided renal colic for which a CT scan of abdomen and pelvis was undertaken. The CT scan showed a large, solid and homogeneous mass in the prostate gland which had predominantly a peripheral contrast enhancement (**see figure 1**). The lesion had extended superiorly on the posterior aspect to the left, and had involved the left ureter resulting in dilatation

of the upper calyceal system. The patient subsequently underwent trans-rectal ultra-sound guided biopsy of the prostate gland, magnetic resonance imaging scan, and hybrid positron emission tomography / computed tomography (PET/CT) scan for staging of the disease. Trans-rectal ultra-sound scan undertaken during the time of the biopsy of the prostate (see figure 2) revealed a hypo-echoic mass which had involved the entire prostate, distorting the architecture of the prostate, causing interruption of the anatomic capsule, as well as infiltrating the adjacent planes. The seminal vesicle was noted to be enlarged due to tumour infiltration. The histological and immunohistochemistry features of the biopsy specimen were adjudged to be consistent with a diagnosis of embryonal rhabdomyosarcoma of the prostate gland. The endo-rectal coil magnetic resonance imaging which he had (see figure 3) showed an ill-defined mass which had infiltrative aspect, intermediary signal on T1-, hyper-signal on T2- weighted sequences which had intense and heterogeneous gadolinium enhancement involving the left neuro-vascular bundle, the left seminal vesicle and the medial portion of the right seminal vesicle. The lesion was in contact with the wall of the urinary bladder at the level of the trigone with probable involvement of the urinary bladder. The PET/CT scan (see figure 4), also showed hypermetabolic lesions in the left, posterior cervical, left lower para-tracheal, left supra-clavicular fossa, and left retroperitoneal lymph nodes which had extended from the renal hila to the pelvic cavity. He also had biopsy of a left supra-clavicular lymph node and histological examination of the specimen confirmed metastatic embryonal rhabdomyosarcoma of prostate. The case was reported after the diagnosis was established therefore there was no report relating to the treatment and outcome of the disease. Almeida et al. [15] stated the following:

- (i) Some authors [1] [25] are of the opinion that rhabdomyosarcoma is a malignant tumour which originates from mesenchymal cells with sarcomatous differentiation.
- (ii) It had been stated that the disease progresses extremely fast and aggressively and is most of the time found in children in whom it tends to correspond with the main tumour of the prostate gland. [26] [27]
- (iii) The tumour is rare in adults and at the time of publication of their paper in 2007 to their knowledge only 30 cases of the tumour had been reported in the English literature. [27] [28] [29]

- (iv) Logani et al. [27] stated that rhabdomyosarcomas tend to present aggressively and at the time of initial presentation 25% of the tumours are associated with metastases. In decreasing order of frequency of metastases the following organs tend to be affected: lungs, bones, lymph nodes, liver, and serosas. [1] [26] [30] In rhabdomyosarcomas, bony metastases tend to be disseminated and osteolytic in comparison with adenocarcinomas which tend to be associated with osteoblastic metastases which tend to be concentrated in the axial skeleton. [1]
- (v) Locally, rhabdomyosarcomas of the prostate gland tend to infiltrate peri-urethrally, perivesically, and peri-rectally thus displacing the urinary bladder and the rectum. [31] Histologically rhabdomyosarcomas can be divided into embryonal, alveolar, a quite aggressive sub-type occurring in soft tissues of children; and pleomorphic, a rare and aggressive sub-type which tends to be found in adults. [25] [32]
- (vi) The embryonal pattern of rhabdomyosarcoma is found in approximately two thirds of all rhabdomyosarcomas [25]
- (vii) The presentation of rhabdomyosarcoma of the prostate include: obstructive urinary symptoms, haematuria, incontinence, pelvic pain requiring analgesia, intestinal obstipation due to per-rectal plane invasion or compression by the tumour. [1] [26] [27] [30]
- (viii) Diagnosis of rhabdomyosarcoma of the prostate gland can be confirmed by means histological examination of trans-rectal ultrasound scan biopsies of the prostate in view of the fact that it had been stated that there is no pattern of radiological imaging that define the diagnosis. [27] [33] Nevertheless, some radiological findings may suggest the diagnosis of rhabdomyosarcoma of the prostate for example, presence of a large mass on the bed of the prostate gland, infiltrating the adjoining planes in a young man whose serum PSA levels have not been elevated. [1] [33]
- (ix) It has been documented that in rhabdomyosarcoma of the prostate ultra-sound scan tend to show hyper-echogenic or hypo-echogenic areas with sonolucent areas which correspond to sites of necrosis or haemorrhage. [26] Hyperemia and high diastolic flow velocity may also be seen in rhabdomyosarcomas in children as stated by Aprons et al. [26]
- (x) With regard to CT scan in rhabdomyosarcomas of the prostate, an infiltrative, and on many

occasions an ill-defined mass which has heterogeneous attenuation has been described in which the origin of the whether prostatic or vesical site of origin could not be determined. [26] [34]

- (xi) With regard to MRI scan, the primary tumour tends to show non-specific low signal intensity on T1-weighted sequences, and high signal intensity on T2-weighted sequences. Heterogeneous signal intensity could also be observed in areas of haemorrhage. [26] In comparison with ultrasound scan and CT scan, MRI scan tends to allow a more accurate assessment of the extent of the local tumour and adjacent plane involvement. [26] [35]
- (xii) The use of PET/CT scan in rhabdomyosarcomas in adults has not yet been consolidated in the literature; nevertheless, cases involving children had illustrated the relevance of PET/CT scan in the detection of the primary focus in metastatic disease, obscure metastasis, and tumours in unusual sites. [36]

