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CASE REPORT

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Granulocytic sarcoma: An uncommon cause of systemic inflammatory response syndrome

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Key Clinical Message

Granulocytic sarcoma rarely arises from adrenal glands. Its necrosis can lead to systemic inflammatory response syndrome (SIRS), causing clinical difficulty in diagnosis without imaging and both biochemical and histological analysis. Compressive effects of the tumor may mask its source, and therefore, prompt resuscitation, symptom control, and investigation are vital in preventing clinical deterioration.

KEYWORDS

abdominal mass, granulocytic sarcoma, myeloproliferative disorders, surgery, systemic inflammatory response syndrome

1 | INTRODUCTION

Granulocytic sarcoma (GS) is a neoplasm consisting of myeloid precursors in an extramedullary site. It is generally associated with myeloproliferative disorders especially with myeloid neoplasias. It may present in association with acute myeloid leukemia, myelodysplastic syndrome, and chronic myelogenous leukemia.[1] With the presentation of this rare case, we review relevant literature and discuss the importance of early diagnosis and management of GS.

2 | PATIENT DETAILS

We report a rare case of a 73-year-old woman presenting with a 2-month history of progressively worsening abdominal distension, epigastric pain, and early satiety. Her epigastric pain reached nine out of ten in severity, radiated to her back, was exacerbated by eating, and partially relieved by lying still. In addition, she had felt feverish over the last week and her general practitioner had recently prescribed a course of trimethoprim 1 week prior to hospital admission for a suspected urinary tract infection. No per rectal bleeding, hematemesis, or weight loss had been reported, and her bowels had been opening normally. She had a past medical history of hypertension, gout, and recurrent cystitis. She occasionally consumed alcohol drinking approximately 6 units per week and was a nonsmoker. She has no family history of gastrointestinal malignancy.

On general physical examination, she was apyrexial, tachycardic at 104 bpm, and otherwise hemodynamically normal. On abdominal examination, there was a large 10×15 cm mass occupying the entire left side of her abdomen extending into the umbilical and epigastric region. There was mild tenderness over the mass. On day 3 of admission, her tachycardia persisted and she developed a temperature of 38.5° demonstrating systemic inflammatory response syndrome (SIRS).

3 | INVESTIGATIONS

Blood tests revealed raised inflammatory markers with white cell count of 30.8 (10^9/L) and a C-reactive protein of 366 (mg/L), hemoglobin was 107 (g/L), platelets 234 (10^9/L), bilirubin 14 (umol/L), alkaline phosphatase 380 (U/L), alanine

Declaration: I declare the information stated in this article is accurate to the best of my knowledge.

transaminase 71 (iu/L), and amylase 42 (U/L). She had mildly impaired renal function with an estimated glomerular filtration rate of 52 (mL/min/1.73 m^2). Serial blood and urine cultures were negative, and chest x-ray showed no evidence of consolidation. Initial differential diagnosis included possible left renal or adrenal mass, splenic flexure mass, pancreatic mass, or a phaeochromocytoma. A computed tomography (CT) scan of the abdomen showed a large cystic lesion predominantly occupying the left upper and central abdomen. It was suggested that the tumor was most likely arising from either the pancreas or the left adrenal gland and low-grade malignancy should be within the differential diagnosis (Figure 1). Suspecting abdominal sepsis on admission and given the patient's chemical and clinical evidence of SIRS, the broad-spectrum antibiotics co-amoxiclav and metronidazole were commenced but were eventually stopped on day 7 as no source of sepsis had been identified. In view of the history of hypertension, 24-hour urine collection for catecholamines was performed to exclude phaeochromocytoma proving negative. Following multidisciplinary team discussion, it was decided to operate to excise the mass for further analysis.

4 | OPERATIVE DETAILS

At laparotomy, there was a giant cystic tumor occupying the entire abdominal cavity. The cystic tumor displaced the stomach, spleen, and pancreas upwards and left kidney and transverse colon downwards. The tumor was found to arise from the left adrenal gland. It was dissected from the pancreas, stomach, spleen, left kidney, and colon (Figure 2). Toward the end of the operation, the cyst ruptured with a small leakage of blood-stained fluid. The mass was sent for histological analysis. The abdomen was closed after insertion of a size 20 Robinson's drain. The cystic lesion weighed 3 kg. She made a good recovery postoperatively without complications and discharged on day 9.

