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Systematic Review

Features and Management of Incidental Prostatic Lymphoma Obtained in Lower Urinary Tract Symptoms Surgery: A Systematic Review

Jeremy Cheng [1], Samith Minu Alwis [1], Nathan Papa [1,2,3], Joseph Ischia [1,4], Damien Bolton [1,4] and Dixon Woon [1,4,*]

[1] Department of Urology, Austin Health, Melbourne 3084, Australia; jeremycheng1996@gmail.com (J.C.); minu.alwis@austin.org.au (S.M.A.); nathan.papa@monash.edu (N.P.); joseph.ischia@unimelb.edu.au (J.I.); damien.bolton@unimelb.edu.au (D.B.)
[2] School of Public Health and Preventive Medicine, Monash University, Melbourne 3800, Australia
[3] Garvan Institute of Medical Research, Sydney 2010, Australia
[4] Department of Surgery, University of Melbourne, Melbourne 3010, Australia
* Correspondence: dixon.woon@unimelb.edu.au

Abstract: Background/Objectives: Prostatic lymphoma is a rare malignant tumour that frequently causes urinary tract obstruction. It is uncommon for patients to present with systemic features or B-symptoms. As a result, it is often diagnosed incidentally during surgical lower urinary tract symptoms (LUTS) treatment. This systematic review aims to identify any common clinical features of prostatic lymphoma diagnosed incidentally during surgical LUTS treatment and summarise disease treatment and outcomes. **Methods**: The study protocol was registered with Prospective Register of Systematic Reviews (PROSPERO). A search was performed across the following electronic databases: MEDLINE, Embase, Web of Science, and Cochrane Database of Systematic Reviews. Full texts of eligible studies were analysed and data were extracted. The review was performed in accordance with PRISMA guidelines. **Results**: A total of 24 case reports compromising 25 cases were included. The median (IQR) age was 67 (61–73) years. All patients reported LUTS as their primary complaint, and the median duration of LUTS prior to diagnosis was 17 (4–44) months. Serum prostate-specific antigen (PSA) was normal in 10 cases and prostatomegaly present on imaging in 16 cases. A total of 10 different subtypes of lymphoma were reported. Extra-prostatic involvement was reported in eight patients. Chemotherapy, with or without adjuvant radiotherapy, was the mainstay of lymphoma treatment. The majority of articles reported positive outcomes, with complete remission in 17 cases. **Conclusions**: Prostatic lymphoma is a difficult clinical diagnosis due to its similar presentation to benign prostatic hyperplasia (BPH). Although rare, prostatic lymphoma may need to be considered as a diagnosis in patients with an atypical presentation of BPH. Prognosis is often favourable after prompt referral to haematology or oncology.

Keywords: prostatic lymphoma; lymphoma; incidental diagnosis; lower urinary tract symptoms surgery; benign prostatic hyperplasia

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1. Introduction

Prostatic lymphoma is a rare malignant tumour, with primary lymphoma of the prostate accounting for 0.1% of all newly diagnosed lymphomas and less than 0.09% of all prostate neoplasms [1]. Diagnosis is most often made in the seventh decade of life during surgical treatment for lower urinary tract symptoms (LUTS) or investigation and treatment

of prostate adenocarcinoma, with a rate of up to 0.17% in prostate biopsy, prostatectomy, and transurethral resection of the prostate (TURP) specimens [2,3].

Prostatic lymphoma frequently causes urinary tract obstruction, and patients may present with LUTS such as urgency, hesitancy, weak urinary stream, and acute urinary retention (AUR) [2,4]. Results from traditional diagnostic tools such as digital rectal examination (DRE) and serum prostate-specific antigen (PSA) are often indistinguishable from those found in benign prostatic hyperplasia (BPH), highlighting the challenges in diagnosing prostatic lymphoma [2,5]. DRE often mimics BPH, with most cases demonstrating a diffusely enlarged or nodular gland [2]. Similarly, there is no clear relationship between PSA and prostatic lymphoma, with PSA generally not elevated [5]. It is uncommon for patients to present with systemic features or B-symptoms of lymphoma such as fever, weight loss, and night sweats [4]. Consequently, diagnosis of prostatic lymphoma is often incidentally made during histopathological review of prostatic tissue obtained from surgical LUTS treatment.

No systematic review exists exploring incidental prostatic lymphoma diagnosed during surgical LUTS treatment. There are limited case series describing prostatic lymphoma; however, these contain a large proportion of cases in which lymphoma was already a suspected or known diagnosis, and furthermore lack clinical details such as initial patient presentation and eventual treatment [3,4]. In addition, due to its rarity, there is no consensus on the optimal treatment of prostatic lymphoma [6]. This systematic review aims to identify any common clinical features of incidental prostatic lymphoma diagnosed during surgical LUTS treatment and summarise disease treatment and outcomes.

2. Materials and Methods

2.1. Protocol, Registration, and Ethics

The protocol was registered with the International Prospective Register of Systematic Reviews (PROSPERO) in May 2024 (registration ID: CRD42024528863) in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [7]. Ethics approval and patient consent were not required given the nature of the review (derived from previously published work).

2.2. Search Strategy

A comprehensive search across four electronic databases (MEDLINE, Embase, Web of Science, and Cochrane Database of Systematic Reviews) was conducted in May 2024. Backwards citation searching (backwards pearl growing/mining/referencing) was also performed on retrieved articles in order to identify any missed additional articles.

The Medical Subject Headings (MeSH) terms 'transurethral resection of prostate', 'prostatectomy', 'lower urinary tract symptoms', 'prostatic hyperplasia', 'lymphoma', and 'leukemia' were combined with keywords 'transurethral resection', 'TURP', 'HOLEP', 'holmium laser', 'prostatectomy', 'lympho*', and 'leuk?emia'.

The search was limited to the English language and human species.

There were no limitations placed on the year of publication.

The complete final search strategy is provided (Figure S1).

2.3. Eligibility Criteria

Articles were included if:

1. They reported on lymphoma of the prostate diagnosed on TURP, simple prostatectomy, or holmium laser enucleation of the prostate (HoLEP) performed for LUTS or AUR;
2. They included sufficient clinical information to answer the review aims;
3. Patients were aged over 18 years;

4. The full text was available in English.

Articles were excluded if:

1. Patients already had a known diagnosis of lymphoma;
2. There was a pre-existing clinical suspicion of lymphoma based on the patient presentation;
3. Diagnosis was made on prostatic biopsy;
4. TURP, simple prostatectomy, or HoLEP were performed for indications other than LUTS or AUR;
5. They were in the form of grey literature, conference abstracts, or letters to the editor.

