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Case report

Retroperitoneal unicentric Castleman's disease—A case report and review of literature

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ABSTRACT

Introduction and importance: Castleman's disease is not so commonly diagnosed worldwide due to non-specific symptoms Clinical findings are variable.

No definite blood investigation or any biomarkers are established to diagnose this disease. Radiological investigations do not play much role in diagnosing. It can be unicentric or multicentric. Etiological factors are not well understood except predilection of this disease towards immune-compromised persons. Surgery is considered as a prime modality to treat, if resectable.

Case presentation: Patient had recurrent abdominal pain in left lumbar region which was intermittent for last 6 months, dull aching with no aggravating and relieving factors. There was no history of abnormal bowel habits, urinary complaints, fever, night sweats, weight loss, rashes in body, joint pains and loss of appetite. On examination, there was a single, firm, non-tender, intra-abdominal, retroperitoneal mass of approximately size 10 * 7 cm in left lumbar region encroaching inferiorly towards left inguinal region. Digital rectal examination (DRE) and external genitalia were normal.

Clinical discussion: All routine blood investigations along with relevant tumour markers were normal. Magnetic Resonance Imaging (MRI) abdomen showed a well-defined mass suggestive of stromal tumour or retroperitoneal sarcoma. Patient underwent surgery in which complete excision of the mass was done. Postoperative event was uneventful and currently doing well.

Conclusion: Take away lesson in this case report is that we should not presume all retroperitoneal mass as cancer or sarcoma, we have to think about other rare causes like Castleman's disease, if clinical picture, blood and radiological investigation are discordant.

1. Introduction

The work has been reported in line with the SCARE 2020 criteria [1].

Castleman's disease is a rare and an incompletely understood entity also known as angiofollicular hyperplasia, lymphoid hamartoma & giant cell nodal hyperplasia. The main reason cited for the development of this disease is inflammatory, autoimmune, viral Infection [Human herpes virus-8(HHV-8), Human immunodeficiency virus (HIV)] and immunocompromised state. This entity was first described by Benjamin Castleman in 1956. He studied this disease in 13 patients who were evaluated for mediastinal pathology [2,3]. Main sites affected by this disease are mediastinum (75%), neck (15%) and abdomen (15%) and rare subsites like mesentery, meninges, muscles and lungs can also be involved [4,5,6].

Histologically this disease can be divided broadly into Hyaline Vascular type (HV), Plasma Cell type (PC) and Mixed type [5,7] and morphologically divided into Unicentric and Multicentric types. Diagnosis is a big dilemma as well as a challenge for a clinician as it can mimic inflammatory as well as malignant pathology. Computed tomography (CT) or Magnetic Resonance Imaging (MRI) helps mainly in road mapping of surgical planning, but unfortunately doesn't help much in making diagnosis of this disease. Surgery is the mainstay of treatment in unicentric Castleman disease (CD), while non-surgical options like chemotherapy, radiotherapy and steroids has a role mainly in multicentric Castleman disease (CD). The final diagnosis is only made after histopathology. Retroperitoneum is a rare localization, where initial imaging diagnosis is unclear and surgical resection is the preferred treatment [8].

We are reporting a case with a diagnostic difficulty as it seems to be retroperitoneal sarcoma or gastro intestinal stromal tumour (GIST) on

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imaging, but turned out to be Castleman's disease on histopathology after surgery.