Niimi et al. [37] reported a 20-year-old man who presented with visible haematuria and high fever. He had a history of acute lymphatic leukemia at the age of six years. His serum prostate-specific antigen (PSA) was 27.9 ng / ml. He had computed tomography (CT) scan of abdomen and pelvis which

showed a suspected infectious cyst in the prostate gland. He received antibiotic treatment and his serum PSA subsequently normalized. Nevertheless, he subsequently suffered urinary bladder tamponade. He had biopsy of his prostate gland and histological examination of the specimen revealed embryonal rhabdomyosarcoma of the prostate gland. According to the treatment protocol of the Japan Rhabdomyosarcoma Study Group he was commenced on chemotherapy which comprised of vincristine, actinomycin D, cyclophosphamide, and ifosfamide. The tumour shrank in size, and partial remission was achieved after he had received 1 course of chemotherapeutic treatment. Niimi et al. [37] stated that with regard to the patient's past medical history, during his earlier treatment for acute lymphatic leukemia at the age of 6 years, he had been exposed to a cumulative radiotherapy dose of 10 Gy across the whole of his body. Niimi et al. [37] further stated that it had been reported that 88% of post-radiotherapy sarcomas are KIT-positive, and they had suspected that their patient had suffered a post-radiotherapy sarcoma in view of the fact that his tumour was KIT-positive. Niimi et al. [37] additionally stated that their case of rhabdomyosarcoma of the prostate gland was the first report of post-radiotherapy sarcoma manifesting as an embryonal rhabdomyosarcoma of the prostate gland.

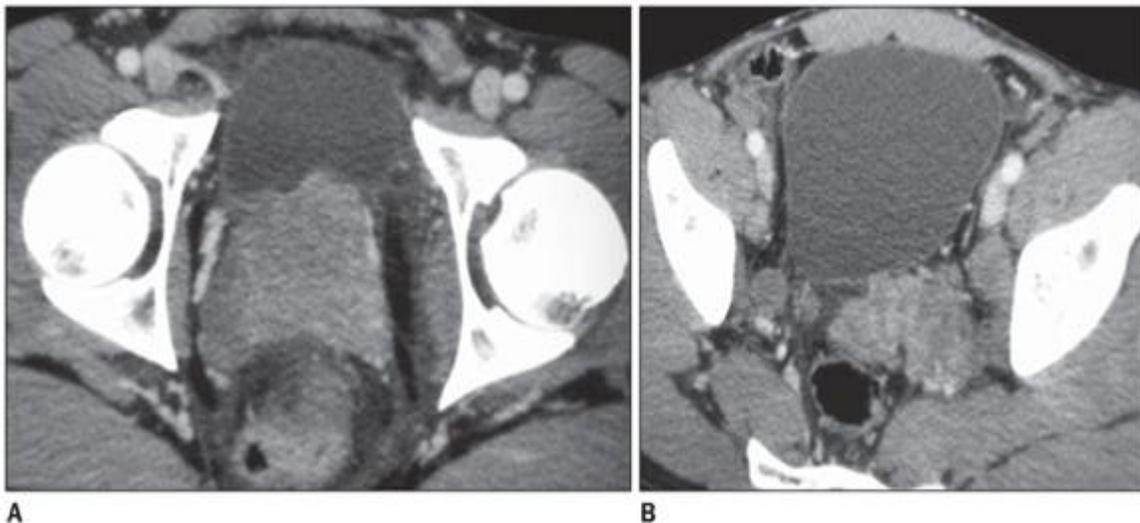


Figure 1. Computed tomography. Expansive prostatic growth with invasion of the left seminal vesicle.

Figure 1: Computed tomography. Expansive prostatic growth with invasion of the left seminal vesicle. Reproduced from: [15] Almeida F A G D, Filho C L D M, Melo E L A, Cerri L M D O, Cerri G G. Prostatic rhabdomyosarcoma in an adult patient: a case report. *Radiologia Brasileira Sao Paulo* 2007 Nov – Dec; 40(6): <http://dx.doi.org/10.1590/50100-39842007000600013> under the terms of the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

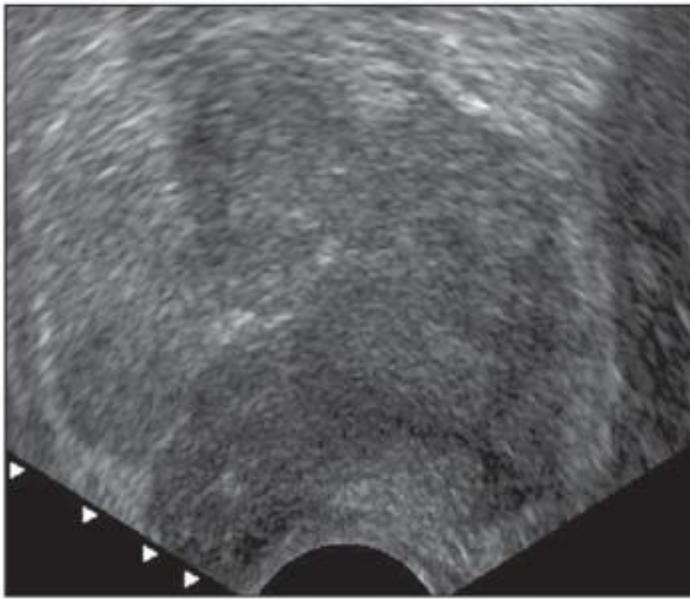


Figure 2: Trans-rectal ultrasound. Hypo-echoic prostatic mass with irregular hypo-echogenic anatomical planes. Reproduced from: [15] Almeida F A G D, Filho C L D M, Melo E L A, Cerri L M D O, Cerri G G. Prostatic rhabdomyosarcoma in an adult patient: a case report. Radiologia Brasileira Sao Paulo 2007 Nov – Dec; 40(6): <http://dx.doi.org/10.1590/5010039842007000600013> under the terms of the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