2.4. Article Selection

All identified citations following the search were collated and uploaded onto Covidence (Veritas Health Innovation, Melbourne, Australia) and duplicates removed. Title and abstract screening was then performed by two independent reviewers (J.C. and S.M.A.). The full texts were then reviewed in detail, with those not fitting eligibility criteria excluded. All disagreements were resolved by a third reviewer (D.W.).

2.5. Data Extraction

Data extraction was performed by two independent reviewers (J.C. and S.M.A.) and collated in an Excel spreadsheet (Microsoft Corporation, Redmond, WA, USA). Variables included patient age, presenting symptoms, examination findings such as DRE and presence of lymphadenopathy, investigations such as PSA results and prostate volume on ultrasound, type of lymphoma and histopathological findings, treatment, follow-up, and patient outcomes. Data not included in individual articles were recorded as 'not specified'.

2.6. Assessment of Methodological Quality

All articles meeting eligibility criteria were case reports. Therefore, the methodological quality of included articles was assessed with a modified tool proposed by Murad et al. [8]. The original tool comprises a total of eight questions from four domains (Table S1). Two questions relating to drug reactions were removed as they were irrelevant. The methodological quality of article was rated as high, intermediate, or low. High quality was defined as a 'yes' answer to four or more of the included questions, intermediate quality as a 'yes' answer to three questions, and low quality was a 'yes' answer to less than three questions.

2.7. Data Synthesis

Given all included studies were case reports, data were reported through summative statistics with a narrative synthesis approach. This summary of data is reported in Table 1.

Table 1. Patient demographics, presentation, pathology, and outcomes.

Total Cases *n* = 25	**Median (IQR)/*n* (%)**
Baseline demographics	
Age (years)	67 (61–73)
History	
LUTS duration (months) [n = 14]	17 (4–44)
AUR	8 (32)
Haematuria	5 (20)
Previous TURP	3 (12)
Fever	1 (4)
Physical examination	
DRE (including multiple findings per case)	
Enlarged	9 (36)

Table 1. *Cont.*

Total Cases *n* = 25	**Median (IQR)/*n* (%)**
Hard	3 (12)
Swollen/tender	2 (8)
Normal	3 (12)
Not specified	10 (40)
Lymphadenopathy	1 (4)
Investigations	
PSA	
Normal	10 (40)
Elevated	7 (28)
Not specified	8 (32)
PSA level (ng/mL) [n = 12]	2.3 (1.6–6.6)
PSA level in elevated subgroup (ng/mL) [n = 5]	8.5 (4.5–474.9)
Abnormal blood/urine tests	
Elevated lactate dehydrogenase	2 (8)
Lymphocytosis/atypical lymphocytes	2 (8)
Thrombocytopaenia	1 (4)
Elevated erythrocyte sedimentation rate	1 (4)
Sterile pyuria	1 (4)
Imaging (CT/US/MRI)	
Prostatomegaly	16 (64)
Estimated prostate volume (cc) [n = 12]	51 (31–105)
Surgical intervention	
TURP	21 (84)
Open prostatectomy	3 (12)
HoLEP	1 (4)
Lymphoma subtype	
Intravascular large B-cell lymphoma	6 (24)
Mucosa-associated lymphoid tissue lymphoma	6 (24)
Follicular lymphoma	3 (12)
Chronic lymphocytic leukaemia	2 (8)
Diffuse large B-cell lymphoma	2 (8)
Mantle cell lymphoma	2 (8)
Burkitt lymphoma	1 (4)
Mixed lymphocytic–histiocytic-type lymphoma	1 (4)
Non-Hodgkin lymphoma	1 (4)
Small-cell lymphocytic lymphoma	1 (4)
Staging (imaging)	
Imaging modality (including multiple modalities per case)	
CT	12 (48)
PET/CT	6 (24)
Bone scan	2 (8)
Abdominal US	1 (4)
Not specified	8 (32)
Lymphadenopathy	5 (20)
Extra-prostatic organ involvement	5 (20)
Bone involvement	1 (4)
Staging (invasive)	
Bone marrow aspirate	10 (40)
Lymph node aspiration/biopsy	1 (4)
Lumbar puncture	1 (4)
Management	
Chemotherapy alone	9 (36)
Chemotherapy + adjuvant radiotherapy	5 (20)
Radiotherapy alone	2 (8)
Observation	1 (4)
Patient refusal	3 (12)
Not specified	5 (20)

IQR, interquartile range; AUR, acute urinary retention; HoLEP, holmium laser enucleation of prostate; PET/CT; positron emission tomography/computed tomography; US, ultrasound.

3. Results

3.1. Article Selection

The electronic search resulted in a total of 3225 studies as follows: MEDLINE (310), Embase (1421), Cochrane Database of Systematic Reviews (2), Web of Science (1490), and backwards citation searching (2). After 617 duplicates were removed, 2608 titles and abstracts were screened, of which 52 full texts were reviewed. A total of 28 articles were excluded due to meeting exclusion criteria as detailed in Figure 1. Specifically, a large series of 62 cases by Bostwick et al. [4] was excluded as numerous cases were not incidental or were diagnosed on biopsy; furthermore, individual patient data were not available and clinical information was lacking, as the series was presented only as an overall summary of all cases.

In total, 24 articles were included, with publication years ranging from 1984 to 2023 [9–32]. These were all case reports, compromising a total of 25 patient cases. All articles were deemed to be of high overall methodological quality (Table S1). A condensed summary of all cases and clinical information is presented in Table 2, with complete details provided in Table S2.