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

2. Case report

38 year old male, belonging to a developing nation of Asian continent, medical representative by occupation, non-smoker and non-alcoholic with no known co-morbidities. There was no significant medical history and any surgical intervention in past and no contributory family history. He presented to us in a tertiary care hospital on outdoor patient clinic basis. He was evaluated for having recurrent abdominal pain in left lumbar region which was intermittent for last 6 months, dull aching with no aggravating and relieving factors. There was no history of abnormal bowel habits, urinary complaints, fever, night sweats, rashes in body, joint pains, loss of appetite and weight. On examination, he was of average built with body mass index (BMI) of 24.9 kg/m^2 and having performance status as per Eastern cooperative oncology group (ECOG) 1 out of 4. His General physical examination (GPE) was within normal limits. On per abdomen(P/A) examination, there was a single, firm, non-tender, intra-abdominal, retroperitoneal mass of approximately size 10 * 7 cm in left lumbar region encroaching inferiorly towards left inguinal region. Digital rectal examination (DRE) and external genitalia were normal. All blood investigations were normal. Tumour markers i.e. S. CEA (Carcinoembryonic antigen), Lactate Dehydrogenase (LDH), Alpha-fetoprotein (AFP) all were within normal limit. Human immunodeficiency virus (HIV1/2) was non-reactive. Ultrasonography (USG) abdomen showed a hyperechoic mass on left side of the abdomen. Contrast enhanced computed tomography (CECT) abdomen showed well defined enhancing solid mass in left paravertebral location pushing left ureter anteriorly, abutting left psoas muscle and having multiple small calcifications and necrotic foci and having maintained fat planes with surrounding structures. Left kidney, spleen, liver, all were normal. Contrast enhanced computed tomography (CECT) chest was within normal limits.

Magnetic Resonance Imaging (MRI) abdomen showed isointense to hyperintense mass along with calcifications and necrotic foci abutting psoas muscle and causing the displacement of inferior mesenteric artery (IMA) and vein (IMV) (Figs. 1 and 2). Retroperitoneal sarcoma (RPS) and gastro-intestinal stromal tumour (GIST) possibility were kept and patient was planned for surgery. We didn't attempt any invasive intervention like needle aspiration or biopsy preoperatively as it seems a resectable mass and even after getting a tissue diagnosis preoperatively it will not going to change our management. Preoperatively Double-J (DJ) stenting of ureter (7 Fr) was done in order to facilitate identification during surgery. Patient was operated by an experienced surgical oncologist. Open laparotomy with full length midline incision was given and intraoperatively there was no evidence of ascites, liver, peritoneal or omental metastasis. There was a large encapsulated solid, yellowish mass, 12 * 8 cm in size in left retroperitoneal space having maintained fat planes with left ureter and gonadal vessel and both were draped anteriorly over the mass (Fig. 3). The mass was pushing aorta towards right side with maintained fat planes. Mass had a contact of approximately 180° for a length of 3–4 cm along with left external iliac vessel from which the 2–3 feeder vessels were going into the mass which were meticulously separated and feeder vessel were ligated. The whole mass was removed completely with R0 resection without any capsular breach (Fig. 4). Postoperative event was uneventful and patient discharged on day seven (POD-7). An imprint smear of the mass showed lymphoid hyperplasia.

Final histopathology on gross examination showed 12.5 cm * 3.5 cm * 4 cm with outer surface smooth, shiny grey, white and brown. Cut surface was solid with focal tan, brown areas (Fig. 1). On microscopic examination, numerous medium sized inflated follicular centers were evenly distributed throughout the parenchyma. Atretic germinal centers traversed by penetrating vessels. Follicles were surrounded by a mantle zone, which was thickened by lymphocytes arranged in onion skin layering. Inter-follicular area showed hyalinization, follicular dendritic cell proliferation with few scattered plasma cells. All these findings were consistent with a hyalinised vascular type of Castleman disease (angio-follicular hyperplasia).

