CASE REPORT

Ewing sarcoma of the adrenal gland: a rare entity

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SUMMARY

A 63-year-old man was referred to our office with an enlarging left adrenal mass found on work-up for prostate cancer. Imaging performed over the course of 6 months demonstrated an increasing left adrenal mass from 2.8 to 3.6 cm. Functional testing of the adrenal lesion was performed. The adrenal mass was non-functional. Owing to the enlarging size, the patient underwent a laparoscopic left adrenalectomy without complication and was discharged home the following day. Gross pathological evaluation demonstrated a 3.2 cm, well-encapsulated, partially cystic mass. Histological evaluation demonstrated a small round blue cell tumour suspicious of sarcoma. Immunohistochemical testing revealed strong CD99 positivity consistent with Ewing family of tumours. Reverse transcriptase PCR demonstrated the presence of the Ewing sarcoma fusion transcript. The patient is currently enrolled in an ongoing research chemotherapy protocol at our institution using vincristine, doxorubicin, cyclophosphamide, ifosfamide and etoposide.

BACKGROUND

Ewing sarcoma is predominantly a malignancy of children and adolescents thought to arise from cells of neuroectodermal origin.¹ Ewing sarcoma in adults comprises only 5% of all Ewing sarcoma cases, and up to 5% of all cases occur outside of skeletal muscle.²⁻⁴ Primary adrenal Ewing sarcoma has only been reported in six cases with most cases occurring in adolescents and young adults.⁵⁻⁹ Our patient is the oldest reported case of a primary adrenal Ewing sarcoma. Enlarging adrenal masses or functional adrenal masses are typically treated with operative intervention. It is our feeling that this rare phenomenon should remain in the differential diagnosis of all adrenal masses. Laparoscopic adrenalectomy has been shown to be safe and effective for benign adrenal diseases and support is growing for malignant lesions. Multimodal therapy with chemotherapy and surgery is felt to be indicated; however, no published guidelines exist to direct optimal treatment for primary adrenal Ewing sarcoma. Our patient is currently undergoing chemotherapeutic treatment under an investigative protocol to help answer this question.

CASE PRESENTATION

A 63-year-old Caucasian man with a history of coronary artery disease and type 2 diabetes mellitus was referred for evaluation of haematuria and an elevated prostate-specific antigen (PSA). He was

eventually diagnosed with stage I Gleason 7 prostate adenocarcinoma, but during his evaluation he underwent an extensive radiological work-up including a CT scan of the abdomen demonstrating a 2.8 cm left adrenal mass (figure 1). The patient did not exhibit any signs or symptoms of adrenal pathology. No personal history of malignancy was reported. He reported a 10-year history of tobacco use and denied any history of ethanol or illicit substance use. His family history was remarkable for leukaemia in his brother and one child, and colon cancer in one cousin.

INVESTIGATIONS

During evaluation for prostate cancer, he underwent a CT scan of the abdomen demonstrating a 2.8 cm left adrenal mass with delayed contrast washout, peripheral enhancement and Hounsfield unit measurements of 36 during the parenchymal phase and 30 after 10 min (figure 1). Follow-up CT of the abdomen showed an increase in size to 3.1 and 3.6 cm at 3 and 6 months, respectively, after the initial study with unchanged imaging characteristics (figure 2). MRI of the abdomen was also performed, for additional characterisation, and demonstrated the same lesion with intensity similar to splenic parenchyma and increased signal intensity with T2-weighted imaging (figures 3 and 4). Functional adrenal testing was performed with 24-h urinary cortisol, fractionated catecholamines and metanephrine studies, plasma renin activity and aldosterone, plasma DHEA-S and plasma estradiol concentrations. All functional testing were within normal limits.

Figure 1 CT scan of abdomen demonstrating a 2.8 cm left adrenal mass.

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Figure 2 CT scan of the abdomen after 6 months of observation demonstrating interval enlargement in the left adrenal mass to 3.6 cm.

DIFFERENTIAL DIAGNOSIS

Differential diagnoses for adrenal masses include primary disease including cortical adrenal tumours (eg, functional and non-functional tumours), medullary adrenal tumours (eg, neuroblastoma), adrenal cortical carcinoma, metastatic neoplasms (eg, melanoma or small bowel neoplasms), adrenal hyperplasia or infiltrative adrenal disorders (eg, amyloidosis).

TREATMENT

A laparoscopic left adrenalectomy was performed to remove the enlarging, non-functional left adrenal mass. He was subsequently discharged on postoperative day 1 without complication.

OUTCOME AND FOLLOW-UP

Gross pathological evaluation showed a 74 g left adrenal gland containing a 3.2 cm×2 cm×1.2 cm well-circumscribed, partially cystic mass within the parenchyma. Histological evaluation demonstrated a small round blue cell tumour with central areas of necrosis (figure 5). The tumour cells were diffusely positive for pancytokeratin and showed membranous CD99 positivity by immunohistochemistry (figure 6). Reverse transcriptase PCR (RT-PCR) studies were performed for the EWSR1-FLI1 and EWSR1-ERG fusion transcripts. The tumour was positive for the EWSR1-FLI1 fusion transcript, supporting the diagnosis of

Ewing sarcoma. Staging CT scan of the chest performed before initiation of treatment did not demonstrate any metastatic or primary lesion.

Our patient is currently undergoing multimodal therapy with adjuvant chemotherapy consisting of vincristine–doxorubicin–cyclophosphamide/ifosfamide–etoposide (VDC/IE) under an ongoing research protocol at our institution (MCR 19–19–08). There has been no evidence of recurrent disease after 13 months of follow-up and surveillance imaging.

