EMBRYONAL CARCINOMA PRESENTING AS CERVICAL LYMPHADENOPATHY: A CASE REPORT ON THE DIAGNOSTIC DILEMMA OF ORIGIN

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Abstract

The presence of an embryonal carcinoma in a cervical lymph node, in the absence of a palpable testicular mass, presents a diagnostic dilemma regarding whether this represents a rare primary extragonadal germ cell tumor (EGCT) of the neck or a metastasis from an occult spontaneously regressed testicular cancer. We report the case of a 34-year-old male presenting with isolated left cervical lymphadenopathy. Initial physical examination of the testes was unremarkable, potentially supporting a diagnosis of primary cervical origin. However, markedly elevated serum tumor markers (lactate dehydrogenase [LDH] and alpha-fetoprotein [AFP]), alongside a beta-human chorionic gonadotropin (beta-hCG) level within normal limits, prompted a search for a gonadal primary. Scrotal ultrasound revealed a calcified scar in the left testis, and subsequent orchiectomy confirmed a fibrotic nodule with no viable malignancy, consistent with the spontaneous regression of a primary tumor. The patient was treated for Stage IIIC non-seminomatous germ cell tumor (NSGCT) with bleomycin, etoposide, and cisplatin (BEP) chemotherapy and remains disease-free at 3 years. This case illustrates that primary cervical EGCT is a diagnosis of exclusion. The spontaneous regression phenomenon must be rigorously investigated via ultrasound and orchiectomy to avoid misdiagnosis and ensure appropriate multimodal therapy.

Keywords: embryonal carcinoma, germ cell tumor, lymphadenopathy, extragonadal germ cell tumor, BEP protocol, spontaneous neoplasm regression

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Introduction

Pure embryonal carcinoma (EC) is a rare and aggressive type of non-seminomatous germ cell tumor (NSGCT) that predominantly arises in the testes, typically affecting men between the ages of 20 and 40. EC is characterized by undifferentiated, primitive cells resembling early embryonic tissue and is known for its rapid growth, early lymphatic spread, and aggressive behavior.[1] Although the testes are the most common primary site, EC can occasionally occur extragonadally in locations such as the mediastinum, retroperitoneum, or, very rarely, the cervical region.[2]

Clinically, patients with EC typically present with testicular swelling or pain. However, due to the tumor's aggressive nature and tendency for early spread, clinical findings may occasionally arise from metastatic sites rather than the primary tumor. Unusual presentations, such as isolated lymph node enlargement, can complicate diagnosis. Cervical lymph node involvement as the first sign of EC is extremely rare and has been reported in only a few cases.[3, 4] We report this case to emphasize the importance of considering occult testicular malignancy in the differential diagnosis of cervical lymphadenopathy. By describing the diagnostic workup and management of a patient with a spontaneously regressed primary tumor, we aim to highlight the critical role of scrotal ultrasound and tumor markers in avoiding misdiagnosis.

A case report

A 34-year-old male with an unremarkable past medical history. The patient presented with a painless neck mass persisting for several weeks. The patient reported a progressive enlargement of the swelling, which had recently begun to cause discomfort. Review of systems was negative for constitutional symptoms (fever, night sweats, weight loss) and dysphagia. Social history was regular alcohol consumption (30 g/day); however, the patient was a non-smoker and denied substance abuse. Family history was negative for cancer.

On physical examination, the patient appeared well-nourished and hemodynamically stable. Head and neck examination identified a prominent, firm, non-tender enlarged mass in the left cervical chain. The mass was fixed and non-mobile, with a discrete nodal character. The overlying skin was non-erythematous and intact. No other palpable lymphadenopathy was noted elsewhere. A testicular examination was performed and was unremarkable, with no palpable masses. The remainder of the physical examination was non-contributory.