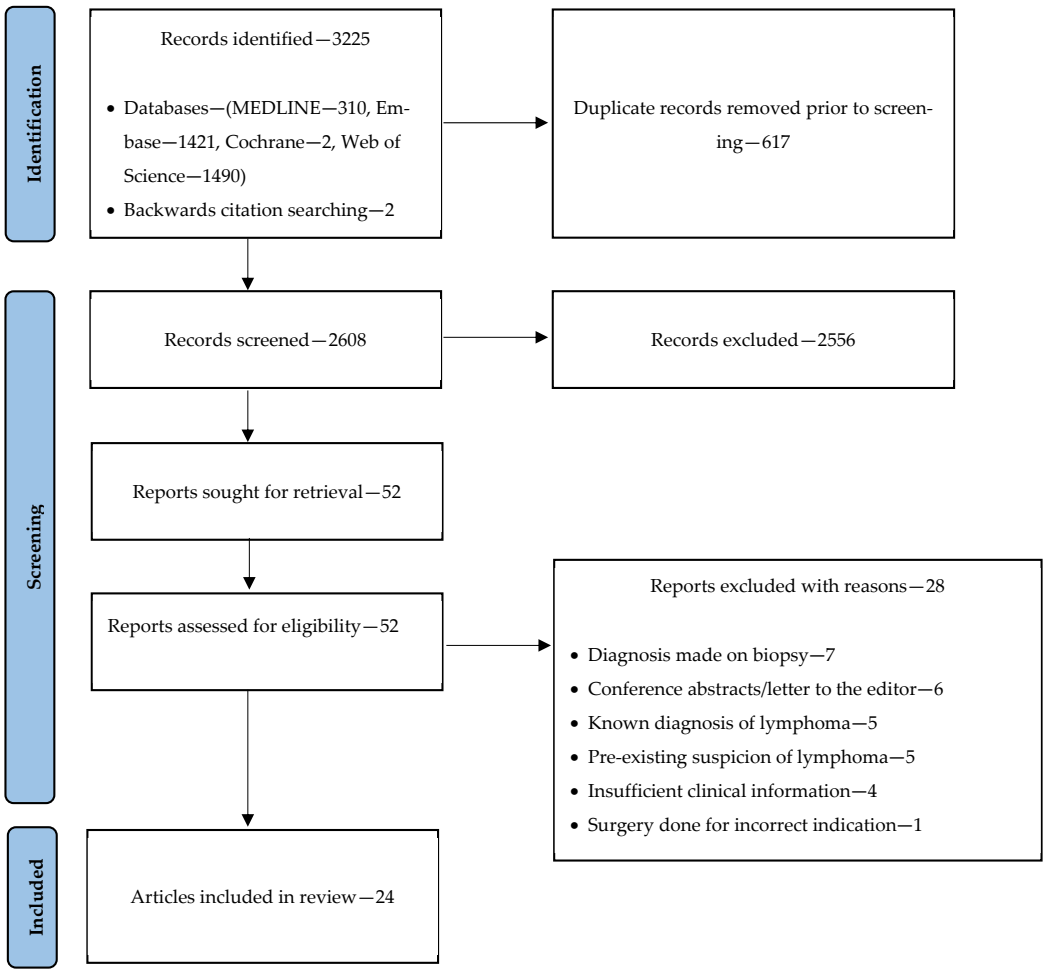

Figure 1. Study search strategy: Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Table 2. Summary of 25 included articles.

Title	Author	Year	Country	Number of Cases	Lymphoma Subtype	Age (Years)	LUTS Duration (Months)	AUR	DRE	Serum PSA (ng/mL)	Prostate Volume (cc)	Intervention	Staging Imaging	Extraprostatic Involvement on Imaging	Management	Outcome
"Presentation of mantle cell lymphoma with symptoms of prostatism" [9]	Atay	2013	Turkey	1	MCL	71	2	No	Not specified	Not specified	Not specified	TURP	CT	Yes	Chemotherapy—rituximab/cyclophosphamide/daunorubicin/vincristine/prednisolone (R-CHOP) ×4 cycles; radiotherapy—residual lymph nodes	Remission—follow-up duration not specified
"Primary non-Hodgkin lymphoma of prostate presenting as benign prostatic hyperplasia" [10]	Cos	1984	USA	1	NHL	62	3	No	Enlarged, symmetrical, rubbery	Not specified	Not specified	TURP	CT and bone scan	Yes	Chemotherapy—chlorambucil/prednisolone	Not specified
"Prolonged survival using anti-CD20 combined chemotherapy in primary prostatic intravascular large B-cell lymphoma" [11]	Csomor	2008	Hungary	1	IVLBCL	73	Not specified	No	Not specified	Elevated	51	TURP	CT and bone scan	No	Chemotherapy—R-CHOP ×8 cycles	Initial remission; first systemic relapse eight months later, retreated 25 months post-initial diagnosis; second systemic relapse five months later—death from pneumonia
"Primary Extranodal Diffuse Large B-Cell Lymphoma of the Prostate: A Case Report" [12]	Ezekwudo	2017	USA	1	DLBCL	54	Not specified	No	Firm, enlarged, no nodularity	Normal (2.0)	Normal—not further specified	TURP	CT and PET/CT	Yes	Chemotherapy—R-CHOP; radiotherapy—not further specified	Remission on PET—two years follow-up
"Primary lymphoma of prostate presenting as bladder outflow obstruction" [13]	Fell	1987	Ireland	1	Mixed lymphocytic–histiocytic-type lymphoma	23	10	No	Normal	Not specified	Not specified	TURP	Not specified	Not specified	Radiotherapy—five fractions to prostate gland	Remission—two years follow-up
"Prostate primary intravascular large B-cell lymphoma: A case report" [14]	Gu	2022	China	1	IVLBCL	76	60	No	Tough and hard, disappearing central sulcus, no nodularity or tenderness	Normal (2.1)	109	TURP	Not specified	Not specified	Patient refusal of treatment	Death—six months follow-up
"A case of recurrent hematuria in primary prostatic low grade mucosa associated lymphoid tissue" [15]	Hashemzadeh	2017	Iran	1	MALT lymphoma	63	6	Yes	Enlarged, no nodularity	Not specified	Normal—not further specified	TURP x2	CT	No	Not specified	Remission—eight months follow-up
"Primary extranodal mucosa associated lymphoid tissue (MALT) lymphoma of the prostate" [16]	Jhavar	2001	India	1	MALT lymphoma	67	4	No	Mildly enlarged, smooth and firm with diffuse margins	Normal	Prostatomegaly—not further specified	TURP	CT	No	Radiotherapy—4400 centigray, 22 fractions	Remission—two years follow-up
"Unexpected hematologic malignancies after prostatectomy: Case report and literature review" [17]	Karademir	2021	Turkey	2	Case 1: CLL	60	72	No	Grade 2 prostate	Normal (1.0)	154	Open suprapubic prostatectomy (Freyer's)	CT	Yes	Haematology follow-up—not further specified	Not specified
					Case 2: MCL	62	48	No	Grade 1 prostate	Normal (1.9)	52	TURP	CT	No	Chemotherapy—R-CHOP ×8 cycles	Remission—five years follow-up
"Primary mucosa-associated lymphoid tissue lymphoma of the prostate: tumor relapse 7 years after local therapy" [18]	Li	2008	Japan	1	MALT lymphoma	79	Not specified	Yes	Elastic hard mass in right lobe	Normal	Normal—not further specified	TURP x2	Not specified	Not specified	Chemotherapy—R-CHOP; radiotherapy—not further specified	Remission—two years follow-up

