e-ISSN: 0975-9506, p-ISSN: 2961-6093

Available online on www.ijpqa.com

International Journal of Pharmaceutical Quality Assurance 2026; 17(10); 104-110

Original Research Article

A Tale of Two Tumors: Peripheral Schwannoma and Testicular Non-Hodgkin's Lymphoma

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Received: 25-07-2026 / Revised: 23-08-2026 / Accepted: 26-09-2026
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Conflict of interest: Nil

Abstract:

Background: Schwannoma is a common, benign, encapsulated tumour of the peripheral nerve sheath, whereas primary testicular lymphoma (PTL) is a rare, aggressive extranodal non-Hodgkin lymphoma (NHL) that predominantly affects elderly men. The simultaneous occurrence of the two neoplasms in the same patient is exceptionally uncommon.

Case Presentation: A 74-year-old man presented with a painless, left-sided scrotal mass of one month's duration and a slowly enlarging mass in the right arm of three months' duration. Both masses were large and firm on examination, and routine blood investigations were normal. A left orchidectomy and an excision biopsy of the arm swelling were performed. Grossly, the testis harboured a well-encapsulated, lobulated, grey-white tumour measuring 8 × 6 × 5 cm, while the arm lesion (7.5 × 4 × 3.5 cm, with overlying skin) was a well-encapsulated, grey-yellow to grey-brown mass with cystic spaces.

Histopathology: The testicular tumour was composed of diffuse sheets of large round to oval cells with a high nuclear–cytoplasmic ratio, vesicular nuclei and prominent nucleoli, replacing the entire testicular parenchyma, with necrosis, frequent mitoses, epididymal involvement and lymphovascular invasion, diagnostic of non-Hodgkin lymphoma. The arm lesion showed alternating hypercellular Antoni A and hypocellular, myxoid Antoni B areas, Verocay bodies and focal cystic change, diagnostic of schwannoma.

Conclusion: The coexistence of these two tumours is most likely coincidental, as they arise from unrelated tissues (haematolymphoid system and peripheral nerve sheath) and share no established biological, genetic or syndromic link. The case underscores the need to obtain independent histopathological confirmation of every clinically distinct lesion in a patient with a known or suspected malignancy, and to manage each tumour along its own treatment pathway under multidisciplinary care.

Keywords: Schwannoma; Non-Hodgkin's lymphoma; Primary testicular lymphoma; Peripheral nerve sheath tumour; coincidental tumours; Case report.

DOI: 10.25258/ijpqa.17.10.16

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Introduction

Schwannomas, also called neurilemmomas, are common, well-encapsulated benign tumours arising from the Schwann cells of the peripheral nerve sheath. [1,2] They occur most frequently in mixed nerves and account for approximately 5% of all soft tissue tumours. [3] Their anatomical distribution is wide: they are encountered most often in the ear, nose and throat region, followed by the trunk, and then by the upper limb (19%) and lower limb (17.5%). [4]

The tumour is more common between 30 and 60 years of age. [5,6] Because of its rarity at any single site, its slow growth and the absence of specific symptoms, the diagnosis is often difficult, delayed or incorrect. [3,7] Schwannomas are typically located on the large nerve trunks. In the upper limb they lie more often on the anterior aspect and frequently involve the ulnar nerve, in over 75% of cases occurring distal to the elbow. [8] Imaging, notably ultrasonography (USG) and above all magnetic resonance imaging (MRI), plays a major role in pre-operative diagnosis and is considered helpful in establishing the correct diagnosis in about 90% of cases; the definitive diagnosis, however, rests on histopathological examination. [2]

Primary testicular lymphoma (PTL) is an extranodal lymphoma that originates in the testis

and accounts for about 5% of all testicular tumours. [9,10] It predominantly affects the elderly and is the most common testicular tumour after the age of 60 years. [11] In the 5th edition of the World Health Organization classification, testicular large B-cell lymphoma is grouped with the large B-cell lymphomas of immune-privileged sites. [12] Its clinical behaviour is characterised by a marked tendency toward extranodal relapse, including relapse in the contralateral testis and the central nervous system. [13]

Schwannoma, a WHO grade I tumour that only very rarely undergoes malignant transformation, [14] and testicular lymphoma, an aggressive haematolymphoid malignancy, differ completely in cell of origin, biology, behaviour and treatment.