Initial laboratory workup revealed a normal complete blood count and metabolic profile. However, given the clinical presentation, a tumor marker panel was obtained, revealing a significantly elevated Lactate Dehydrogenase (LDH) of 1087 U/L (reference range: < 289 U/L) and an elevated Alpha-Fetoprotein (AFP) of 25.03 ng/mL (reference range: 0 - 9 ng/mL). Beta-hCG was within normal limits (**Table 1**).

Table 1. Serial laboratory workup results from initial diagnosis through 3-year follow-up after chemotherapy

Analyte (Unit)	Reference Range	Initial	After Cycle 1	After Cycle 4	3-Year Follow-up
alpha-Fetoprotein (AFP) (ng/mL)	0 – 9	**25.0**	8.9	7.7	4.7
Lactate Dehydrogenase (LDH) (U/L)	< 289	**1087**	286	242	207
beta-Human Chorionic Gonadotropin (beta-hCG) (mIU/mL)	< 1	0.58	< 0.1	< 0.1	< 0.1
Creatinine (mg/dL)	0.7 – 1.3	0.69	0.72	0.72	0.85

Diagnostic imaging was performed to locate the primary site and complete clinical staging. Scrotal ultrasound revealed occult pathology in the left testis, characterized by hypoechoic lesions with associated macrocalcifications (**Figure 1C**). Whole-body Computed Tomography (CT) confirmed systemic lymphadenopathy, identifying multiple bilateral cervical nodes (levels I–IV) measuring up to 3 cm in diameter, as well as significant intra-abdominal and inguinal lymphadenopathy with nodes measuring up to 2.5 cm (**Figures 1A and 1B**).

Subsequently, a diagnostic biopsy of a cervical lymph node was performed. Histopathological examination revealed embryonal carcinoma (Figures 2A and 2B). The diagnosis was confirmed via immunohistochemistry, which showed positive staining for CD30 and PLAP (**Figures 2C and 2D**) and negative staining for AFP, beta-hCG, synaptophysin, and chromogranin. Biopsies of the intra-abdominal and inguinal lymph nodes were not performed, as the histological confirmation from the cervical node was sufficient to guide systemic management.

To definitively identify the suspected occult primary tumor and rule out residual viable malignancy, the patient underwent a left radical orchiectomy. The patient underwent a left radical orchiectomy. Subsequently, a diagnostic biopsy of a cervical lymph node was performed. Histopathological examination revealed sheets of large, primitive epithelioid cells with amphophilic cytoplasm, marked nuclear pleomorphism, and prominent nucleoli, consistent with embryonal carcinoma (**Figures 2A and 2B**).