DISCUSSION

To date, only six cases of primary adrenal Ewing sarcoma have been reported in the literature.^{5–9} Our patient adds to the existing literature of primary Ewing sarcoma in the adrenal gland. Most cases occur in the paediatric, adolescent and young adult population. One patient was 57-year-old making this one the oldest reported case. In osseous Ewing sarcoma, only 5% of all cases occur in adults older than 40-year-olds. Five of six patients with adrenal Ewing's sarcoma reported in the literature underwent multimodal therapy with surgery, chemotherapy and/or radiation therapy. One patient refused therapy and died after 6 months. The chemotherapeutic regimen administered was standard for the treatment of osseous Ewing sarcoma. Follow-up data were available for all but one patient. Mean follow-up time after surgery was 7.8 months. One patient has 14 months of follow-up with no documented recurrence. Two patients died after multimodal therapy: one after surgery and chemotherapy, the other after surgery and radiation therapy. One patient had a recurrence 1 month after surgery and is currently undergoing further chemotherapy. This patient is currently undergoing multimodal therapy with adjuvant chemotherapy consisting of VDC/IE under an ongoing research protocol at our institution (Mayo Clinic Rochester MCR protocol 19–19–08). No studies have thus been published evaluating optimal chemoradiotherapy for patients of this age group. Furthermore, no extensive experience has been published regarding multimodal chemotherapy in patients with adrenal Ewing sarcoma given the rarity of the disease. Specifically, our institution has no published experience with treatment of Ewing sarcoma of the adrenal gland. Some studies have demonstrated worse prognosis for adults with Ewing sarcoma compared with their younger counterparts.¹⁰ However, treatment with similar chemotherapeutic regimes has demonstrated similar outcomes in adults and children for skeletal Ewing sarcoma.¹¹

Figure 3 MRI of the abdomen demonstrating high signal intensity on T2-weighted imaging of the left adrenal mass.

Figure 4 MRI of the abdomen demonstrating an indeterminate left adrenal mass on T1-weighted imaging. Signal is isointense with splenic parenchyma.

Figure 5 600× magnification of the adrenal gland specimen demonstrating a small round blue cell tumour.

Guidelines for the workup and management of incidentally found adrenal lesions have been published and our practice is concurrent with these recommendations.¹² Diagnosis of adrenal tumours can, at times, be readily made with CT or MRI. The imaging characteristics to help distinguish benign from malignant adrenal lesions are well established.¹³ No specific imaging characteristics regarding adrenal Ewing sarcoma could be elucidated from CT or MRI performed in this case. [18F]fluorodeoxyglucose positron emission tomography (FDG-PET) has been used for detection, staging and assessment of response to therapy in Ewing sarcoma, principally in paediatric patients. FDG-PET scans combined with conventional CT scans have been shown to be more accurate than just FDG-PET alone for small lesions. However, studies using PET/CT for adrenal Ewing sarcoma have not been published. No FDG-PET scan was performed on this case given the absence of lesions by conventional chest CT and the published efficacy of this modality compared with FDG-PET for pulmonary lesions.¹⁴ Conventional CT scans have been the imaging modality of historical choice; however, some centres are utilising FDG-PET/CT for initial diagnosis, staging and identification of recurrent disease. Identifying specific imaging characteristics for adrenal sarcomas is one of the aims of an ongoing study at our institution.

Historically, adrenal malignancy has been managed with radical open surgical techniques. Our patient underwent a laparoscopic adrenalectomy which is considered safe and effective

for uncomplicated adrenal lesions. In fact, support is growing for laparoscopic adrenalectomy for malignant lesions.¹⁵

Ewing sarcoma of the adrenal gland presents extremely rare and likely is not typically in the differential for an incidentally discovered adrenal lesion. Though Ewing sarcoma of the adrenal has only been documented seven times with our case, it should remain in the differential diagnosis of all adrenal masses. Currently, we are undergoing a retrospective review of all adrenalectomy cases over the last 5 years to identify other adrenal sarcomas and assess treatment modalities that were employed. We believe that a larger cohort study may be able to improve our current diagnostic and therapeutic strategies for patients with adrenal sarcomas. Comprehensive multimodal therapy for adrenal Ewing sarcoma is felt to be indicated, just as with osseous Ewing sarcoma. Long-term data are lacking, however, regarding optimal therapy for adrenal Ewing sarcoma, and further studies are needed.

Learning points

- ▶ Adrenal Ewing sarcoma is a rare entity.
- ▶ Ewing sarcoma should remain in the differential diagnosis of all adrenal masses.
- ▶ Laparoscopic adrenalectomy can be performed safely and effectively for adrenal Ewing sarcoma.
- ▶ Multimodal treatment with chemotherapy and surgery remains the mainstay of therapy for Ewing sarcoma.
- ▶ Further studies are needed to determine optimal chemotherapeutic treatment for select patients with extraskeletal Ewing sarcoma.

Contributors JB is the principal author who conceived the manuscript, collected data, interpreted and analysed the data, and authored the preliminary and final manuscripts. MS provided pathology interpretation of our surgical specimen, provided insight for conception, analysis of data and input with final draft approval. CC contributed to the conception, revisions and final draft of our manuscript. NW participated in the conception of our manuscript, editing and interpretation of data and final draft approval. RS was the surgical consultant who directly was involved in the conception and design of the draft, data collection and interpretation and the final approval of the manuscript.

Competing interests None.

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Figure 6 CD 99 immunostaining demonstrating positivity.

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