Table 2. *Cont.*

Title	Author	Year	Country	Number of Cases	Lymphoma Subtype	Age (Years)	LUTS Duration (Months)	AUR	DRE	Serum PSA (ng/mL)	Prostate Volume (cc)	Intervention	Staging Imaging	Extraprostatic Involvement on Imaging	Management	Outcome
"Diagnosis of monoclonal B cell lymphocytosis (MBL) through transurethral resection of prostate for obstructive lower urinary tract symptoms" [19]	Mansbridge	2020	Australia	1	CLL	73	Not specified	No	Mildly enlarged, smooth	Normal (0.9)	31	TURP	CT	No	Clinical observation—yearly flow cytometry	Not specified
"Primary non-Hodgkin lymphoma of the prostate: A case report" [20]	Martin	2017	Colombia	1	MALT lymphoma	68	36	No	Regular size, no nodularity, normal consistency, no masses	Normal (1.4)	50	TURP	CT	No	Chemotherapy—rituximab/ cyclophosphamide/ vincristine/ prednisolone (R-CVP) ×6 cycles	Remission and resolution of LUTS—five years follow-up
"Primary Non-Hodgkin Lymphoma of Prostate: a Case Report" [21]	Nerli	2020	India	1	Follicular NHL	73	36	Yes	Not specified	Elevated (46.8)	147	TURP	CT	No	Patient refusal of treatment	Not specified
"Hematolymphoid tumor of prostate: Diffuse large B cell lymphoma case report" [22]	Ochirjav	2023	Mongolia	1	DLBCL	67	6	Yes	Not specified	Not specified	Enlarged—not further specified	TURP	PET/CT	Yes	Not specified	Remission and improvement in LUTS—follow-up duration not specified
"Intravascular Large B-Cell Lymphoma Diagnosed on Prostate Biopsy: A Case Report" [23]	Özsan	2014	Turkey	1	IVLBCL	65	Not specified	No	Not specified	Normal (2.4)	31	TURP	PET/CT and abdominal US	Yes	Patient refusal of treatment	Death—eight months follow-up
"Intravascular large B cell lymphoma of prostate, a rare entity" [24]	Rallabandi	2021	India	1	IVLBCL	76	0.5	Yes	Grade 2 prostate	Normal	Normal—not further specified	TURP	PET/CT	No	Chemotherapy—not further specified	Death—follow-up duration not specified
"Extra-nodal Small Cell Lymphocytic Lymphoma of Prostate: An Unusual Cause of Lower Urinary Tract Symptoms" [25]	Singh	2008	India	1	SCLL	60	Not specified	Yes	Enlarged	Elevated (8.5)	30	TURP	CT	Yes	Oncology follow-up—not further specified	Remission and decreased PSA—six months follow-up
"Primary follicular lymphoma of the prostate" [26]	Terada	2016	Japan	1	Follicular lymphoma	68	Not specified	No	Swollen, elastic, hard	Elevated (4.6)	Normal—not further specified	TURP	Not specified	Not specified	Chemotherapy—R-CHOP; radiotherapy—local radiation, 40 gray	Remission and decreased PSA—five months follow-up
"Primary lymphoma of the prostate with features of low grade B-cell lymphoma of mucosa associated lymphoid tissue: A rare cause of urinary obstruction" [27]	Tomaru	1999	Japan	1	MALT lymphoma	84	Not specified	Yes	Firm, moderately enlarged with tenderness	Elevated (903)	Normal—not further specified	TURP	Not specified	Not specified	Not specified	Remission and decreased PSA—two years follow-up
"Primary prostatic lymphoma of mucosa-associated lymphoid tissue" [28]	Tomikawa	1998	Japan	1	MALT lymphoma	50	24	No	Not specified	Not specified	Prostatomegaly —not further specified	TURP	Not specified	Not specified	Chemotherapy—CHOP ×6 cycles	Remission—eighteen months follow-up
"Primary follicular lymphoma of an extraordinarily large prostate: A case report and review of the literature" [29]	Williams	2023	Australia	1	Follicular lymphoma	74	Not specified	No	Not specified	Not specified	Massive prostatomegaly —not further specified	Millen retropubic prostatectomy	Not specified	Not specified	Chemotherapy—rituximab/cyclophosphamide then R-CHOP/intrathecal methotrexate	Remission—six months follow-up
"Primary prostate Burkitt's lymphoma resected with holmium laser enucleation of the prostate: A rare case report" [30]	Wu	2023	China	1	Burkitt lymphoma	57	Not specified	Yes	Not specified	Elevated (4.3)	36	HoLEP	PET/CT	Yes	Chemotherapy—pre-treatment regime then rituximab/vinpocetine/ methotrexate/doxorubicin/ cyclophosphamide/ dexamethasone x4 cycles	Remission—follow-up duration not specified

Table 2. *Cont.*

Title	Author	Year	Country	Number of Cases	Lymphoma Subtype	Age (Years)	LUTS Duration (Months)	AUR	DRE	Serum PSA (ng/mL)	Prostate Volume (cc)	Intervention	Staging Imaging	Extraprostatic Involvement on Imaging	Management	Outcome
"Prostate involvement by intravascular large B-cell lymphoma: a case report with literature review" [31]	Xu	2011	China	1	IVLBCL	65	Not specified	No	Not specified	Elevated	29	Transvesical prostatectomy	Not specified	Not specified	Chemotherapy—CHOP ×5 cycles	Remission—thirteen months follow-up
"A case report of primary prostate intravascular large B cell lymphoma presenting as prostatic hyperplasia" [32]	Zhu	2019	China	1	IVLBCL	71	48	No	Not specified	Not specified	100	TURP	PET/CT	No	Chemotherapy—R-CHOP ×4 cycles then further unspecified chemotherapy; radiotherapy—prostate 45 gray, 25 fractions	Remission and improvement in LUTS—one year follow-up

AUR, acute urinary retention; CLL, chronic lymphocytic leukaemia; CT, computed tomography; DLBCL, diffuse large B-cell lymphoma; DRE, digital rectal examination; HoLEP, holmium laser enucleation of prostate; IVLBCL, intravascular large B-cell lymphoma; LUTS, lower urinary tract symptoms; MALT, mucosa-associated lymphoid tissue; MCL, mantle cell lymphoma; NHL, non-Hodgkin's lymphoma; PET, positron emission tomography; PSA, prostate-specific antigen; R-CHOP, rituximab/cyclophosphamide/doxorubicin/vincristine/prednisone; SCLL, small-cell lymphocytic lymphoma; TURP, transurethral resection of prostate; US, ultrasound.

3.2. Patient Demographics and Clinical Presentation

The age range of patients was 23 to 84 years, with a median (interquartile range [IQR]) age of 67 (61–73).