Their presence together in a single patient is exceptionally rare. We describe an elderly man who presented concurrently with a testicular mass and an arm mass, in whom histopathology revealed non-Hodgkin lymphoma in the testis and a schwannoma in the arm, and we discuss the clinicopathological features of each entity, the diagnostic pitfalls, and the implications of such a dual presentation.

Case Report

Clinical Presentation: A 74-year-old man presented with a painless mass on the left side of the scrotum that had been present for one month. He also reported a slowly growing mass in the right arm for the preceding three months. On physical examination, there was a large, firm left testicular mass together with a large, firm mass in the right arm. Routine blood laboratory investigations were within normal limits. The patient underwent a left orchidectomy, and the swelling in the right arm was removed by excision biopsy. Both specimens were submitted separately for histopathological evaluation.

Gross Findings

Left Testis: The left orchidectomy specimen, with its tunica sac, measured 8.5 × 6 × 5 cm. The cut surface showed a well-encapsulated, lobulated, grey-white tumour measuring 8 × 6 × 5 cm (Figure 1). The tumour replaced most of the testis and had a firm, fleshy, relatively homogeneous appearance with well-demarcated borders.



Figure 1: Gross photograph of the left orchidectomy specimen, cut section. A well-encapsulated, lobulated, grey-white tumour measuring 8 × 6 × 5 cm replaces the testicular parenchyma (scale in centimetres).

Right arm lesion. The excision biopsy from the right arm swelling was received as a grey-brown, globular mass covered by skin, measuring 7.5 × 4 × 3.5 cm. On sectioning, it was a well-encapsulated mass with a grey-yellow to grey-brown cut surface and multiple cystic spaces (Figure 2).



Figure 2: Gross photograph of the right arm lesion, cut section. A well-encapsulated mass with a grey-yellow to grey-brown cut surface and cystic spaces (scale in centimetres).

Microscopic Findings

Left Testicular Mass: Haematoxylin and eosin (H&E)-stained sections showed a malignant neoplasm composed of cells arranged in diffuse sheets that had replaced the entire testicular parenchyma.

The neoplastic cells were large and round to oval, with a high nuclear–cytoplasmic ratio, well-defined cytoplasmic borders, vesicular nuclei and prominent nucleoli (Figure 3). Areas of necrosis were present, mitotic figures were frequent, and a chronic inflammatory infiltrate was seen in the background.

The tumour also infiltrated the epididymis (Figure 4) and the rete testis. Lymphovascular invasion was identified. On the basis of these features, a diagnosis of non-Hodgkin lymphoma was made.

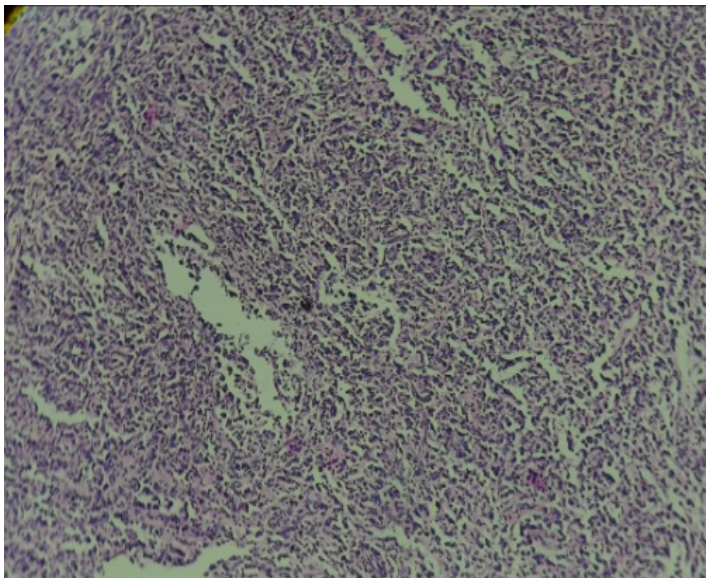


Figure 3: H&E section of the testicular tumour showing a malignant neoplasm composed of cells arranged in diffuse sheets that replace the entire testicular parenchyma.