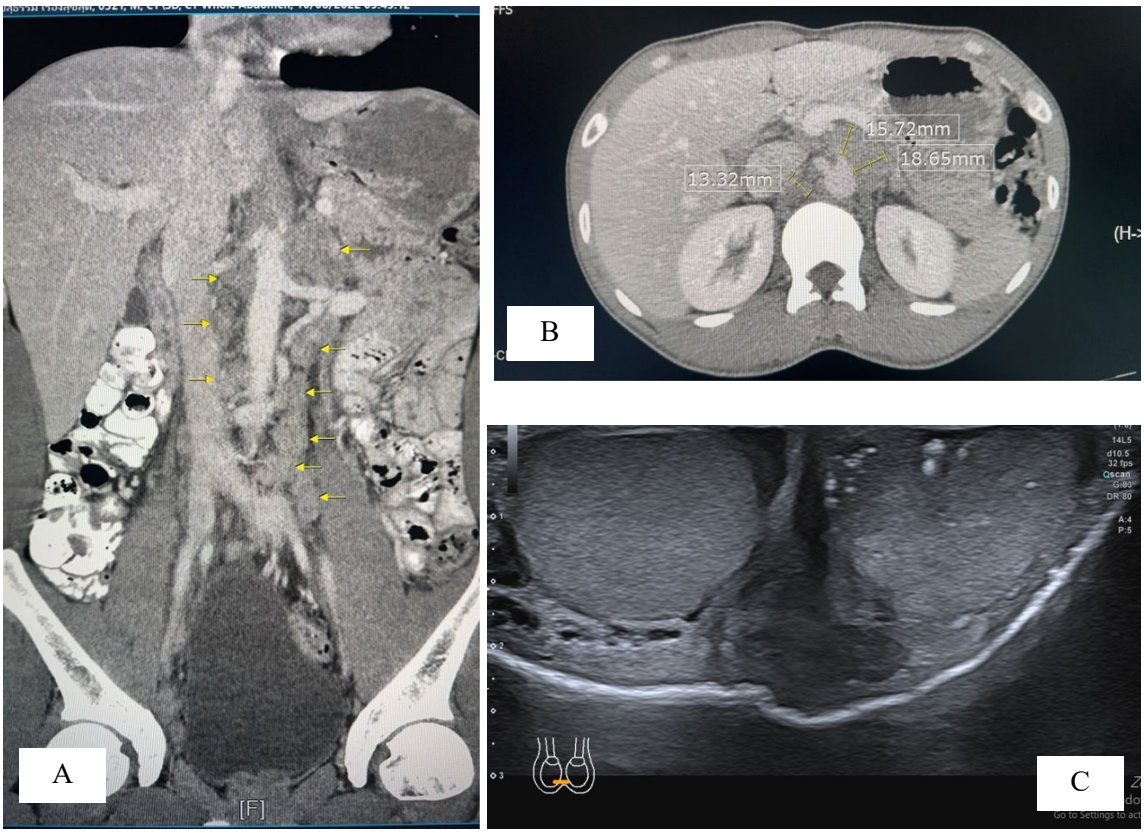

Figure 1. (A, B) Computed Tomography (CT) scan showing systemic lymphadenopathy. (C) Scrotal ultrasound of the left testis demonstrating homogenous echogenicity of the parenchyma with few hypoechoic lesions containing macrocalcifications (measured up to 0.7 × 0.6 cm) and mult iple small hyperechoic foci.

The diagnosis was confirmed via immunohistochemistry. While the tumor demonstrated strong positivity for PLAP (**Figure 2D**)—a marker often associated with seminoma—the diagnosis of embryonal carcinoma was confirmed by diffuse CD30 expression (**Figure 2C**). This CD30 positivity, combined with the solid and glandular morphologic patterns, effectively excluded seminoma and other germ cell tumors. Staining was negative for AFP, beta-hCG, synaptophysin, and chromogranin.

Given the rare presentation, the case was reviewed by a multidisciplinary team (MDT) and reached consensus on a diagnosis of Stage IIIC Non-Seminomatous Germ Cell Tumor (NSGCT). Risk stratification according to the IGCCCG classified the patient as Intermediate Risk, based on the marked elevation of LDH (3.7x ULN) (5). The patient was treated with 4 cycles of BEP chemotherapy (Bleomycin, Etoposide, and Cisplatin). He demonstrated a rapid biochemical response with normalization of all tumor markers following the first cycle. Post-treatment imaging confirmed a Complete Response (CR). At 3-year follow-up, the patient remains disease-free on both serologic and radiographic surveillance.

Discussion

Primary Extragonadal Germ Cell Tumors (EGCT)

A key diagnostic dilemma in this case was determining whether the cervical mass represented a metastasis or a primary extragonadal germ cell tumor (EGCT). Primary EGCTs are rare tumors that arise from primordial germ cells arrested during their migration along the urogenital