All 25 patients reported LUTS as their primary complaint. In the 14 articles that reported symptom duration, the median duration of LUTS prior to diagnosis was 17 months (IQR 4–44 months). Haematuria was the next most common symptom, reported in eight patients. Three patients had undergone a previous TURP. One patient experienced fevers of unknown cause as an additional symptom, but B-symptoms were not reported in any other cases.

DRE findings were reported in 15 cases. The most common DRE finding was of an enlarged prostate (nine cases), followed by a hard prostate (three cases) and a swollen/tender prostate (two cases).

Lymphadenopathy was only reported in a single patient, with axillary and inguinal nodes involved.

3.3. Investigations

Serum PSA testing was reported in 17 patients, with 10 in the normal range. In those with an elevated result, the median PSA was 8.5 ng/mL (IQR 4.5–474.9); this included an outlier of 903 ng/mL [27].

Overall, the majority of other blood and urine results were either normal or not specified. Lactate dehydrogenase (LDH) was elevated in two cases, lymphocytosis or atypical immature lymphocytes were present in two cases, and thrombocytopaenia, elevated erythrocyte sedimentation rate (ESR), and sterile pyuria were all reported in one case each.

Baseline imaging was in the form of computed tomography (CT), ultrasound (US), and magnetic resonance imaging (MRI). Prostatomegaly was present in 16 cases, and in the 12 cases that reported prostate volume, median prostate size was 50 cc (IQR 31–105). Aside from prostatomegaly, other described imaging findings included T2-weighted intense nodules on MRI and echogenic areas on US.

Prostate biopsy was performed in three out of seven patients who had an elevated serum PSA, with all demonstrating BPH alone.

3.4. Surgical Intervention

In the vast majority of cases, lymphoma diagnosis was made during TURP (21 cases), followed by simple prostatectomy (three cases) and HoLEP (one case).

3.5. Lymphoma Subtype

A total of 10 different subtypes of lymphoma were reported. The most common subtypes were intravascular large B-cell lymphoma (IVLBCL) and mucosa-associated lymphoid tissue (MALT) lymphoma, with six reported cases each. Table 3 summarises the treatment modalities and patient outcomes for each subtype.

Table 3. Treatment and outcomes by lymphoma subtype.

Lymphoma Subtype	Treatment	Outcome
Intravascular large B-cell lymphoma (n = 6)	1. Chemotherapy (R-CHOP) 2. No treatment (patient refusal) 3. No treatment (patient refusal) 4. Chemotherapy (not specified) 5. Chemotherapy (CHOP) 6. Chemotherapy (R-CHOP) with adjuvant chemotherapy	1. Death after initial remission (30 months post-initial diagnosis) 2. Death (six months follow-up) 3. Death (eight months follow-up) 4. Death (follow-up duration not specified) 5. Remission (13 months follow-up) 6. Remission (one year follow-up)
Mucosa-associated lymphoid tissue lymphoma (n = 6)	1. Not specified 2. Radiotherapy (22 fractions) 3. Chemotherapy (R-CHOP) with adjuvant radiotherapy 4. Chemotherapy (R-CVP) 5. Not specified 6. Chemotherapy (CHOP)	1. Remission (eight months follow up) 2. Remission (two years follow-up) 3. Remission (two years follow-up) 4. Remission (five years follow-up) 5. Remission (two years follow-up) 6. Remission (18 months follow-up)
Follicular lymphoma (n = 3)	1. No treatment (patient refusal) 2. Chemotherapy (R-CHOP) with adjuvant radiotherapy 3. Chemotherapy (R-CHOP)	1. Not specified 2. Remission (five months follow-up) 3. Remission (six months follow-up)
Chronic lymphocytic leukaemia (n = 2)	1. Haematology follow-up (not specified) 2. Clinical observation (annual flow cytometry)	1. Not specified 2. Not specified
Diffuse large B-cell lymphoma (n = 2)	1. Chemotherapy (R-CHOP) with adjuvant radiotherapy 2. Not specified	1. Remission (two years follow-up) 2. Remission (follow-up duration not specified)
Mantle cell lymphoma (n = 2)	1. Chemotherapy (R-CHOP) with adjuvant radiotherapy 2. Chemotherapy (R-CHOP)	1. Remission (follow-up duration not specified) 2. Remission (five years follow-up)
Burkitt lymphoma (n = 1)	1. Chemotherapy (R-CHOP)	1. Remission (follow-up duration not specified)
Mixed lymphocytic–histiocytic-type lymphoma (n = 1)	1. Radiotherapy (five fractions)	1. Remission (two years follow-up)
Non-Hodgkin lymphoma (n = 1)	1. Chemotherapy (chlorambucil/prednisolone)	1. Not specified
Small-cell lymphocytic lymphoma (n = 1)	1. Oncology follow-up (not specified)	1. Remission (six months follow-up)

R-CHOP, rituximab/cyclophosphamide/doxorubicin/vincristine/prednisolone; CHOP, cyclophosphamide/doxorubicin/vincristine/prednisolone; R-CVP, rituximab/cyclophosphamide/vincristine/prednisolone.

3.6. Staging—Imaging

Following a diagnosis of lymphoma, further staging imaging was performed in 17 patients. Cross-sectional imaging in the form of CT (12 cases) and positron emission tomography/computed tomography (PET/CT) (six cases) were the most common modalities, followed by bone scan (two cases) and abdominal US (one case).

Extra-prostatic involvement in the form of lymphadenopathy, solid organ involvement, or bone involvement was reported in eight patients.

Lymphadenopathy was reported in five patients, with periaortic, pericaval, pre-sacral, perirectal, common iliac, mesenteric, and inguinal nodes affected.

Extra-prostatic solid organ involvement was also reported in five patients. Local involvement included the bladder, seminal vesicles, penis, and rectum, and more distant organs affected included the spleen, sigmoid colon, caecum, ileum, oesophagus, gastric wall, and adrenal gland.

Intense focal hypermetabolic bone lesions in the cranium, clavicle, scapulae, sternum, humerus, and femur were reported in a single patient [22].

3.7. Staging—Invasive

Bone marrow aspirate was the most common invasive staging procedure, occurring in ten cases. Only one patient had a positive aspirate result, demonstrating 60% atypical immature lymphocytes and a cyclin D1-positive marker [9].

Axillary lymph node aspiration and cervical node excisional biopsy were reported in one case, with both being positive for lymphoma [25]. This corresponded with physical examination and CT findings.

Lumbar puncture was performed in one patient, with cerebrospinal fluid (CSF) fluid analysis indicating no tumour involvement [30].

3.8. Management

Chemotherapy, with or without adjuvant radiotherapy, was the mainstay of treatment. Nine patients received chemotherapy alone and five in combination with adjuvant radiotherapy. Most patients underwent a regime including cyclophosphamide, daunorubicin/doxorubicin, vincristine, and prednisolone (CHOP) +/− rituximab (R-CHOP).

