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CASE REPORT

Retroperitoneal extragonadal germ cell tumor with duodenal infiltration: A challenging endo-luminal tissue diagnosis

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Abstract

A 32-year-old Malay male was referred to our hospital for a second opinion. An abdominal and pelvic CT scan at the previous medical facility showed a large retroperitoneal tumor, which was subjected to ultrasound-guided fine-needle aspiration cytology (FNAC) with a provisional diagnosis of malignant lymphoma. However, after reviewing the existing results, a repeat biopsy was deemed necessary and this was performed endoluminally via gastroduodenoscopy in view of the close proximity of the tumor and the third part of the duodenum. The first biopsy failed to detect any abnormal cells, but a repeat biopsy with supporting evidence from other laboratory results led to a final diagnosis of extragonadal germ cell tumor (GCT) with duodenal infiltration.

Introduction

Retroperitoneal tumors often pose a challenging problem to clinicians when it comes to tissue diagnosis. Imaging-guided fine-needle aspiration biopsies are commonly employed for tissue diagnosis, but this is sometimes hampered by inadequate tissue sampling for accurate diagnosis to be made. Germ cell tumors (GCTs) are a rare case of retroperitoneal tumors, which are potentially curable with chemotherapy. We report a case of retroperitoneal extragonadal GCT with duodenal infiltration diagnosed after repeated biopsies from the duodenum.

Case Report

A 32-year-old Malay male presented to a local hospital with a 2-week history of intermittent upper abdominal pain associated with bloating. There was no history of vomiting, weight loss, or overt gastrointestinal bleeding. An abdominal and pelvis CT scan showed a large soft tissue mass (5.5 × 7 × 6 cm) in the retroperitoneal space abutting the third part of the duodenum (D3) and encasing the inferior vena cava (IVC) (Figs 1 and 2).

An ultrasound (UC)-guided fine-needle aspiration cytology (FNAC) exam was performed, and the initial cytopathologic report showed the presence of cells suspicious of malignant lymphoma. The patient was then referred to our hematologist for further opinion. Upon reviewing the existing results, it was felt that the cytopathologic specimen was insufficient to make a definitive diagnosis of lymphoma with further subtyping and hence a repeat biopsy was warranted. This was initially planned to be done percutaneously by our radiologist, but given the CT scan findings, we decided to attempt biopsies endoluminally using a gastroduodenoscope because the mass was abutting D3 without a clear plane of demarcation.

The patient underwent gastroduodenoscopy, which showed a nodular lesion in D3 with a central area of ulceration (Fig. 3).

Multiple biopsies from the surface as well as ulcerated areas were taken. Urease test for *Helicobacter pylori* was negative. Unfortunately, the subsequent histopathologic report showed nonspecific duodenitis with no malignant cells detected. This prompted a repeat gastroduodenoscopy and biopsies targeting mainly the ulcerated areas, as we believed the yield of a positive result would be higher.

A repeat gastroduodenoscopy and biopsies were performed, targeting a same spot in the ulcerated region to ensure adequate depth of reach. A total of 15 biopsy samples were taken, which were subjected to immediate frozen section examination to confirm the presence of abnormal cells. Histopathologic examination of the second biopsies (Fig. 4) showed invasion of the ulcerated mucosa by atypical glandular structures surrounded in areas by cellular spindled-cell stroma. The spindled stromal cells displayed nuclear hyperchromasia and increased mitotic activity, suggestive of an immature mesenchymal stroma. Although there was absence of unequivocal immature neuroectordermal tubules/rosettes and classical GCT elements such as yolk sac tumor, embryonal carcinoma, or choriocarcinoma, immature teratoma component of an underlying GCT was highly consistent with the biopsy results given the raised serum levels of alpha-fetoprotein (AFP) of 792 ng/mL and beta-hCG of 92.5 mIU/mL in this patient. His hemoglobin count was normal and screenings for hepatitis B and C virus were negative. Physical examination of his testicles by two separate physicians found them to be normal.

This finally led to the diagnosis of extragonadal GCT (EGCT) with duodenal infiltration. Following discussions with