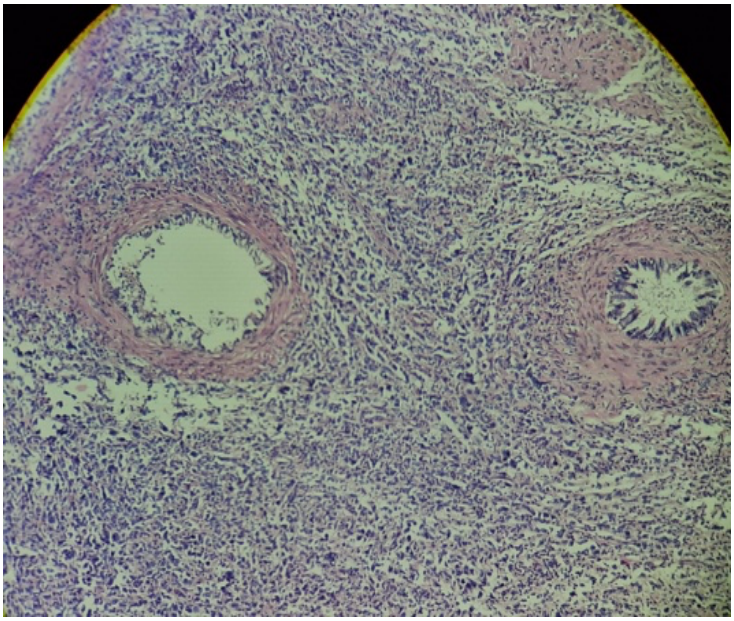


Figure 4: H&E section showing infiltration of the epididymis by the tumour; neoplastic cells lie between and around the epididymal ducts.

Right Arm Mass: Sections from the arm lesion showed an encapsulated neoplasm composed of hypercellular Antoni A areas alternating with hypocellular Antoni B areas. In the myxoid, hypocellular zones the individual cells were narrow and elongated, with wavy nuclei and tapered ends. Verocay body formation and focal cystic areas were noted. These features are characteristic of schwannoma, and a diagnosis of schwannoma was made (Figure 5).

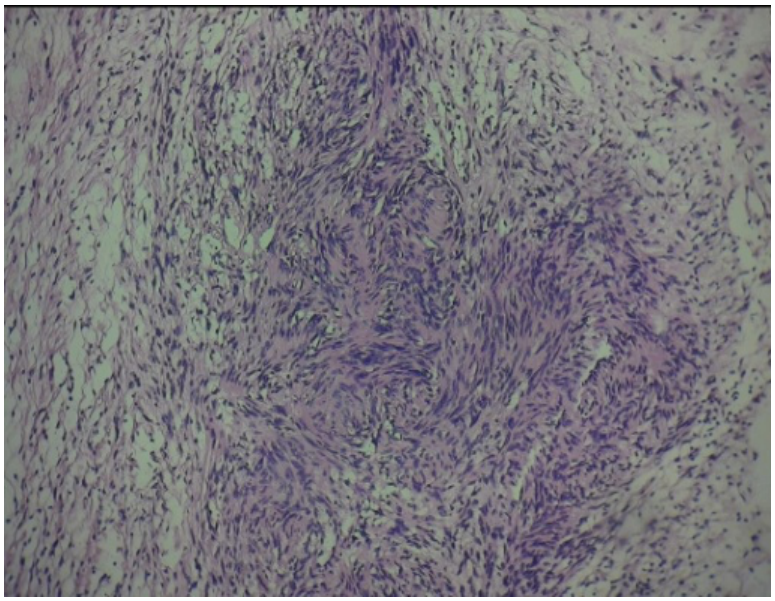


Figure 5: H&E section of the arm lesion showing a neoplasm composed of hypercellular Antoni A areas and hypocellular, myxoid Antoni B areas, consistent with schwannoma.

Discussion

Schwannoma: Schwannomas, also known as neurilemmomas, are common soft tissue tumours of the extremities. They may be classified as proximal, involving the brachial plexus and upper arm, or distal, involving the forearm and hand. They emerge from nerves invested by Schwann cell sheaths and are surrounded by a true capsule formed by the epineurium. Some are found incidentally as painless masses, while others cause neurological symptoms through compression of adjacent structures; symptomatic tumours may present with neurogenic pain in the extremity, local swelling, paraesthesia and motor weakness. [1] Most schwannomas are sporadic, but they may also arise in the setting of neurofibromatosis type 2 (NF2), schwannomatosis or Carney complex. They

behave as WHO grade I tumours, and the central molecular event in their pathogenesis is loss of function of the merlin protein, through alteration of the NF2 gene on chromosome 22 or secondary merlin inactivation. [14] Larger tumours such as the present 7.5 cm lesion may show secondary degenerative change, including cystic spaces, hyalinised vessels and, occasionally, necrosis. [14] The cystic spaces seen grossly in our case are consistent with this phenomenon.