Two patients underwent radiotherapy alone. Radiotherapy targeted both the prostate alone as well as other affected sites.

A single patient underwent annual clinical observation in the form of flow cytometry. Three patients refused planned treatment, and five articles did not specify management.

3.9. Outcomes

Most articles reported positive outcomes, with complete remission reported in 17 cases. Remission was achieved with each form of active management. Of the 14 studies that specified remission follow-up duration, the median follow-up was 21 months (8–24).

Patient death was reported in four cases. The time to death was six, eight, and 38 months post-diagnosis and not specified in one article. In two cases, the patient refused any treatment. One patient died despite initial chemotherapy. This patient experienced systemic disease relapse following initial successful R-CHOP chemotherapy and was recommenced on further chemotherapy. They then suffered a second systemic relapse and later died of pneumonia and neutropaenia secondary to systemic treatment.

Seven cases reported improvement or resolution of obstructive LUTS following surgery. The remaining articles did not specify LUTS outcomes.

4. Discussion

Prostatic lymphoma appears to be difficult to differentiate clinically from BPH, with limited findings to suggest this diagnosis prior to histological examination. Clinical presentation often mimics BPH, with typical LUTS including hesitancy, poor stream, frequency, and AUR. DRE does not appear to provide any indication of lymphoma and lymphadenopathy was initially reported in only one case. However, in another article, cervical, axillary, and inguinal lymphadenopathy was noted only upon retrospective examination following lymphoma diagnosis [25]. Of course, a complete thorough haematological physical

examination prior to surgical intervention for LUTS may be more than what is expected of urologists.

It is well known that BPH can cause an elevated PSA [33], but the relationship between lymphoma and PSA is not well established, with some case series reporting a mean PSA of only 3.5–5.3 ng/mL [4,34] but with other studies supporting a raised PSA [35]. Nerli et al. described a 73-year-old man with a raised PSA of 46.8 ng/mL, which decreased to 1.9 ng/mL following TURP [21]. Similarly, Tomaru et al. reported on a patient with an initial PSA of 903 ng/mL, which subsequently decreased to 8.6 ng/mL three months post-TURP [27]. Both these cases did not receive any treatment for lymphoma. Therefore, it is difficult to ascertain whether elevated PSA was due to BPH alone or related to lymphoma too. Clearly, the most likely cause of a persistently elevated PSA after surgical treatment of an enlarged prostate with lymphoma is a concurrent diagnosis of prostatic adenocarcinoma [36,37].

A diagnosis of prostatic lymphoma should not be definitively excluded despite previous benign histopathology. Williams et al. reported a case with two previous benign TRUS biopsies who underwent a retropubic prostatectomy six years later which demonstrated follicular lymphoma in a 350 cc specimen [29]. Similarly, another patient by Li et al. was diagnosed with MALT lymphoma on second TURP, and similar histological features were present on retrospective examination of the initial TURP specimen from seven years prior [18]. Three patients underwent needle biopsy of the prostate prior to TURP which demonstrated BPH only [11,21,25]. This reflects that prostatic biopsy is not completely sensitive, and similar to adenocarcinoma, prostatic lymphoma may also be missed on initial biopsy.

Similarly, a diagnosis of lymphoma should be considered in younger patients with symptoms of bladder outlet obstruction, especially given the low pre-test possibility of BPH. Fell et al. reported on a 23-year-old with bladder outlet obstruction but normal investigations aside from sterile pyuria and mildly elevated ESR [13]. Tuberculous prostatitis was excluded with further investigations, and mixed lymphocytic–histiocytic-type lymphoma was diagnosed on TURP.

Disease type was largely varied, with 10 different lymphoma subtypes as detailed in Table 3. This is consistent with the wide diversity of the disease in general, with over 80 subtypes described [38,39]. Treatment centred around chemoradiotherapy, with R-CHOP/CHOP being the mainstay regime of choice, and other combinations such as rituximab/cyclophosphamide/vincristine/prednisolone and chlorambucil/prednisolone less common. However, there was a wide array of different chemotherapy regimens and radiotherapy dosages utilised, ranging from four to eight cycles of chemotherapy and five to 25 fractions of radiotherapy. The use of adjuvant radiotherapy was sporadic, and the articles did not specify the indication for its use. Overall, there was no particular apparent pattern predicting the prescribed treatment, reflecting the heterogeneity of the disease and thus treatment. Similar difficulties have been described in the literature, as there is no consensus for treatment due to the rarity of disease [6,12]. This is reflected in literature exploring genitourinary lymphoma in general. A recent 2024 article by Al-Maghrabi et al. described the treatment and outcomes of 11 patients with various lymphoma subtypes of the urinary bladder, testes, spermatic cord, ureter, and prostate [40]. There was a similar degree of heterogeneity in treatment regime and outcomes, but again treatment was predominantly R-CHOP, supporting its efficacy in most genitourinary lymphomas. R-CHOP was also shown to be an effective treatment in an analysis of 195 patients with primary bladder lymphoma [41]. This analysis also suggested that patients with low-grade tumours appear to respond well to local therapy such as transurethral resection. Several articles included in our review described patients who successfully demonstrated cancer

remission despite no further documented specified treatment; perhaps local resection of prostatic lymphoma, in the form of TURP alone, may be a valid treatment in select cases. Overall, the particulars of treatment are beyond the scope of practice for urologists, but prompt referral to oncology or haematology is warranted. Most patients had good outcomes with treatment, with only four total deaths including two occurring in patients refusing treatment. This demonstrates the often indolent and curable nature of lymphoma [42,43], particularly with early diagnosis.

A limitation of this review is the diverse nature of case reports and the subsequent reporting inconsistencies and biases both within and between articles. Several papers had missing datapoints which predisposes to inaccuracies if you were to pool data, but these have been highlighted in this systematic review. Missing data classified as 'not specified' may not have been available or reported. For example, several articles did not specify if treatment was implemented (including if no treatment was given) but did report on patient outcomes. Furthermore, aggregation of case reports is inherently biased given not all cases are published. Therefore, results derived from this review are not expected to be an exact reflection of clinical practice but rather serve to enhance our knowledge of a rare subject matter [44].

5. Conclusions

In conclusion, this systematic review summarises the features and management of incidentally diagnosed prostatic lymphoma. It is difficult to diagnose clinically due to its similar presentation to BPH. Although rare, prostatic lymphoma may need to be considered as a diagnosis in patients with an atypical presentation of BPH. Prompt referral to haematology or oncology is warranted and prognosis is often favourable with systemic treatment. Additional cases in the literature are required to further understand this uncommon entity but this review provides a broad overview of the disease.