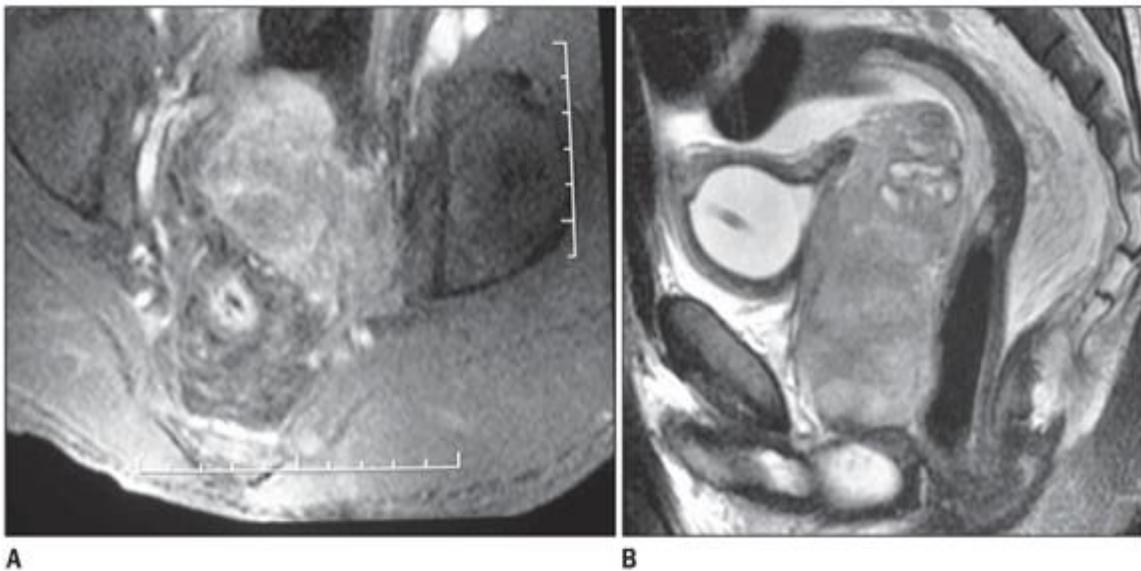


Figure 3. Endorectal coil magnetic resonance imaging, axial, contrast-enhanced T1-weighted fat-saturated sequence (A) and sagittal T2-weighted (B). Mass with an infiltrative aspect, with heterogeneous gadolinium enhancement involving the vasculonervous bundle and left seminal vesicle.

Figure 3: Endo-rectal coil magnetic resonance imaging, axial, contrast-enhanced T1-weighted fat-saturated sequence (A) and sagittal T2-weighted (B). Mass with an infiltrative aspect, with heterogeneous gadolinium enhancement involving the vasculo-nervous bundle and left seminal vesicle. Reproduced from: [15] Almeida F A G D, Filho C L D M, Melo E L A, Cerri L M D O, Cerri G G. Prostatic rhabdomyosarcoma in an adult patient: a case report. Radiologia Brasileira Sao Paulo 2007 Nov – Dec; 40(6): <http://dx.doi.org/10.1590/50100-39842007000600013> under the terms of the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

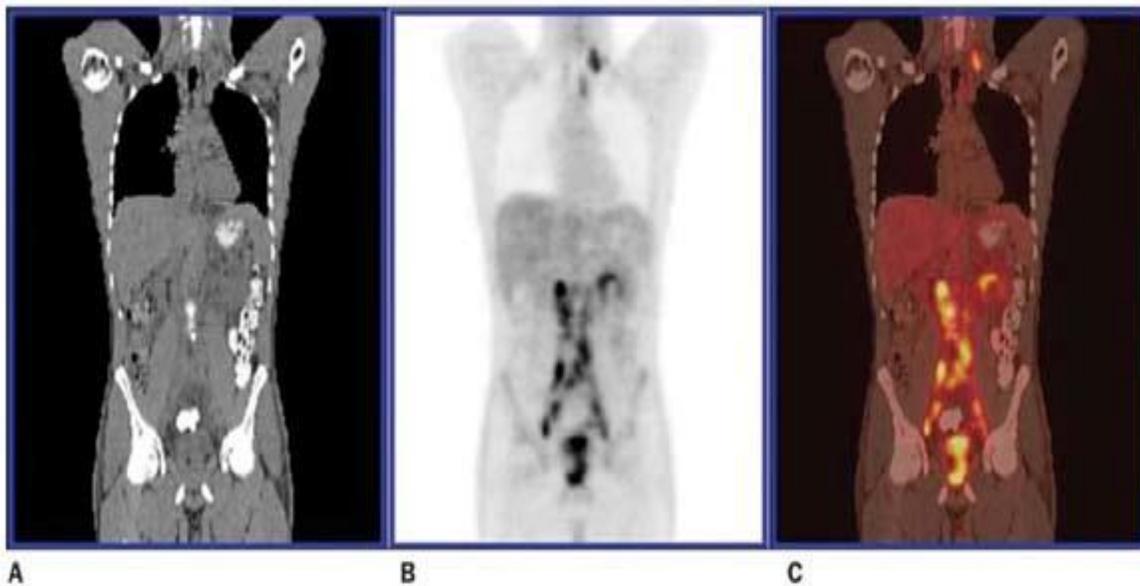


Figure 4. PET/CT image. Multiple, retroperitoneal and left supraclavicular metastatic lymph nodes.

Figure 4: PET/CT image. Multiple, retroperitoneal and left supraclavicular metastatic lymph nodes. Reproduced from: [15] Almeida F A G D, Filho C L D M, Melo E L A, Cerri L M D O, Cerri G G. Prostatic rhabdomyosarcoma in an adult patient: a case report. *Radiologia Brasileira Sao Paulo* 2007 Nov – Dec; 40(6): <http://dx.doi.org/10.1590/50100-39842007000600013> under the terms of the Creative Commons Attribution License which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Singh et al. [11] reported a 16-year-old Asian-Indian male student who presented with worsening shortness of breath on exertion and new onset skin nodules which had developed over the preceding one week. He had poly-arthritis and low-grade pyrexia of two months. His past medical history was unremarkable. He had received broad spectrum antibiotics empirically for his constitutional symptoms without any improvement. On examination he was found to be febrile, pale. His blood pressure was normal and he had sinus tachycardia. He had multiple non-tender, subcutaneous nodules which were two to four centimeters in size and they were predominantly located on the scalp, face and upper trunk. He had crackles on examination of the respiratory system and splenomegaly on abdominal examination. His prostate gland was found to be enlarged but non-tender. He had laboratory investigations which revealed: normocytic normochromic anemia, hypercalcemia, and hyperuricemia, normal urinalysis, no laboratory test evidence for tuberculosis, no laboratory test evidence to suggest immunocompromised state or autoimmune disorder. He had tomographic imaging of the chest which showed multiple bilateral nodular densities (see figure 5). He was rehydrated, transfused with blood and he received empirical broad spectrum