USG and MRI play an important role in guiding the pre-operative diagnosis, although neither is 100% accurate. [2] On USG, schwannomas are usually seen as homogeneous, well-defined, often ovoid hypoechoic masses, and the study can demonstrate the origin of the tumour and its relationship to the affected nerve. MRI remains the most useful investigation, with a diagnostic value above 90%; like other peripheral nerve tumours, schwannoma appears moderately bright on proton-density-weighted images and bright on T2-weighted images. [2] Radiologic–pathologic correlation studies further describe a well-circumscribed mass that is isointense to skeletal muscle on T1-weighted images and that often lies eccentric to the parent nerve. [15]

The definitive diagnosis is histopathological. Microscopically, schwannomas are characterised by two distinct areas, the compact hypercellular Antoni A pattern and the loose, myxoid, hypocellular Antoni B pattern, with nuclear palisading around fibrillary processes (Verocay bodies) in the cellular areas. [2] Both features were present in our case (Figure 5). Neurofibroma, the principal differential diagnosis, is usually distinguished by the absence of a capsule, a mixed cell population and the lack of Antoni A and B patterns, [14] and immunohistochemistry, typically diffuse S-100/SOX10 positivity in schwannoma, helps to separate schwannoma from other nerve sheath tumours, including malignant peripheral nerve sheath tumour. [16]

Treatment of schwannoma is surgical and consists of tumour enucleation under the surgical microscope. [2] Large institutional experiences with peripheral nerve sheath tumours, such as the 30-year Louisiana State University series, document the results of surgical management of these lesions. [17]

Primary Testicular Lymphoma: The testis is an uncommon site of extranodal lymphoma, with a reported annual incidence of 0.26 cases per 100,000 person-years and a reported median age at diagnosis of about 67 years; it is rare in children. [10] In the International Extranodal Lymphoma Study Group (IELSG) survey of 373 patients, the median age at diagnosis was 66 years. [13] PTL accounts for less than 2% of all NHL and approximately 5% of all testicular neoplasms, yet it is the most prevalent histological type of testicular cancer in men older than 60 years. [10,11] Population-based data from the United States indicate that the incidence of testicular diffuse large B-cell lymphoma is increasing. [18] Histologically, 80–90% of PTLs are diffuse large-cell lymphomas of B-cell phenotype. [13]

The most frequent presenting symptom is a unilateral testicular mass of variable size, usually painless, as in our patient. [9] Contiguous invasion of the epididymis and the spermatic cord can be seen in 60% and 39% of cases, respectively. [9] Our case showed involvement of the epididymis and rete testis. Lymphovascular invasion, also present here, reflects the tendency of PTL to disseminate: a continuous risk of extranodal relapse exists even in localised disease, with the central nervous system, the contralateral testis, skin and other extranodal sites most often affected. [13,19] Cutaneous metastasis of testicular diffuse large B-cell lymphoma has been documented. [9]

Grossly, lymphomas present as an enlarged testis with a fleshy, lobulated, diffuse grey-white firm mass having a homogeneous cut surface and well-demarcated borders, which corresponds closely to the specimen in Figure 1. Microscopic examination with routine H&E shows diffuse sheets of large lymphoma cells that infiltrate between the seminiferous tubules and eventually replace the entire parenchyma. Frequent mitotic figures are observed and necrosis is common. Most cases of testicular lymphoma exhibit centroblastic morphology (90%), followed by immunoblastic morphology (10%). [11]

Immunohistochemistry (IHC) in testicular lymphoma commonly shows expression of pan-B-cell antigens, including CD19, CD20, CD79a and PAX5. BCL6 is expressed in 75–90% of cases, MUM1 in 40–70% and CD10 in 20–40%. The proliferative index, as indicated by Ki-67 staining, ranges from 40% to 90%, with a mean of 70%. Virtually all cases show IGH rearrangements, and rearrangements involving BCL6 (40%), followed by MYC (15%) and BCL2 (10%), have been reported. [11] At the genomic level, PTL and primary central nervous system lymphoma share a distinctive signature: near-uniform CDKN2A loss, activation of Toll-like receptor signalling through MYD88 mutation and/or NFKBIZ amplification, deregulation of BCL6, and frequent 9p24.1/PD-L1/PD-L2 copy-number alterations that provide a structural basis for immune evasion. [19] These features are consistent with the immune-privileged nature of the testis. [12,19] Testicular lymphoma must be differentiated from other testicular tumours that can show sheet-like growth of large cells. Seminoma is characterised by nests, cords or sheets of tumour cells within thin fibrous septa, and

