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Retroperitoneal mass revealed to be metastatic lymph node of unknown primary origin

Cancer of unknown origin

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ABSTRACT

Cancer of unknown primary origin is a rare form of metastatic solid tumour representing less than 2% of malignancies. These patients tend to have an unfavourable prognosis, with long-term survivors scarcely reported in the literature. Here we present a rare case of a 56- year-old female with eight year survival, after surgical resection of a metastatic retroperitoneal lymph node, despite relapse of her tumour and no adjuvant treatment. We hope that this case report will aid in increasing awareness and understanding of this often overlooked entity.

Key Words: *Cancer of unknown primary; cancer of unknown origin; CUP, retroperitoneal mass; case report*

CASE REPORT

A 56-year-old female was referred to the surgical outpatient service due to an intraabdominal mass noted as an incidental finding in an abdominal computed tomography (CT). The patient was asymptomatic and had a normal physical examination at the time of referral apart from some vague abdominal pain. She had a past medical history of Hashimoto's thyroiditis, two unsuccessful in vitro fertilisation procedures and reported a family history of urinary bladder carcinoma on her father's side.

Her abdominal CT scan and magnetic resonance imaging (MRI) depicted a 6-cm, well-circumscribed solid mass, with heterogeneous enhancement. The mass was located in the retroperitoneum between the head of the pancreas and the great vessels and displaced the inferior vena cava and the third part of duodenum. Differential diagnosis included gastrointestinal stromal tumour (GIST), neurogenic tumour, other tumour of mesenchymal origin or metastatic lymph node (Figure 1).

Since a metastatic lymph node was suspected, a complete workup was scheduled to identify the primary tumour including tumour markers, endoscopy of the upper and lower gastrointestinal tract, chest CT, mammography, cervical smear, transvaginal ultrasound and head MRI without any remarkable findings. In order to establish a conclusive diagnosis, a CT-guided biopsy of the lesion was performed. The results of the histopathological examination showed poorly differentiated adenocarcinoma of unknown origin.

Subsequently, the patient was hospitalised to undergo surgical resection (Performance Status 0). During surgical exploration, two well-circumscribed scleroelastic lesions were identified in the retroperitoneum in close proximity to the great vessels, the right ureter and the lower pole of

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ABBREVIATIONS: *CA-125: cancer antigen 125, CT: computed tomography, CUP: cancer of unknown primary, GIST: gastrointestinal stromal tumor, LDH: lactic dehydrogenase, MRI: magnetic resonance imaging*

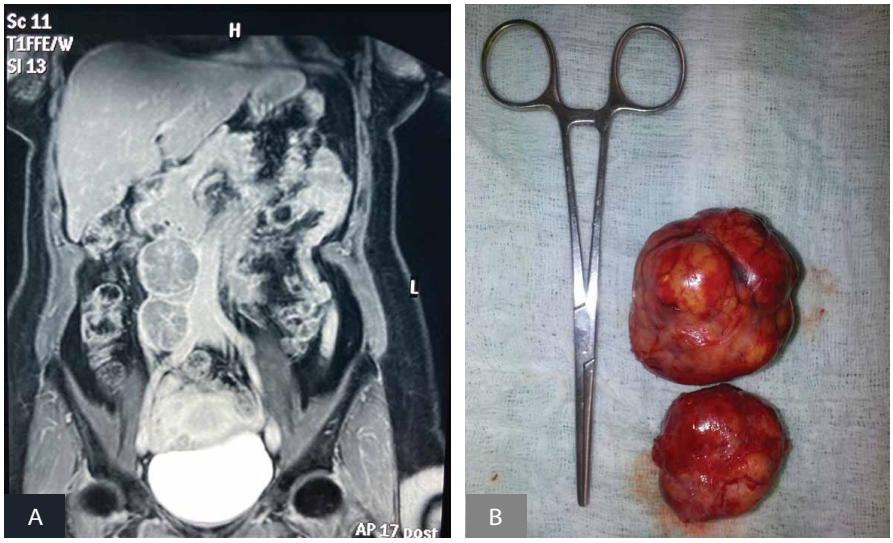

FIGURE 1. (A) Preoperative abdominal MRI depicting a bilobular well circumscribed mass with heterogeneous enhancement in close relation to the great vessels. (B) Surgical specimen after resection. A Kocher forceps is shown, for size reference.

the right kidney, which were resected en bloc. Her postoperative course was uneventful and she was discharged from the hospital on the 7th postoperative day. Histopathological examination reported a metastatic lymph node due to poorly differentiated carcinoma of possible primary pancreatic, breast or ovarian origin. However, as mentioned above, no primary tumour was discovered in these or any other possible location.

The patient denied any further treatment. Two months after surgery, the MRI showed residual tissue at the resection site with a largest diameter of 1,5cm. Her annual follow-up with MRI and blood workup showed no evidence of recurrence. Four years after surgery, cancer antigen 125 (CA-125) level increased to 580 U/ml in parallel with an increase in the diameter of the residual lymphatic tissue to 2.7cm and the appearance of a second enlarged lymph node near the right common iliac artery. The lymph nodes were hypermetabolic in positron emission computed tomography (PET-CT) scanning, while no other lesions were identified. The following years a gradual increase in the CA-125 level and in the diameter of the residual lymphatic tissue was noticed, being 1930 U/ml and 6cm respectively, at her eight year follow up (Figure 2).