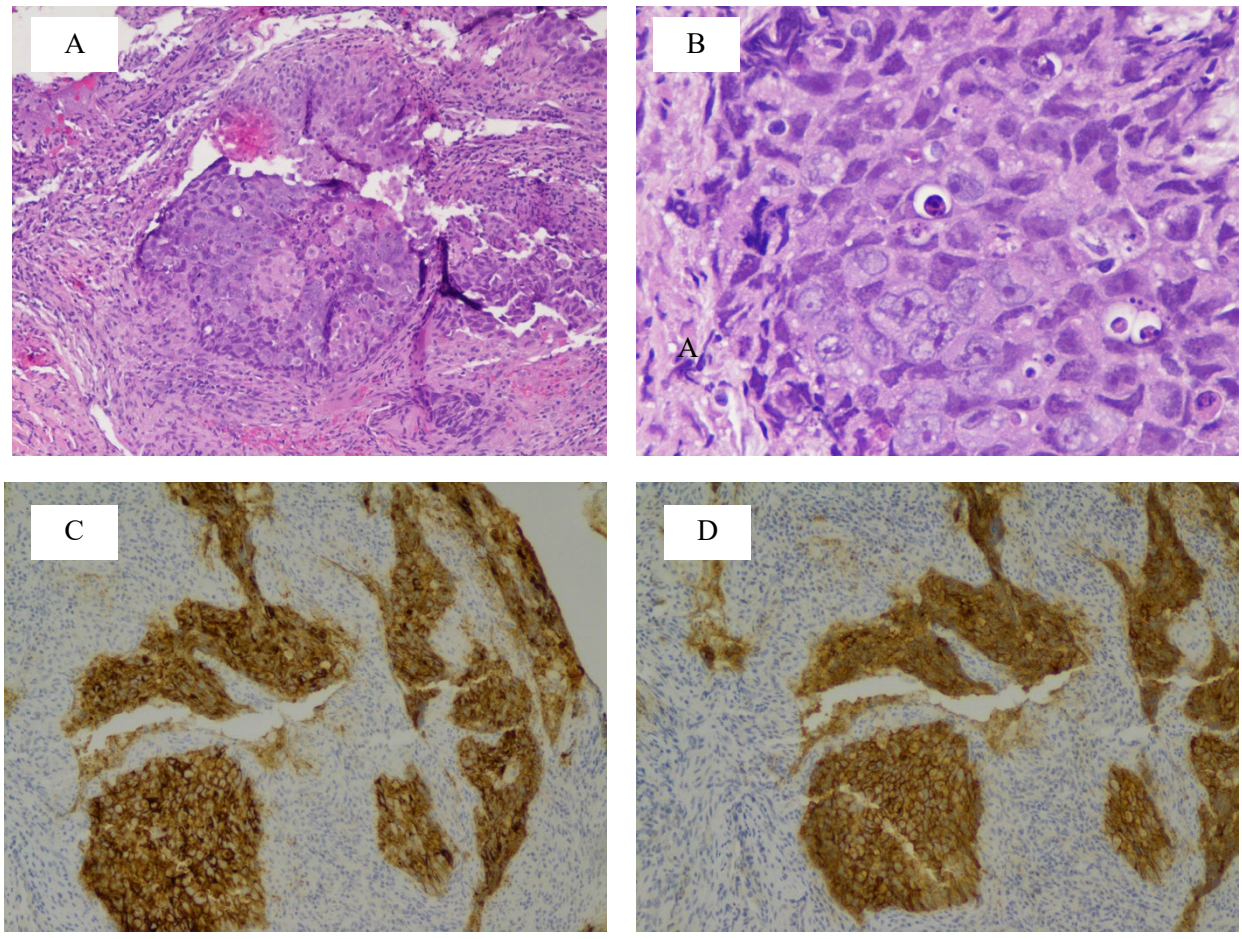

Figure 2. (A, B) Histopathological study of the cervical lymph node biopsy showing proliferation arranged in multiple solid nests surrounded by fibrous septa. Tumor cells are polygonal with atypical, enlarged nuclei and abundant eosinophilic cytoplasm. (C, D) Immunohistochemical staining shows strong positivity of tumor cells for CD30 and PLAP.

ridge. While they most commonly occur in the midline structures of the mediastinum and retroperitoneum, primary EGCTs of the head and neck are exceptionally rare, accounting for less than 5% of all EGCTs.[2]