antibiotics prior to receiving his blood and urine culture results which were normal. He had computed tomography (CT) scan of abdomen and pelvis which revealed a 6 cm x 5 cm x 5 cm homogeneous soft tissue mass in the prostate gland. He had tests done for serum prostate-specific antigen (PSA), and prostatic acid phosphatase (PAP) which were normal. He had trucut biopsy of a nodule on his forehead and histological as well as immunohistochemistry studies of the biopsy specimen revealed features adjudged to be consistent with embryonal rhabdomyosarcoma (see figure 6). He later on, developed osteolytic lesions in the skull, pelvis, and proximal long bones. He had chemotherapy which comprised of Vincristine, Adriamycin and cyclophosphamide regimen. He died 3 weeks later as a result of complications of disseminated disease following a transient initial clinical response. The relatives of the patient did not give consent for an autopsy to be performed. Singh et al. [11] stated that their case was atypical with regard to its inconspicuous manifestation which mimicked a systemic inflammatory response and to the best of their knowledge had not been previously reported. Singh et al. [11] also stated that even though the primary site of the tumour in the prostate gland tends to have a favorable sign of prognosis with regard to rhabdomyosarcomas, the presence of detectable

metastases, tumour size > 5 centimeters, and age > 10 years at the time of initial presentation had been reported to be associated with poor unfortunate outcome. [38] Singh et al. [11] further stated that it had been iterated that debulking of tumour (with excision of equal to or greater than fifty percent of tumour) followed by administration of chemotherapy had improved the overall survival rates to 75% in patients with embryonal rhabdomyosarcomas; [39] however, their patient had distant metastatic spread at the time of initial presentation which had precluded any form of surgical intervention.

Prabhakaran et al. [2] in 2013 reported a 19-year-old gentleman who presented with dysuria and urinary frequency which culminated in him developing urinary retention. He was asymptomatic otherwise. He was found on examination to have a grade 3, enlarged prostate gland and no evidence of lymphadenopathy or hepatomegaly. His full blood count, renal profile and liver function tests and urine microscopy were normal. His serum lactate dehydrogenase was 715 U/L, serum alkaline phosphatase and prostate-specific acid (PSA) levels were normal. He had computed tomography (CT) scan of the abdomen and pelvis which showed a 9 cm x 7 cm x 6.5 cm heterogeneously enhancing mass which had replaced the prostate gland and which had infiltrated the base of the urinary bladder and which had reached inferiorly up to the left ischiorectal fossa (see figure 7). There was no evidence of calcification or enlarged lymph nodes. He underwent biopsy of

the prostate gland and histological examination of the specimen revealed sheets of cells that had moderate amount of eosinophilic cytoplasm and hyperchromatic nuclei (see figures 8 and 9). Immunohistochemistry studies of the biopsy specimen showed that the tumour was positively stained for desmin, and myogenin (see figures 10 and 11) and negatively stained for cytokeratin and leucocyte common antigen (CD45), which was adjudged to be suggestive of embryonal rhabdomyosarcoma of the prostate gland (RMS). He had CT scan of thorax which showed well-defined nodular densities which were scattered within the lung suggestive of pulmonary metastases. There was no bone metastasis and the bone marrow was reported to be normal. He was treated by means of chemotherapy which comprised of cyclophosphamide, doxorubicin, vincristine and actinomycin D and he also had local radiotherapy. He developed haemorrhagic cystitis at 10 months but this settled with supportive measures and he had a CT scan at one year after the start of his chemotherapy and this showed that the prostate gland was normal. Prabhakaran et al. [2] stated that embryonal rhabdomyosarcoma of the prostate commonly occurs in infants and in children, but occurrence of embryonal rhabdomyosarcoma of the prostate gland in young adults is rare and in view of this a high index of suspicion is essential for the diagnosis of the disease and for its treatment.



Figure 5: CECT chest (lung window) shows multiple varying nodules in both lungs. Reproduced from: Singh N K, Gangappa M, Gupta V, Mohan A. Embryonal prostatic rhabdomyosarcoma disguised presentation in an adolescent male: a case report. *Cases Journal* 2009; 2: 7546 DOI: 10.4076/1757-1626-2-7546 © 2009 licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