Remarkably, the patient continues to remain asymptomatic even though she has denied conservative treatment or surgical resection over these years.

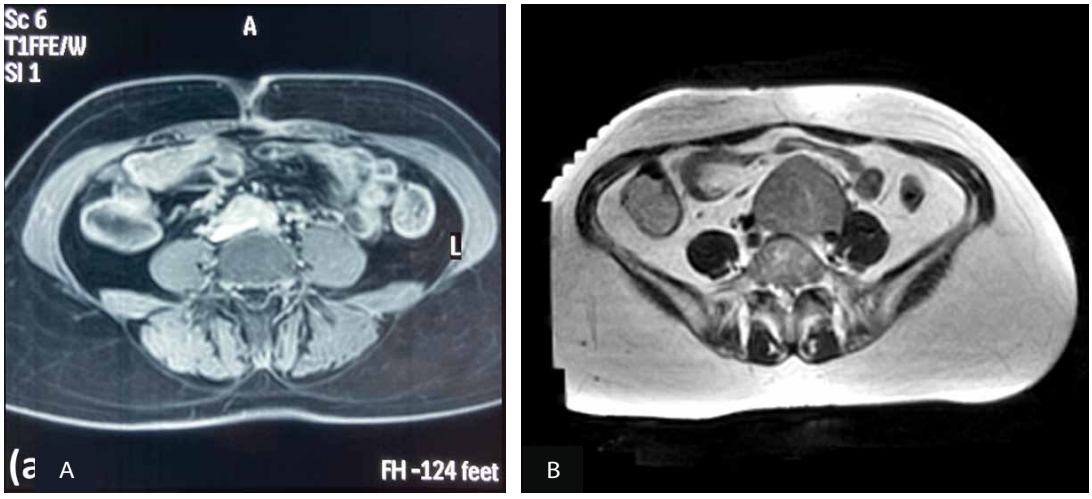

FIGURE 2. (A) Abdominal MRI two months postoperatively, showing residual tissue near the aortic bifurcation. (B) At her last follow-up, abdominal MRI indicates relapse of her tumour.

DISCUSSION

Cancer of unknown primary (CUP) is defined as a metastatic solid tumour, in the absence of a primary cancer after complete diagnostic work up of the patient. [1] This definition excludes patients with a metastatic tumor as the first manifestation, for which the primary tumor was eventually revealed in the diagnostic process. The incidence of CUP has decreased in the course of time, as diagnostic tools have emerged to assist in identifying the primary site, and is currently estimated to be less than 2%. [2] Nevertheless, there is a percentage of patients for whom the primary remains elusive even at autopsy.

Four main histological subtypes of CUP have been described. These include adenocarcinoma (50%), undifferentiated carcinoma (30%), squamous-cell carcinoma (15%) and undifferentiated neoplasms (5%), which are then further subcategorised, after thorough investigation with immunohistochemistry markers [3]. If the origin cannot be identified, genetic assays have recently been used to guide therapeutic decisions [4]. In this case, even after a thorough immunohistochemistry investigation by two independent pathology laboratories and complete diagnostic work up, no primary was identified. She therefore fulfills the criteria for the diagnosis of CUP, specifically CUP of midline distribution.

There is no consensus regarding treatment of CUP according to the published literature. For the majority of patients with CUP that don't belong to a specific subgroup, morbidity and quality of life play an important role in decision-making. Patients with midline distribution CUP show better response rates, as well as better outcomes after platinum-based chemotherapy [5]. Therefore, the appropriate management for this case should include resection with clear margins and adjuvant chemotherapy with a platinum based agent - she was treated by surgical resection, however she refused to receive any adjuvant treatment.

CUP phenotypes with a more favorable prognosis, include women with adenocarcinoma of the axillary lymph nodes, squamous carcinoma involving cervical lymph nodes, CUP with neuroendocrine features, CUP of a single location, men with midline CUP and women with peritoneal papillary serous carcinoma [1].

Several prognostic systems have been developed to predict the survival of CUP patents, irrespective of the specific subtype, including Culine's prognostic score [6], which is the most widely accepted, validated model based on Performance Status and lactate dehydrogenase (LDH) levels (predicted median survival 11,7 months in the favorable prognosis group). Pentheroudakis et al (2010) [5] suggested low tumour bulk, patient fitness, female gender, carcinomatous histology, and absence of visceral metastases as positive predictive markers specifically in CUP of midline distribution, with survival barely touching the one-year mark.

At her six-year follow-up, despite no adjuvant therapy and a relapse of her tumour, our patient is still asymptomatic and in impeccable general condition. Although the favourable outcome is in line with the lack of adverse prognostic indicators (poor Performance Status, liver metastasis, elevated LDH) discussed above, it still surpasses even the most optimistic prognostications.

Even though there have been scarce reports of long-term survivors in the literature [7], this is the only reported case of CUP, to our knowledge, with a long-term survival despite relapse that received no systemic treatment. This case therefore questions our current understanding of CUP, including the overall benefit of adjuvant chemotherapy in prolonging survival and raises the question of the necessity of surgical resection in the first place.

Ethical standards declaration: *This work complies with the current Greek law requirements. No ethics committee approval was required for the case described in this manuscript.*

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