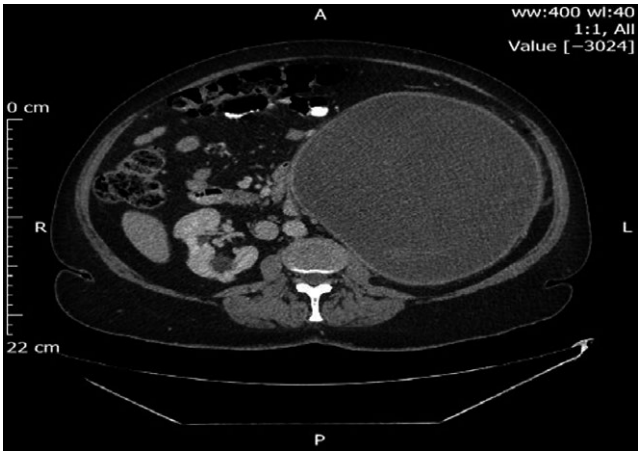

FIGURE 1 Computed tomography (CT) abdomen revealing large cystic mass (17 cm × 16 cm × 17 cm) in the left side of the abdominal cavity with calcification within the wall

5 | HISTOLOGY

Histology revealed features of an extensively necrotic adrenal neoplasm (Figure 3). The specimen included adrenal cortex containing three layers of cortical cells, deep to which there was a band of fibrous tissue intimately associated with an infarcted and necrotic cellular mass centered within the adrenal medulla. The mass was composed of dense sheets of small, immature-appearing, mononuclear cells with occasional blasts, intermixed with cells containing multilobated nuclei. There was no evidence of adipose tissue or other tissue elements within the necrotic debris nor was there evidence of tumor infiltration into, or beyond, the adrenal cortex. Definite lymphovascular and perineural infiltrations were not identified. The neoplastic cells showed positive staining with myeloperoxidase, CD45, and lysozyme, but there was no staining with broad-spectrum cytokeratins, markers of melanocytic differentiation, or neuroendocrine markers.

In summary, the histological features are those of an extensively necrotic adrenal neoplasm. The main histological

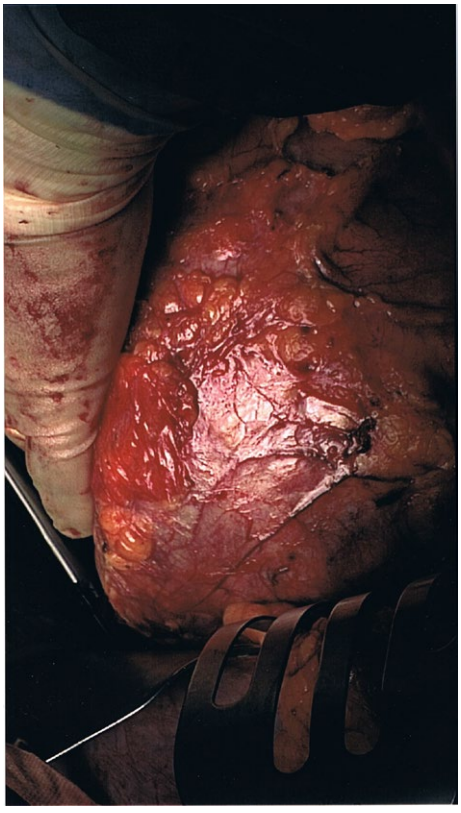

FIGURE 2 Operative resection of large cystic lesion found to arise from the left adrenal gland

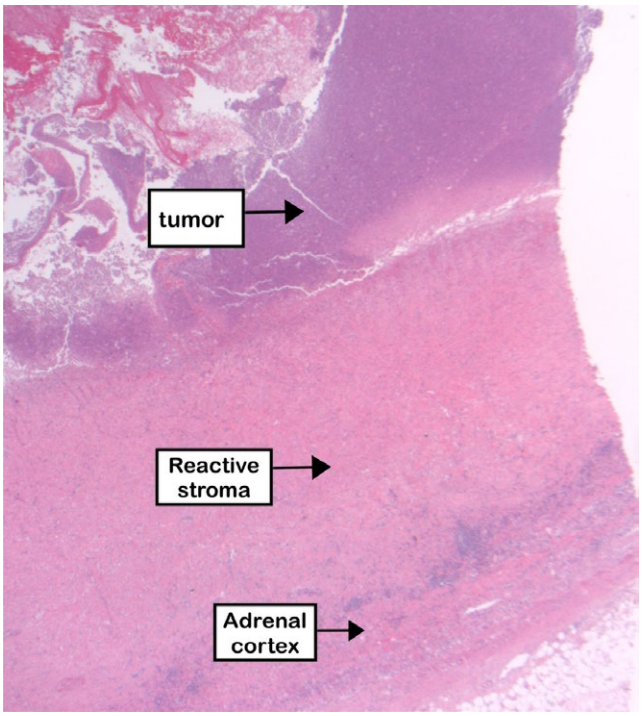

FIGURE 3 Hematoxylin and eosin stained slides, ×12.5 magnification showing adrenal cortex with extensively necrotic tumor filling and distending the adrenal medulla

differential diagnosis lies between a myelolipoma and a myeloid malignancy (granulocytic sarcoma/acute myeloid leukemia). The presence of dense sheets of myeloid cells in the absence of other bone marrow cell lineages and adipose tissue argues against a myelolipoma.