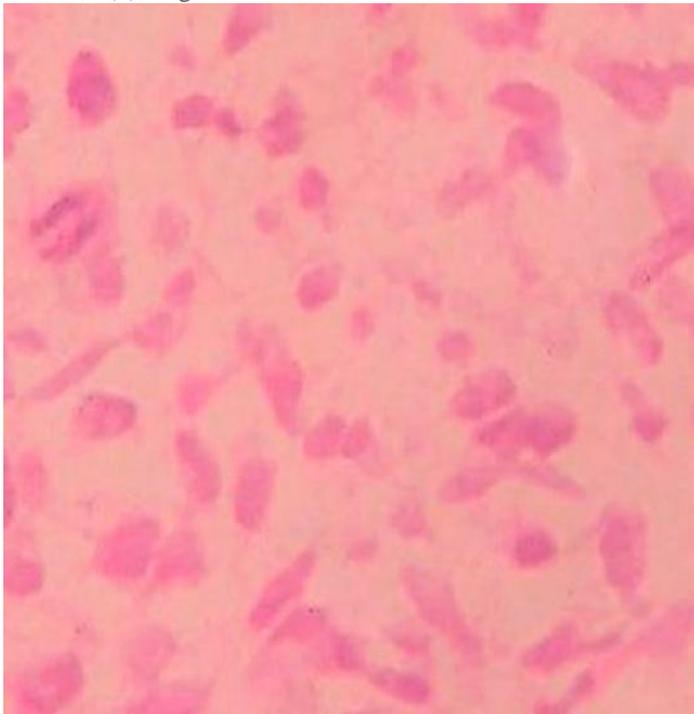


Figure 6: H/E – 400X) showing a malignant small round cell tumor with frequent mitoses and there is no evidence of any differentiation. Immunohistochemistry reveals focal cytoplasmic positivity for desmin, and negativity for leucocyte common antigen, cytokeratin, chromogranin, MIC-2 and S-100 protein. The histological and histochemistry findings are compatible with undifferentiated rhabdomyosarcoma. Reproduced from: Singh N K, Gangappa M, Gupta V, Mohan A. Embryonal prostatic rhabdomyosarcoma disguised presentation in an adolescent male: a case report. Cases Journal 2009; 2: 7546 DOI: 10.4076/1757-1626-2-7546 © 2009 licensee BioMed Central Ltd. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Hamzah et al. [10] reported a 23-year-old single Malay man who was referred to their institution because of persistent acute retention of urine. They reported that the patient had recurrent episodes of acute retention of urine which had started in March 2012. Hamzah et al. [10] stated that the patient had reported that each of his recurrent episodes of acute retention of urine was preceded by two days of haematuria associated with dysuria and culminating in retention of urine for which he was catheterized. He had 3 episodes of retention for which he was catheterized followed by trial without catheter. He had a rectal examination which revealed a firm enlarged prostate. His blood analysis was within normal range. He underwent cystoscopy which revealed a growth at the lateral wall of the prostatic urethra. He underwent trans-urethral resection of the urethral tumour. Histological examination of the specimen revealed blood clots and necrotic tissue which had been diffusely infiltrated by tumour cells. Detailed examination of the tumour infiltration revealed areas of hyper-cellularity with alternating loose arrangement with myxoid background. The tumour cells were highly pleomorphic, and these had ranged from large polygonal to spindle shaped cells. Amidst the cells, there were scattered rhabdomyoblasts seen; some large cells in centrally located nuclei which had encompassing eosinophilic cytoplasm. The histological features of the tumour were adjudged to be consistent with embryonal rhabdomyosarcoma of the prostatic urethra. He had ultra-sound scan of abdomen, renal tract and pelvis

which revealed normal kidneys with regard to echogenicity and size and no evidence of calculus or hydronephrosis on both sides. The ultrasound scan also showed a hypo-echoic lesion on the left lateral aspect of the posterior urethra which was reported as likely to be due to tumour. He also had magnetic resonance imaging (MRI) scan which showed a large soft tissue mass bulging into the lumen of the urinary bladder. The long-term outcome and further management was not reported in the case report. Hamzah et al. [10] stated that the histogenesis of the tumour is believed to arise from undifferentiated mesenchymal cells, which in the distal urogenital tract surround the mesonephric duct and becomes incorporated into the urinary bladder and prostate gland during embryogenesis and that they may undergo rhabdomyoblastic differentiation subsequently in life. Hamzah et al. [10] further stated that the diagnosis of rhabdomyosarcoma of the prostate is usually made by trans-rectal ultra-sound scan guided biopsy of the prostate or trans-urethral resection of the prostate; rectal examination does not reveal any finding specific to rhabdomyosarcoma; the serum prostate specific antigen level may be within normal range in view of the non-epithelial origin of the disease; no definite pathognomonic radiological finding has been documented to confirm the diagnosis of rhabdomyosarcoma of the prostate gland, extensive local invasion of the bladder neck and trigone by the tumour may be ensued by some changes related to obstruction of the ureter(s); Intravenous urogram may reveal ureteric obstruction at the level of the vesico-

ureteric junction which may be seen as elevation and fish hooking of the distal ureter over an enlarged mass; Ultra-sound scan and computed tomography scan may help, they are not valuable for the early detection of the disease; It has been stated that magnetic resonance imaging has been the choice for

the investigation of most sarcomas. [40] The diagnosis is confirmed by histopathological examination findings which tend to reveal variable differentiation along the myogenesis pathway and may show strap cells or myotubes which at times contain muscle cross striations.



Figure 7: CT scan of the pelvis showing heterogeneously enhancing mass replacing the prostate infiltrating the bladder base and Foley's bulb and catheter in situ.

Reproduced from: Prabhakaran P, Sanjayan R, Somanathan T, Narayanan G. Rhabdomyosarcoma of prostate presenting as bladder outlet obstruction in a young adult. *ecancer* 2013; 7: 360 DOI: 10.3332/ecancer.2013.360 Copy: © The authors; licensee *ecancermedicalsecience*. This is an Open Access article distributed under the terms of the Creative Commons Attribution License

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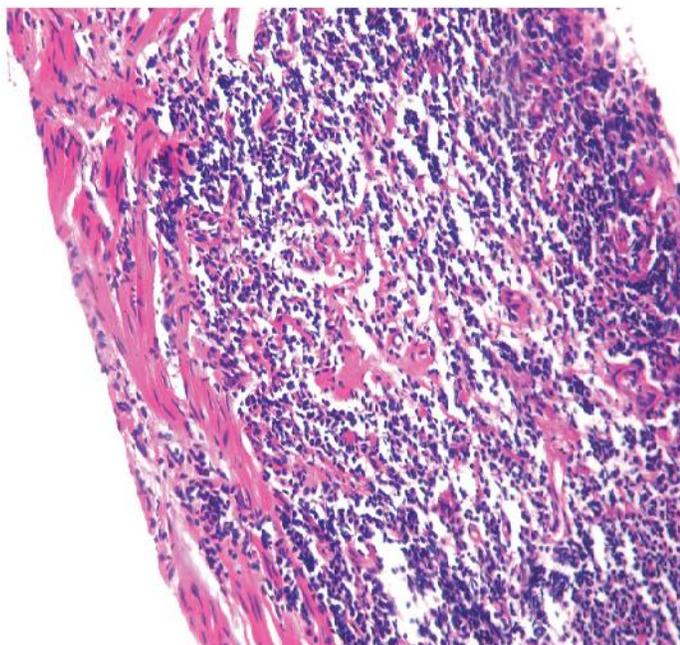


Figure 8: Hematoxylin and eosin (H&E) stained image showing sheets of cells having hyperchromatic nuclei at 10x magnification.