Differentiating primary cervical EGCT from metastasis

Distinguishing between a primary cervical EGCT and a metastasis from an occult testicular primary is crucial for management, as treatment protocols and prognoses differ. A true primary cervical EGCT is a diagnosis of exclusion. It can only be diagnosed if the testes are completely normal on both palpation and high-resolution ultrasonography.[6] In this patient, the initial clinical picture—a solitary neck mass with non-palpable testes—raised the possibility of a primary cervical origin. However, the identification of a calcified, hypoechoic lesion on scrotal ultrasound and the subsequent histopathological finding of a fibrotic, calcified nodule in the orchiectomy specimen provided the definitive evidence against a primary cervical origin.[7]

The "burned-out" phenomenon and spontaneous regression

The term "burned-out" tumor describes a clinical and imaging finding where a testicular mass is non-palpable or appears benign, despite the presence of metastatic disease. Pathologically, this corresponds to the phenomenon of spontaneous regression, characterized by fibrosis, calcification, and lymphoplasmacytic infiltration with no viable tumor cells.[8] While the exact mechanism remains unclear, it is hypothesized to be mediated by a host immune response or by ischemia resulting from tumor outgrowth beyond its blood supply.[9] It is also important to note the histological subtype involved. While spontaneous regression has been reported in various germ cell tumors, it is most frequently associated with choriocarcinomas due to their high metabolic demand and tendency for hemorrhage. The presence of a "burned-out" primary giving rise to a pure embryonal carcinoma metastasis, as seen in this case, is relatively distinct. Embryonal carcinoma is typically aggressive and less prone to hemorrhagic necrosis than choriocarcinoma, making the complete regression of the primary site a notable pathophysiological event.

Prognosis and long-term surveillance

The patient's outcome—remaining disease-free at 3 years following treatment for Stage IIIC NSGCT—is a significant clinical finding. Historically, patients with tumors that have undergone spontaneous regression have a prognosis similar to those with primary testicular germ cell tumors of the same stage and histological classification. Stage IIIC NSGCT generally carries an intermediate or poor prognosis, depending on the International Germ Cell Cancer Collaborative Group (IGCCCG) risk stratification. However, the complete response to BEP chemotherapy in this case aligns with the high chemosensitivity of embryonal carcinoma. Long-term surveillance remains critical, as late relapses (>2 years post-treatment) are rare. This case reinforces that identifying and removing the spontaneously regressed primary tumor, combined with aggressive systemic chemotherapy, can lead to durable remission even in advanced-stage disease.

Clinical implications

This distinction is clinically vital. If this case had been misclassified as a primary cervical EGCT due to a failure to detect the testicular scar, orchiectomy might have been omitted. This would represent a significant management error, as the spontaneously regressed testis often harbors Germ Cell Neoplasia In Situ (GCNIS) or microscopic foci of residual malignancy, which can lead to local recurrence or a new primary tumor if left untreated.[10] Therefore, this case underscores that finding a germ cell tumor in the neck mandates a rigorous search for a testicular "scar," as true primary cervical EGCTs are exceedingly rare in adults compared to the spontaneous regression phenomenon.

Conclusion

The presentation of an embryonal carcinoma in a cervical lymph node without evident disease in the mediastinum or retroperitoneum presents a significant diagnostic challenge. While this

clinical picture may initially suggest a primary extragonadal germ cell tumor (EGCT) of the cervical region, this diagnosis is one of exclusion and is exceptionally rare. This case demonstrates that even when the clinical epicenter of the disease appears to be the cervical lymph nodes, an occult or "burned-out" testicular primary must be rigorously investigated. The identification of a testicular scar via ultrasound and subsequent histopathology confirmed the testicular origin in this patient, ruling out a primary cervical etiology. Distinguishing between a primary cervical EGCT and a metastatic regressed tumor is clinically paramount, as it necessitates radical orchiectomy to eliminate potential residual neoplasia and prevent disease recurrence.

Ethics approval

This research did not require ethical approval, as the IRB committee does not mandate approval for reporting individual cases or case series. The patient provided written informed consent for the publication of this case report and associated images.

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