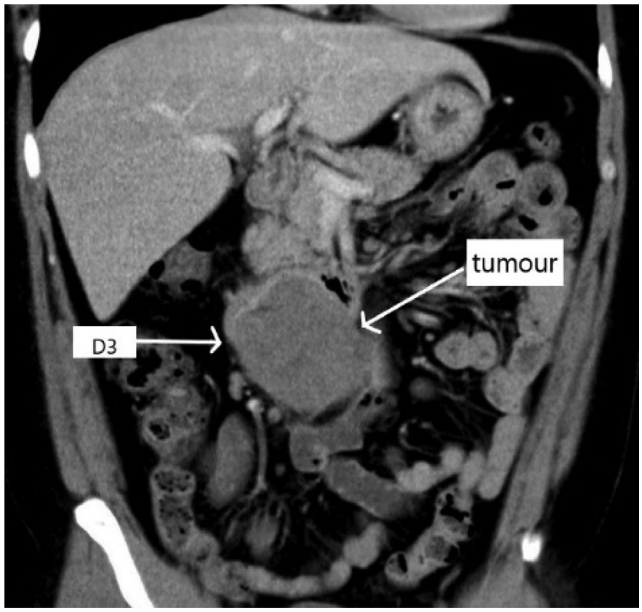

Figure 1 Retroperitoneal soft tissue mass abutting D3.

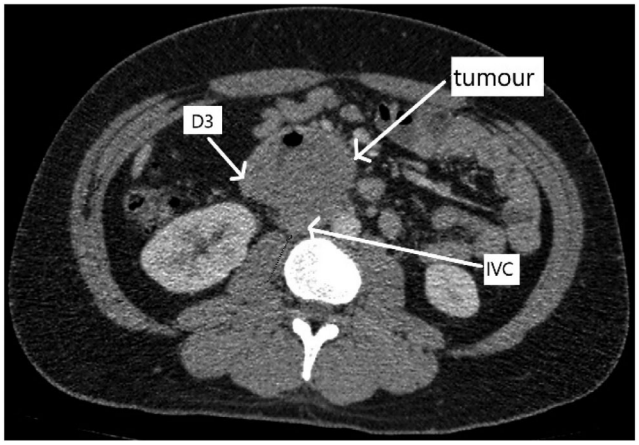

Figure 2 Retroperitoneal soft tissue mass encasing inferior vena cava and abutting D3.

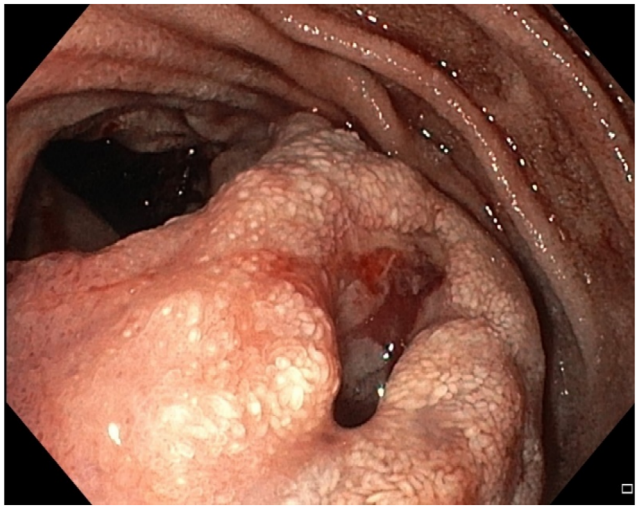

Figure 3 Ulcerated nodular lesion in D3.

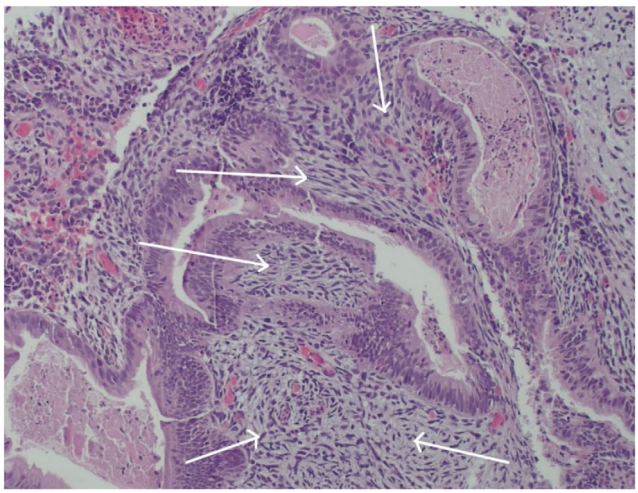

Figure 4 Histology of the biopsy showing immature glands and stroma, white arrows indicate spindle shaped cells. H&E stain, ×100.

our surgeon and oncologist, it was concluded that surgery was not possible at this stage and the only treatment that we could offer was chemotherapy, which would be identical to those with gonadal GCT. However, owing to financial constraints, the patient had requested to be transferred to an oncology unit at a public institution for further treatment.

Discussion

Retroperitoneal tumors often present a challenging situation to clinicians, as they are not easily accessible for tissue diagnosis. However, advances in imaging modalities such as US and CT imaging have made fine-needle aspiration biopsies possible and safe to be performed, obviating the need for more costly and invasive tests such as excision biopsy or surgery. In experienced hands with sufficient tissue sampling, an accurate diagnosis can be reached in most cases.