embryonal carcinoma by solid, papillary or tubular growth patterns. IHC aids in separating these entities: seminoma typically stains positively for SALL4, OCT3/4, CD117 and PLAP and is negative for CD45, CD3, CD20 and CD30, whereas embryonal carcinoma is often positive for SALL4, OCT3/4, SOX2 and CD30 and negative for CD117, CD45, CD3 and CD20. Myeloid sarcoma is another differential diagnosis; it shows diffuse replacement by blasts with thin nuclear membranes, fine chromatin and variably prominent nucleoli, and is positive for MPO on IHC. [11] Because germ cell tumours mainly affect younger men, a large testicular mass in a man in his seventies should prompt early consideration of lymphoma.

Orchidectomy establishes the diagnosis but is not curative on its own. The IELSG retrospective survey found that anthracycline-based chemotherapy, central nervous system prophylaxis and contralateral testicular irradiation appeared to improve outcome. [13] This was supported prospectively by the IELSG-10 phase II trial, in which 53 patients with stage I–II PTL received R-CHOP, intrathecal methotrexate and testicular radiotherapy; there were no contralateral testicular relapses and the 5-year cumulative incidence of CNS relapse was 6%. [20] Accordingly, rigorous staging and multidisciplinary oncological planning are essential once the lymphoma diagnosis is established.

Coexistence of the Two Tumours: The simultaneous occurrence of testicular lymphoma and schwannoma in the same patient is exceptionally rare and is most likely a coincidental presentation, as no established biological, genetic or syndromic association links the two conditions. The tumours have different tissue origins: lymphoma arises from the haematolymphoid system, and schwannoma from the peripheral nerve sheath. Their molecular drivers are also distinct, being dominated by merlin/NF2 loss in schwannoma14 and by MYD88, CDKN2A and 9p24. [1] Alterations in testicular lymphoma. [19] Neither tumour is associated simultaneously with neurofibromatosis or with the germline predisposition syndromes related to lymphoid neoplasms. [12,14] Both are tumours of later adult life, and the rising incidence of testicular lymphoma in the elderly [18] makes chance co-occurrence in a single elderly patient plausible.

Clinical Significance: Even though unrelated, this combination is clinically important because it emphasises the need for histopathological confirmation of each lesion. In a patient with lymphoma, a new soft tissue mass might easily be assumed to represent extranodal dissemination, as skin and soft tissue involvement by testicular lymphoma is well recognised. [9] Treating such a mass as lymphoma without tissue diagnosis would lead to inappropriate staging and unnecessary systemic therapy. Conversely, labelling a slow-growing limb mass as a benign nerve sheath tumour on clinical grounds alone could miss a second malignancy. In our patient, histology resolved the question: a benign, surgically curable schwannoma in the arm and an aggressive lymphoma in the testis, which require separate treatment pathways under multidisciplinary care.

Limitations: This is a single case, and a coincidental association cannot be proven. The work-up reported here does not include germline or tumour genetic testing, which could in principle exclude a shared predisposition. Longer follow-up of the lymphoma would also be informative given the late-relapse tendency of PTL.

Conclusion

We report a rare coincidence of a peripheral schwannoma of the right arm and a non-Hodgkin lymphoma of the left testis in a 74-year-old man. The two tumours are biologically unrelated.

Careful gross examination and histopathological evaluation of each lesion were decisive in reaching the correct diagnosis of each, and they allow each tumour to be managed on its own merits: complete surgical excision for the schwannoma and oncological staging and systemic management for the lymphoma.

Learning points

- A testicular mass in a man older than 60 years should raise suspicion of lymphoma, which is the most common testicular tumour in this age group.
- Schwannoma shows Antoni A and B areas with Verocay bodies, and cystic change is common in larger lesions.
- Every clinically distinct lesion in a patient with malignancy deserves its own tissue diagnosis; a second mass is not necessarily metastatic.
- Concurrent schwannoma and testicular lymphoma is most likely coincidental, but each tumour needs its own management pathway within a multidisciplinary team.

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