Supplementary Materials: The following supporting information can be downloaded at https://www.mdpi.com/article/10.3390/siuj6020028/s1, Figure S1: Complete final search strategy; Table S1: Methodological quality assessment; Table S2: Detailed summary of 25 articles.

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References

1. Sarris, A.; Dimopoulos, M.; Pugh, W.; Cabanillas, F. Primary lymphoma of the prostate: Good outcome with doxorubicin-based combination chemotherapy. *J. Urol.* **1995**, *153*, 1852–1854. [CrossRef] [PubMed]
2. Warrick, J.I.; Owens, S.R.; Tomlins, S.A. Diffuse large B-cell lymphoma of the prostate. *Arch. Pathol. Lab. Med.* **2014**, *138*, 1286–1289. [CrossRef] [PubMed]
3. Chu, P.G.; Huang, Q.; Weiss, L.M. Incidental and Concurrent Malignant Lymphomas Discovered at the Time of Prostatectomy and Prostate Biopsy: A Study of 29 Cases. *Am. J. Surg. Pathol.* **2005**, *29*, 693–699. [CrossRef] [PubMed]
4. Bostwick, D.G.; Iczkowski, K.A.; Amin, M.B.; Discigil, G.; Osborne, B. Malignant lymphoma involving the prostate: Report of 62 cases. *Cancer* **1998**, *83*, 732–738. [CrossRef]
5. Bostwick, D.G.; Mann, R.B. Malignant lymphomas involving the prostate. A study of 13 cases. *Cancer* **1985**, *56*, 2932–2938. [CrossRef]

6. Hu, S.; Wang, Y.; Yang, L.; Yi, L.; Nian, Y. Primary non-Hodgkin's lymphoma of the prostate with intractable hematuria: A case report and review of the literature. *Oncol. Lett.* **2015**, *9*, 1187–1190. [CrossRef]
7. Moher, D.; Shamseer, L.; Clarke, M.; Ghersi, D.; Liberati, A.; Petticrew, M.; Shekelle, P.; Stewart, L.A. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst. Rev.* **2015**, *4*, 1. [CrossRef]
8. Murad, M.H.; Sultan, S.; Haffar, S.; Bazerbachi, F. Methodological quality and synthesis of case series and case reports. *BMJ Evid. Based Med.* **2018**, *23*, 60–63. [CrossRef]
9. Atay, M.H.; Kelkitli, E.; Alici, O.; Cilingir, F.; Turgut, M. Presentation of mantle cell lymphoma with symptoms of prostatism. *Pol. Arch. Med. Wewn.* **2013**, *123*, 643–644. [CrossRef]
10. Cos, L.R.; Rashid, H.A. Primary non-Hodgkin lymphoma of prostate presenting as benign prostatic hyperplasia. *Urology* **1984**, *23*, 176–179. [CrossRef]
11. Csomor, J.; Kaszas, I.; Kollar, B.; Pajor, L.; Egyhazi, Z.; Fekete, S.; Egyed, M.; Timar, B. Prolonged survival using anti-CD20 combined chemotherapy in primary prostatic intravascular large B-cell lymphoma. *Pathol. Oncol. Res.* **2008**, *14*, 281–284. [CrossRef] [PubMed]
12. Ezekwudo, D.E.; Ogunleye, F.; Gbadamosi, B.; Blankenship, L.M.; Kinoyan, M.; Krauss, D.; Hollander, M.; Haberichter, K.; Jaiyesimi, I. Primary Extranodal Diffuse Large B-Cell Lymphoma of the Prostate: A Case Report. *Case Rep. Oncol.* **2017**, *10*, 199–204. [CrossRef] [PubMed]
13. Fell, P.; O'Connor, M.; Smith, J.M. Primary lymphoma of prostate presenting as bladder outflow obstruction. *Urology* **1987**, *29*, 555–556. [CrossRef] [PubMed]
14. Gu, L.; Li, M.; Tong, G.; Wei, W.; Fan, Y.; Zhao, Y. Prostate primary intravascular large B-cell lymphoma: A case report. *Urol. Case Rep.* **2022**, *45*, 102276. [CrossRef]
15. Hashemzadeh, S.; Farrokhi, F.; Hozhabrossadaty, A.; Ghafarzadegan, K.; Ashraf, H. A case of recurrent hematuria in primary prostatic low grade mucosa associated lymphoid tissue. *J. Nephropathol.* **2017**, *6*, 49–52. [CrossRef]
16. Jhavar, S.; Agarwal, J.P.; Naresh, K.N.; Shrivastava, S.K.; Borges, A.M.; Dinshaw, K.A. Primary extranodal mucosa associated lymphoid tissue (MALT) lymphoma of the prostate. *Leuk. Lymphoma* **2001**, *41*, 445–449. [CrossRef]
17. Karademir, B.; Kisa, E.; Ozbilen, M.H.; Bildirici, C.; Karabacakoglu, B.; Suelozgen, T.; Ilbey, Y.O.; Kucuk, U.; Olgun, A. Unexpected hematologic malignancies after prostatectomy: Case report and literature review. *Urologia* **2021**, *88*, 382–385. [CrossRef]
18. Li, C.; Hibino, M.; Komatsu, H.; Sakuma, H.; Sakakura, T.; Ueda, R.; Eimoto, T.; Inagaki, H. Primary mucosa-associated lymphoid tissue lymphoma of the prostate: Tumor relapse 7 years after local therapy. *Pathol. Int.* **2008**, *58*, 191–195. [CrossRef]
19. Mansbridge, M.M.; Parker, J.R.; Francisco, S.; McClintock, S.T. Diagnosis of monoclonal B cell lymphocytosis (MBL) through transurethral resection of prostate for obstructive lower urinary tract symptoms. *Urol. Case Rep.* **2020**, *29*, 101086. [CrossRef]
20. Martin, O.D.; Wadskier, L.A.; Quiroz, Y.; Bravo, H.P.; Cacciamani, G.; Umana, P.; Medina, L. Primary non-Hodgkin lymphoma of the prostate: A case report. *Ecancermedicalscience* **2017**, *11*, 789. [CrossRef]
21. Nerli, R.B.; Sanikop, A.; Sharma, M.; Patel, P.; Kangale, R.; Patil, S.; Ghagane, S.C.; Hiremath, M.B.; Dixit, N.S. Primary Non-Hodgkin Lymphoma of Prostate: A Case Report. *Indian. J. Surg. Oncol.* **2020**, *11*, 274–277. [CrossRef] [PubMed]
22. Ochirjav, E.; Tsedenbal, B.; Enkhjargal, M.; Mendbayar, E.; Sharkhuu, E. Hematolymphoid tumor of prostate: Diffuse large B cell lymphoma case report. *Urol. Case Rep.* **2023**, *50*, 102497. [CrossRef] [PubMed]
23. Ozsan, N.; Sarsik, B.; Yilmaz, A.F.; Simsir, A.; Donmez, A. Intravascular large B-cell lymphoma diagnosed on prostate biopsy: A case report. *Turk. J. Haematol.* **2014**, *31*, 403–407. [CrossRef] [PubMed]
24. Rallabandi, H.B.; Thirukovela, J.; Swain, M.; Meeramira, D.; Gowrishankar, S. Intravascular large B cell lymphoma of prostate, a rare entity. *Indian. J. Pathol. Microbiol.* **2021**, *64*, 575–578. [CrossRef]
25. Singh, I.; Joshi, M.; Agarwal, S.; Singh, U.R.; Saran, R. Extra-nodal small cell lymphocytic lymphoma of prostate: An unusual cause of lower urinary tract symptoms. *Urology* **2008**, *71*, 547 e547–e549. [CrossRef]
26. Terada, T. Primary follicular lymphoma of the prostate. *Case Rep. Clin. Pathol.* **2016**, *3*, 24–28. [CrossRef]
27. Tomaru, U.; Ishikura, H.; Kon, S.; Kanda, M.; Harada, H.; Yoshiki, T. Primary lymphoma of the prostate with features of low grade B-cell lymphoma of mucosa associated lymphoid tissue: A rare cause of urinary obstruction. *J. Urol.* **1999**, *162*, 496–497. [CrossRef]
28. Tomikawa, S.; Okumura, H.; Yoshida, T.; Mochizuki, H.; Miwa, A.; Takayanagi, K.; Yoshino, T.; Ohtake, S.; Fujimura, M.; Nakamura, S.; et al. Primary prostatic lymphoma of mucosa-associated lymphoid tissue. *Intern. Med.* **1998**, *37*, 628–630. [CrossRef]
29. Williams, I.S.C.; Roberts-Thomson, S.; Lawrentschuk, N.; Sathianathen, N.J. Primary follicular lymphoma of an extraordinarily large prostate: A case report and review of the literature. *Urol. Case Rep.* **2023**, *50*, 102530. [CrossRef]
30. Wu, Y.F.; Li, X.; Ma, J.; Ma, D.Y.; Zeng, X.M.; Yu, Q.W.; Chen, W.G. Primary prostate Burkitt's lymphoma resected with holmium laser enucleation of the prostate: A rare case report. *World J. Clin. Cases* **2023**, *11*, 4406–4411. [CrossRef]
31. Xu, M.; Yang, Q.; Li, M.; Geng, W.; Huang, W.; Chen, Y. Prostate involvement by intravascular large B-cell lymphoma: A case report with literature review. *Int. J. Surg. Pathol.* **2011**, *19*, 544–547. [CrossRef] [PubMed]