The diagnosis of retroperitoneal EGCT is often challenging, as a wide range of differential diagnoses exist for any patient presenting with a solid retroperitoneal mass on imaging, with a majority of them being malignant in nature. These include lymphoma, liposarcoma, malignant fibrous histiocytoma, leiomyosarcoma, neurogenic tumors, GCTs, and metastasis from adjacent structures. Hence, an accurate tissue diagnosis is imperative to ensure that prompt and correct treatment is instituted, as this may impact treatment outcome and survival.

Our patient had undergone an FNAC at another hospital with a provisional diagnosis of malignant lymphoma. Upon reviewing the existing results, we felt that the amount of tissue obtained was

insufficient to make a definitive diagnosis of malignant lymphoma with further subtyping, which is crucial in determining the appropriate chemotherapy regimen. Hence, we decided to repeat the biopsy endoluminally using a gastroduodenoscope, given the CT scan findings. The diagnosis of EGCT present in the gastrointestinal tract is not straightforward and requires a high index of suspicion because of the heterogeneity of these groups of tumors mimicking other diagnosis, often resulting in delay in diagnosis.[1]

During the first gastroduodenoscopy, a nodular lesion was seen at D3 with predominantly normal-looking mucosa except a small area of central ulceration. Several differential diagnoses were considered, which included adenocarcinoma of the duodenum, ampullary tumor, gastrointestinal stromal tumor (GIST), neuroendocrine tumor (NET), and external compression from adjacent structures (lymphoma, renal cell carcinoma, pancreatic mass, etc). Ampullary tumor was quickly excluded following direct visualization of an intact papilla.

The first biopsies were performed using a standard biopsy forceps with an opening width of 6.7 mm. Although samples were taken from both the ulcerated and non-ulcerated areas, no malignant cells were detected. During the second biopsy, samples were taken mainly from the same spot in the ulcerated areas, with abnormal cells confirmed by immediate frozen section examinations. In hindsight, biopsies using a larger-sized forceps (such as the 9-mm "Alligator" type) could have increased the chances of a positive yield during the first biopsies and fewer samplings would have been necessary during the second biopsies. The other alternative for endoluminal tissue sampling in this scenario would be an EUS-guided trans-duodenal biopsy; however, this would be considerably more invasive and costly to perform. If endoluminal biopsies failed to provide a positive yield, a percutaneous biopsy would then be necessary.

GCTs are a heterogenous groups of tumors usually arising from the gonads (ovaries and testicles) but rarely outside the gonads. EGCT is an uncommon entity without evidence of a gonadal primary, accounting for 1–5% of all GCTs.[2] Its overall incidence ranges from 1.8 to 3.4 per million, with a higher male preponderance.[3] In adult males, EGCT is sometimes considered debatable, as some authors believe that they represent metastasis originating in the testis in the form of a "burnt out" testicular tumor or a hitherto-undiagnosed testicular primary.[4,5]

Nevertheless, clinical data on this group of tumors show that they are distinct and behave in many different ways compared to their gonadal counterparts.[6] This includes lower survival rates in EGCTs than in primary gonadal GCTs due to the metastatic nature of this disease. The pathogenesis of these tumors remains intriguing and poorly understood. The commonest theory is an aberration in their migration pathway during embryogenesis,[7] although many authors believe that a significant number of them can be traced back to a gonadal primary.[4,5] In adults, EGCT can occur in almost any structure along the midline of the body from the cranium to the coccyx, with mediastinum, retroperitoneum, and brain[3,8,9] being the most commonly affected anatomical locations.

We believe that our patient has EGCT, as both physical examination and imaging of the testicles from abdominal and pelvis CT scan did not show any abnormality. After discussions with our surgeon and oncologist, his condition was deemed to be unsuitable for surgical resection (due to adjacent tissue invasion) and thus chemotherapy was advised. The current consensus for chemotherapy recommends four cycles of bleomycin, etoposide, and cisplatin (BEP). For patients with residual tumor after the initial chemotherapy, salvage chemotherapy with or without surgery may be required. The use of cisplatin-based chemotherapy since the mid-1970s has dramatically improved the prognosis for EGCT.[10]

For patients with non-seminomatous EGCTs similar to our patient, existing data from a multicenter study indicated a 62% 5-year overall survival rate and 45% disease progression-free survival rate following chemotherapy.[10] Nevertheless, in our patient, the adult onset, unfavorable clinical (tumor invasion into duodenum and IVC involvement) and pathological (high mitotic activity, immature cell components) staging, and increased serum β-hCG levels have been recognized as independent prognostic factors for shorter survival.[10]

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