Reproduced from: Prabhakaran P, Sanjayan R, Somanathan T, Narayanan G. Rhabdomyosarcoma of prostate presenting as bladder outlet obstruction in a young adult. *ecancer* 2013; 7: 360 DOI: 10.3332/ecancer.2013.360 Copy: © The authors; licensee *ecancermedicalsecience*. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by3.0>), which permits unrestricted use, distribution, and reproduction in any medium provided the original work is properly cited

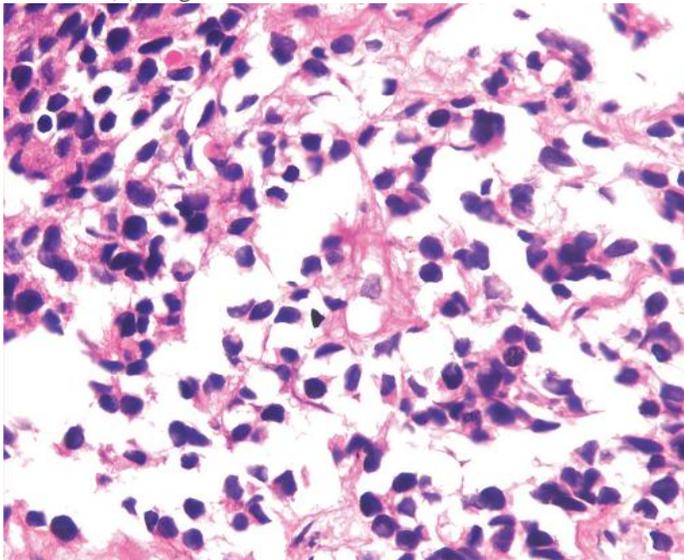


Figure 9: H & E stained image showing sheets of cells having moderate amount of eosinophilic cytoplasm and hyperchromatic nuclei at 40 x magnification.

Reproduced from: Prabhakaran P, Sanjayan R, Somanathan T, Narayanan G. Rhabdomyosarcoma of prostate presenting as bladder outlet obstruction in a young adult. *ecancer* 2013; 7: 360 DOI: 10.3332/ecancer.2013.360 Copy: © The authors; licensee *ecancermedicalsecience*. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by3.0>), which permits unrestricted use, distribution, and reproduction in any medium provided the original work is properly cited

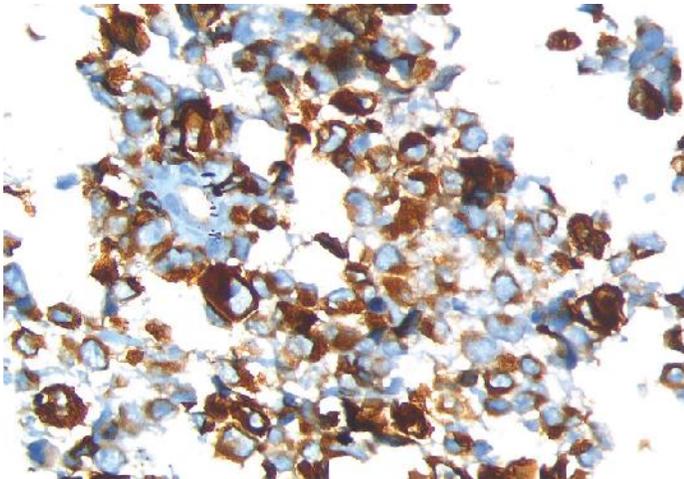


Figure 10: Immunohistochemistry 40 x image showing desmin positivity.

Reproduced from: Prabhakaran P, Sanjayan R, Somanathan T, Narayanan G. Rhabdomyosarcoma of prostate presenting as bladder outlet obstruction in a young adult. *ecancer* 2013; 7: 360 DOI: 10.3332/ecancer.2013.360 Copy: © The authors; licensee *ecancermedicalsecience*. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by3.0>), which permits unrestricted use, distribution, and reproduction in any medium provided the original work is properly cited

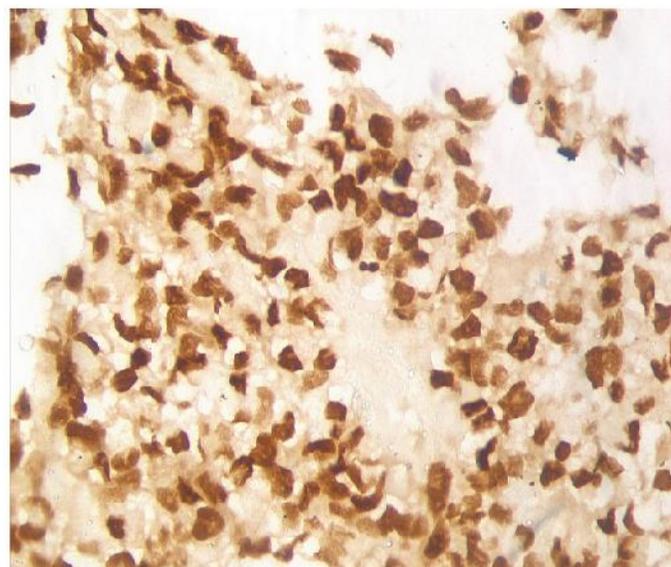


Figure 11: Immunohistochemistry 40x image showing myogenin positivity. Reproduced from: Prabhakaran P, Sanjayan R, Somanathan T, Narayanan G. Rhabdomyosarcoma of prostate presenting as bladder outlet obstruction in a young adult. *ecancer* 2013; 7: 360 DOI: 10.3332/ecancer.2013.360 Copy: © The authors; licensee *ecancermedicalsecience*. This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by3.0>), which permits unrestricted use, distribution, and reproduction in any medium provided the original work is properly cited

Hamzah et al. [10] additionally stated that previously the first line of treatment for rhabdomyosarcoma was radical surgical excision; nevertheless, superior chemotherapy treatment regimes, and radiotherapy regimes have been developed recently; embryonal rhabdomyosarcomas in children do respond well to radiotherapy and chemotherapy; it has been iterated that the advances in multi-modality treatment which include surgery, chemotherapy and radiotherapy had improved the prognosis in children and that the 5-year survival rate with multi-modality treatment in children was 74% [41]; in adults the prognosis tends to be dismal and adults tend to present with non-embryonal sub-types which also tend to be widely disseminated and associated with late presentation and the advanced stage of the disease at presentation. With regard to treatment Hamzah et al. [10] stated the following: the goal of treatment should be to achieve complete removal of the disease which commonly would require radical cystoprostatectomy and pelvic exenteration while preserving all functioning tissue; nevertheless, definite surgery tends to be delayed until neo-adjuvant therapy has caused the shrinkage of large unresectable tumour; [17] chemotherapy and radiotherapy should be adjunct to surgery to prevent local recurrence and distant metastases; radical prostatectomy alone could be an alternative treatment only in cases of small sarcomas which are confined to the prostate; An earlier study had reported a prostate sarcoma which was treated by means of radical prostatectomy, hemicystectomy and ureteroureterostomy and in which no adjuvant treatment was given and the patient was well at his 6th year follow-up. [42]