6 | FOLLOW-UP

The patient was referred to the hematology team who performed a bone marrow biopsy finding blast cells in the bone marrow confirming the diagnosis of acute myeloid leukemia; thus, she was commenced on low-dose cytarabine (LDAC) 3 months postoperatively. At hematology clinic 5 months postoperatively, the patient had responded well to LDAC with white cell count and neutrophil count reducing to within normal range at 5.3 × 10 tp9/L and 3.1 × 10 tp9/L, respectively. She is now in complete remission 4 years after her initial presentation.

7 | DISCUSSION

Granulocytic sarcoma usually involves the skin, lymph node, bone, soft tissue, and testis, while involvement of the gastrointestinal tract is rare.[2] Gastrointestinal GS usually involves the small intestine presenting with abdominal pain and obstruction and has been managed successfully using both laparoscopic-assisted and open surgical approaches.[2,3] Other rare presentations include GS presenting as a rectal mass[1] and GS causing spinal cord compression.[4] Biliary manifestations GS have been reported on 4 occasions in the literature with extramedullary myeloid tumor (EMMT) of the gallbladder and 2 cases of GS of the pancreas and GS of the porta hepatis causing obstructive jaundice demonstrated on autopsy.[5-7] Other intra-abdominal manifestations include testicular swelling in a 26-year-old man in remission from AML. Surgical exploration revealed a granulocytic sarcoma of the right kidney resulting in a right nephrectomy.[8]

Nigam et al presented a rare case of GS involving multiple sites in an 18-year-old female patient. She presented with abdominal pain and swelling of both legs and breasts with imaging revealing bilateral ovarian masses. Histopathological analysis of ovarian masses, breast lump, and leg tissue confirmed GS at all sites.[9] Gynecological presentations of GS include GS of the cervix as the first clinical manifestation of acute myeloid leukemia.[10,11] Acute AML has also been reported to present with GS as an ovarian mass in a 3-month-old infant.[12]

Granulocytic sarcoma rarely presents as an abdominal mass with only 3 cases reported in the published literature.[13-15] These cases include a young female with a huge abdominal mass due to GS associated with a new diagnosis of chronic myelocytic leukemia (CML)[13] and a 50-year-old woman presenting with a large pelvic mass involving the right uterine adnexa region as a relapse of her CML.[14] A 15-year-old girl presented complaining of abdominal pain and weight loss for 3 months with hepatosplenomegaly and a painless mass under the umbilicus evident on examination. Histopathological diagnosis revealed myelodysplastic syndrome on biopsy of her ovotestis on laparoscopy, and cytogenic analysis demonstrated hermaphroditism.[15] Our case of a 73-year-old lady presenting with epigastric pain and a large upper and central abdominal mass is the fourth published case of a GS arising from the adrenal gland.[16-18] Furthermore, our case was exceptional in that there have been no cases of GS presenting as an abdominal mass with SIRS in the published literature. The most likely explanation of the demonstrated SIRS response was the extensive necrosis of the tumor. There had been some compression of the adrenal gland by the tumor which may have further contributed to the presentation; however, the inflammatory cascade that was initiated by tumor necrosis is likely to have caused the fever, raised WCC and tachycardia, which in themselves fulfills the criteria for SIRS.

The most well-documented iatrogenic cause of GS is extramedullary relapse following bone marrow transplantation (BMT) in patients with myelodysplastic syndrome,

CML, and AML as demonstrated by a large retrospective study of 5824 patients. GS was observed in 26 patients (0.45%) occurring 4-56 months after BMT.[19] Although prognosis of patients with GS is not well documented in the published literature, in this retrospective study, nine of 26 patients (33%) were alive at 15-151 months after the onset of GS.[19]

Etiology of GS is uncertain though one small case-control study suggests that cellular immune deficiency may be an underlying cause.[20] Usually, GS presents concurrently with bone marrow disease, and although it may require additional local therapy in the form of intrathecal chemotherapy or radiation, the same principles of systemic treatment apply. The prognostic impact of GS on concurrent bone marrow disease is unclear.[21]

In patients over 60 years of age with AML, remission rates are <10% despite intensive chemotherapy, and thus, the appropriate treatment for each patient is decided on the basis of a risk-benefit analysis.[22] In patients who are not considered candidates for intensive chemotherapy, such as in this case, low-dose cytarabine is one of the commonly used chemotherapeutic options.[22] The use of hematopoietic stem cell transplantation for those in first remission from GS has not yet been established.[21]

8 | CONCLUSION

General surgeons must retain granulocytic sarcoma as a differential in any patient presenting with epigastric pain, abdominal distension, and an abdominal mass of unknown origin. Prompt imaging and surgical intervention in conjunction with hematological management are essential to ensure optimal patient outcome.

CONFLICT OF INTEREST

None declared.

AUTHORSHIP

NR: is the primary author of the case report. JWB: is the secondary author and assistant in operation during patient admission. PM: involved in the analysis of the specimen with concurrent contribution in the multidisciplinary team as histopathologist. SA: admitted and operated the patient during this hospital admission as consultant surgeon, involved in multidisciplinary team discussions, and help edit the manuscript.

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