32. Zhu, F.; Pan, H.; Xiao, Y.; Li, Q.; Liu, T.; Liu, X.; Wu, G.; Li, J.; Zhang, L. A case report of primary prostate intravascular large B cell lymphoma presenting as prostatic hyperplasia. *Medicine* **2019**, *98*, e18384. [CrossRef] [PubMed]
33. Roehrborn, C.G.; Boyle, P.; Gould, A.L.; Waldstreicher, J. Serum prostate-specific antigen as a predictor of prostate volume in men with benign prostatic hyperplasia. *Urology* **1999**, *53*, 581–589. [CrossRef]
34. Péricart, S.; Syrykh, C.; Amara, N.; Franchet, C.; Malavaud, B.; Gaulard, P.; Girard, J.P.; Ysebaert, L.; Laurent, C.; Brousset, P. Exclusive B-cell phenotype of primary prostatic lymphomas: A potential role of chronic prostatitis. *Histopathology* **2020**, *76*, 767–773. [CrossRef]
35. Oosterheert, J.J.; Budel, L.M.; Vos, P.; Wittebol, S. High levels of serum prostate-specific antigen due to PSA producing follicular non-Hodgkin's lymphoma. *Eur. J. Haematol.* **2007**, *79*, 155–158. [CrossRef]
36. Ballario, R.; Beltrami, P.; Cavalleri, S.; Ruggera, L.; Zorzi, M.G.; Artibani, W. An unusual pathological finding of chronic lymphocitic leukemia and adenocarcinoma of the prostate after transurethral resection for complete urinary retention: Case report. *BMC Cancer* **2004**, *4*, 95. [CrossRef]
37. Dhillon, J.; Pow-Sang, J.M.; Poch, M.A.; Zhang, L. Concurrence of prostatic adenocarcinoma and lymphoma: Clinical and pathological characteristics–Single institutional experience. *J. Clin. Oncol.* **2015**, *33*, e16101. [CrossRef]
38. de Leval, L.; Jaffe, E.S. Lymphoma Classification. *Cancer J.* **2020**, *26*, 176–185. [CrossRef]
39. Sapkota, S.; Shaikh, H. Non-Hodgkin Lymphoma. In *StatPearls*; StatPearls Publishing Copyright © 2024; StatPearls Publishing LLC.: Treasure Island, FL, USA, 2024; Disclosure: Hira Shaikh declares no relevant financial relationships with ineligible companies.
40. Al-Maghrabi, H.; Al-Maghrabi, J. Non-Hodgkin's primary lymphoma involving the genitourinary tract: Histopathological experience from two tertiary hospitals, Western region, Saudi Arabia. *Am. J. Clin. Exp. Urol.* **2024**, *12*, 288–295. [CrossRef]
41. Sellman, D.P.; Simpson, W.G.; Klaassen, Z.; Jen, R.P.; DiBianco, J.M.; Reinstatler, L.; Li, Q.; Madi, R.; Terris, M.K. Characterization and outcomes of local treatment for primary bladder lymphoma: A population-based cohort analysis. *Urol. Ann.* **2018**, *10*, 249–253. [CrossRef]
42. Horning Sandra, J.; Rosenberg Saul, A. The Natural History of Initially Untreated Low-Grade Non-Hodgkin's Lymphomas. *New Engl. J. Med.* **1984**, *311*, 1471–1475. [CrossRef]
43. Zinzani, P.L. Lymphoma: Diagnosis, staging, natural history, and treatment strategies. *Semin. Oncol.* **2005**, *32*, 4–10. [CrossRef]
44. Jackson, D.; Daly, J.; Saltman, D.C. Aggregating case reports: A way for the future of evidence-based health care? *Clin. Case Rep.* **2014**, *2*, 23–24. [CrossRef] [PubMed]