Conclusions

Primary rhabdomyosarcoma of the prostate gland is an uncommon aggressive disease which tends to be found more often in children in comparison with adults. The disease tends to be associated with worse prognosis in adults in comparison with children. Multi-modality treatment including surgery, new chemotherapy regimens and radiotherapy has been reported to result in improved survival in a number of cases and the use of chemotherapy and radiotherapy prior to surgery has enabled organ preserving surgical treatment of the disease. Developments in radiological imaging techniques may aid in the diagnosis and staging of the disease which would enable therapeutic planning. A high index of suspicion is required for the early diagnosis of the disease.

Conflict of Interest: None

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References

1. Waring P M, Newland R. Prostatic embryonal rhabdomyosarcoma in adults: a clinicopathologic review. *Cancer* 1992; 69: 755 – 762 DOI: 10.1002/1097-0142(19920201)69:3&it: 755:

- AID-CNCR2820690324>3.0.CO:2-Y PMID: 1730126
- Prabhakaran P, Sanjayan R, Somanathan T, Narayanan G. Rhabdomyosarcoma of prostate presenting as bladder outlet obstruction in a young adult. *ecancer* 2013; 7: 360 DOI: 10.3332/ecancer.2013.360
 - Carpentieri D F, Nichols K, Chou P M, Mathews M, Pawel B, Huff D.. Expression of WT1 in the differentiation of rhabdomyosarcoma from other paediatric small round blue cell tumors *Mod Pathol* 2002; 15: 1080 1086 DOI: 101097/01.MP.0000028646.03760.6B PMID: 12379755
 - Arora K Prostate Other malignancies Embryonal rhabdomyosarcoma *PathologyOutlines.com* 2012 June 2; [http:// pathologyoutlines.com/topic/prostateembryonalrhab.html](http://pathologyoutlines.com/topic/prostateembryonalrhab.html) last accessed 4th September 2015.
 - Rodeberg D A, Anderson J R, Amdt C A, Ferrer F A, Raney R B, Jenney M E, Brecht I B, Koscielniak E, Carli M, Biscogno G, Oberlin O, Rey A, Ullrich F, Stevens M C, Meyer W H. Comparison of outcomes based on treatment algorithms for rhabdomyosarcoma of the bladder/prostate: combined results from the Children Oncology Group, German Cooperative Soft Tissue Sarcoma Study, Italian Cooperative Group, and International Society of Pediatric Oncology Malignant Mesenchymal Tumors Committee. *Int J Cancer* 2011 Mar; 128(5): 1232 1239 DOI: 10.1002/ijc.25444
 - Bisceglia M, Magro C, Carosi I, Cannazza V, Ben Dor D. Primary embryonal rhabdomyosarcoma of the prostate in adults: report of a case and review of the literature *Int. J Surg Pathol* 2011 Dec; 19(6): 831 – 837: DOI: 10.1177/1066896910395585. Epub 2011 Mar 21
 - Hazard F K G Rhabdomyosarcoma Surgical Pathology Criteria *Stanford* URL: surgpathcriteria.stanford.edu/srbc/rhabdomyosarcoma/printable.html Surgical Pathology Criteria <http://surgpathcriteria.stanford.edu/>
 - Nabi G, Dinda A K, Dogra P N. Primary embryonal rhabdomyosarcoma of prostate in adults: diagnosis and management. *Int Urol. Nephrol* 2002-2003; 34(4); 531 – 534
 - Dalal D D, Tongaokar H B, Krishnamurthy S, Kulkarni J N. Embryonal rhabdomyosarcoma of prostate in an adult a diagnostic dilemma. *Indian J Cancer* 2000 Mar; 37(1): 50 – 53
 - Hamzah A A, Adnan A S, Jummaat F, Aftab R A. Embryonal rhabdomyosarcoma of the prostatic urethra *Journal of Clinical Practice and Health Sciences* 2015 Jul – Sep; 1(1): URL: www.jcphs.com] www.jcphs.com/sites/default/files/JCPHS_1_1_3pdf
 - Singh N K, Gangappa M, Gupta V, Mohan A. Embryonal prostatic rhabdomyosarcomas disguised presentation in an adolescent male: a case report. *Cases Journal* 2009; 2: 7546 DOI: 10.4076/1757-1626-2-7546
 - Figueiredo A A, Brandao G, Dentz L C, Alves C M, Stroppa A E. Bilateral pulmonary alveolar infiltrate and prostate tumour in a 54-year-old man. *Thorax* 2007 Nov; 62(11): 1002 - 1018
 - Lazar E B, Whitman G J, Chew F S. Embryonal rhabdomyosarcoma of prostate *A J R* 1996; 166(1): 72 DOI: 10.2214/ajr.166.1.8571909
 - Levin T, Berdon W E, Ruzal-Shapiro C, Abramson S, Garvin J, Altman R P, Hensle T, Ablin D S. Three pediatric patients with extension of prostatic embryonal rhabdomyosarcoma anterior to the bladder into the space of Retzius *Pediatr Radiol* 1992; 22(3): 200 - 202
 - Almeida F A G D, Filho C L D M, Melo E L A, Cerri L M D O, Cerri G G. Prostatic rhabdomyosarcoma in an adult patient: a case report. *Radiologia Brasileira Sao Paulo* 2007 Nov – Dec; 40(6): <http://dx.doi.org/10.1590/50100-39842007000600013>
 - Ashlock R, Johnstone P A S. Treatment modalities of bladder/prostate rhabdomyosarcoma: a review. *Prostate cancer and prostatic disease* 2003; 6: 112 – 120 Doi: 10.1038/sj.pcan.4500652
 - Ferrer F A, Isakof M, Koyle M A. Bladder/Prostate rhabdomyosarcoma: past, present and future. *J Urol.* 2006; 176(4 Pt 1): 1283 – 1291 DOI: 10.16/jjuro.2006.06.019 PMID: 16952614
 - McLone G A, Abara O E, Churchill B M, Greenberg M, Mancer K. Rhabdomyosarcoma of the prostate in childhood: Current challenges. *Journal of Pediatric Surgery* 1989 Oct; 24(10): 977 - 981
 - Ruszkiewicz A, Vernon-Roberts E. Incidental rhabdomyosarcoma of the prostate gland in sudden infant death syndrome *Am J Forensic Med Pathol* 1994 Mar; 15(1): 79 - 81
 - Bapna B C, Chakrabarty A K, Singh S M, Bhargava S, Thomas K. Rhabdomyosarcoma of the prostate. *Indian J Pediatr* 1968 May, 35(5): 232 - 236
 - Munoz Velez Rebeca Llull M, Anton Valenti E, Ramos Asensio R, Riera Mari V, Gutiérrez Sanz-Gadea C, Ozonas Moragues M. Prostatic

- rhabdomyosarcoma in adults *Arch Esp Urol*. 1998 Nov; 51(9): 883 - 888
22. Timmons J W Jr, Burgert E O, Jr, Soule E H, Gilchrist G S, Kelalis P P. Embryonal rhabdomyosarcoma of the bladder and prostate in childhood. *J Urol*. 1975 May; 113(5): 694 - 697
 23. Nagata Y, Hoshino H, Kawamura N, Suzuki K. A case of rhabdomyosarcoma of the prostate in children *Hinyokika Kyo* 1985 Feb; 31(2): 319 - 326
 24. Carvarjal Busslinger M I, Plaschkes J. Rhabdomyosarcoma of the prostate and bladder in a child: radical or conservative surgery? *Helv Chir Acta* 1994 Dec; 60(6): 1097 – 1100
 25. Nigro K G, McLennan G T. Rhabdomyosarcoma of the bladder and prostate *J Urol*. 2005; 173: 1365
 26. Agrons G A, Wagner B J, Lonergan G J, Dickey G E, Kaufman M S. From the Archives of the AFIP Genitourinary rhabdomyosarcoma in children: radiologic – pathologic correlation *Radiographics* 1997; 17: 919 – 937
 27. Logani S, Cabrera R A, Amin M B. Embryonal rhabdomyosarcoma of the adult prostate: differential diagnostic consideration. *Path Cas Rev* 2003; 8: 82 – 87
 28. Hawkins W G, Hoos A, Antonescu C R, Clinicopathologic analysis of patients with adult rhabdomyosarcoma. *Cancer* 2001; 91: 794 – 803
 29. Ferrari A, Dileo P, Casanova M, et al. Rhabdomyosarcoma in adults: A retrospective analysis of 171 patients treated at a single institution. *Cancer* 2003; 98: 571 - 580
 30. Bos S D, Siao E T. An adult man with a rhabdomyosarcoma of the prostate: A case report. *Scan J Urol. Nephrol* 1991; 25: 329 - 330
 31. Little D J, Ballo M T, Zagars G K, Pisters P W T, Patel S R, El-Naggar A K, Garden A S, Benjamin R S. Adult rhabdomyosarcoma: outcome following multimodality treatment. *Cancer* 2002; 95: 377 – 388
 32. Miettinen M. Rhabdomyosarcomas in patients older than 40 years of age. *Cancer* 1988; 62: 2060 - 2065
 33. Sexton W J, Lance R E, Reyes A O, Pisters P W, Tu S M, Pisters L L. Adult prostate sarcoma: the M.D. Anderson Cancer Center Experience. *J Urol*. 2001; 166: 521 - 525
 34. Baker M E, Silverman P M, Korobkin M. Computed tomography of prostatic and bladder rhabdomyosarcomas. *J Comput Assist Tomogr* 1985; 9: 780 - 783
 35. Bartolozzi C, Selli C, Olmastroni M, Menchi I, Di Candio G. Rhabdomyosarcoma of the prostate: MR findings. *A J R Am J Roentgenol* 1988; 150: 1333 - 1334
 36. McCarville M B, Christie R, Daw N C, Spunt S L, Kaste S C. PET/CT in the evaluation of childhood sarcomas. *A J R Am J Roentgenol* 2005; 184: 1293 - 1304
 37. Niimi K, Hashimoto Y, Kurokawa S, Okada A, Tozawa K, Kohri K. Embryonal rhabdomyosarcoma of the prostate. *Int. J. Clin. Oncol*. 2010 Feb; 15(1): 93 – 96 doi: 10.1007/s10147-009-0004-6. Epub 2010 Jan 20
 38. Raney R B, Anderson J R, Barr F G, Donaldson S S, Pappo A S, Qualman S J, Wiener E S, Maurer H M, Crist W M. Rhabdomyosarcoma and undifferentiated sarcoma in the first two decades of life: a selective review of intergroup rhabdomyosarcoma study group experience and rationale for Intergroup Rhabdomyosarcoma Study V. *J Pediatr Hematol Oncol* 2001 May; 23(4): 215 - 220
 39. Raney R B, Stoner J A, Walterhouse D O, Andrassy R J, Donaldson S S, Laurie F, Meyer W H, Qualman S J, Crist W M. Results of treatment of fifty-six patients with localized retroperitoneal and pelvic rhabdomyosarcoma: a report from The Intergroup Rhabdomyosarcoma Study –IV, 1991-1997. *Pediatr Blood Cancer* 2004 Jun; 42(7): 618 - 625
 40. Pappo A S, Shapiro D N, Crist W M. Rhabdomyosarcoma. *Biology and treatment* *Pediatr Clin North Am* 1997; 44: 953 – 972
 41. Crist W M, Garnsey L, Beltangady M S, Gehan E, Ruymann F, Webber B, et al. Prognosis in children with rhabdomyosarcoma studies I and II. Intergroup Rhabdomyosarcoma Committee: *J Clin. Oncol*. 1990; 8: 443 - 452
 42. Quinlan D M, Stutzman R E, Peters C A, Walsh P C. Unilateral nerve-sparing radical prostatectomy and hemicystectomy in management of prostate sarcoma. *Urology* 1993; 41: 308 - 310