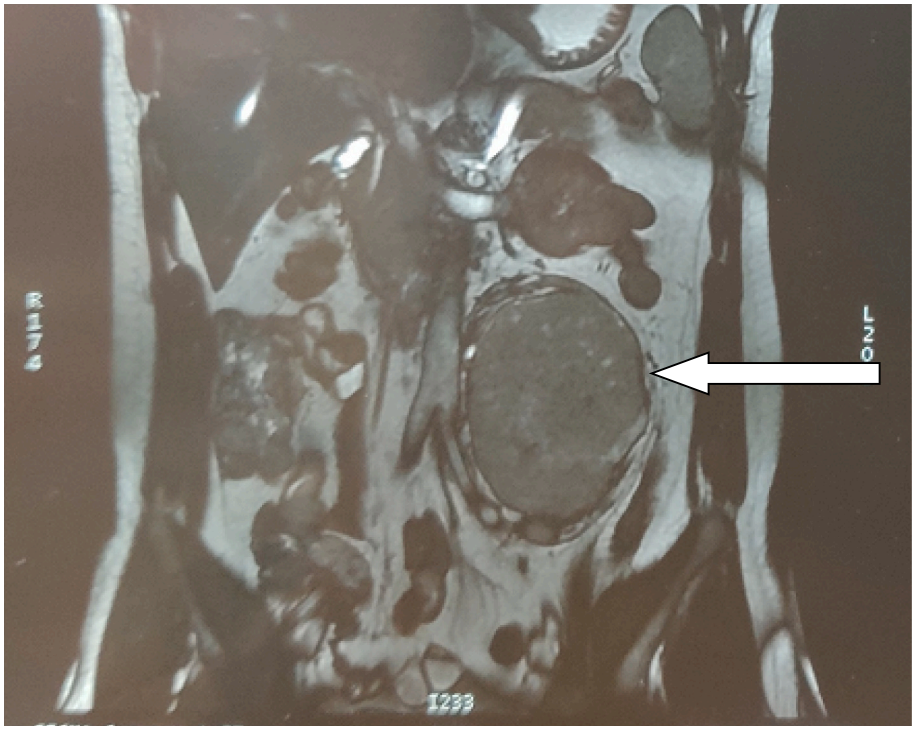

Fig. 1. Magnetic Resonance Imaging (MRI) abdomen showed isointense to hyperintense mass (as pointed by white arrow) closely abutting inferior vena cava (IVC) pushing it medially.

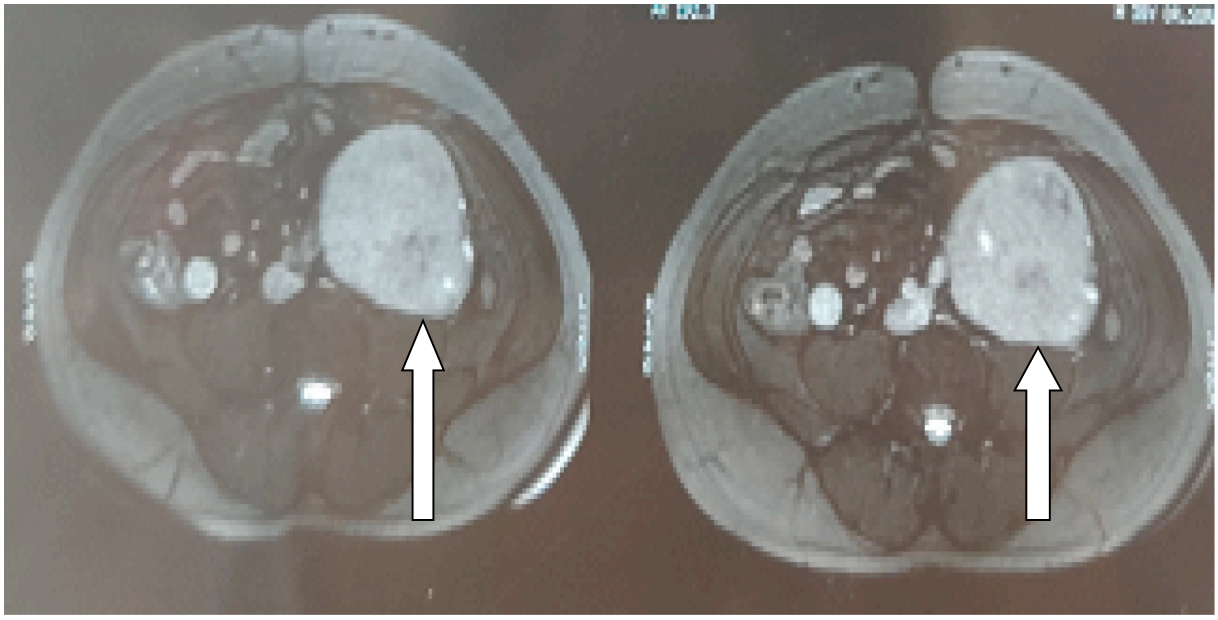

Fig. 2. Showing Magnetic Resonance Imaging (MRI) isointense to hyperintense mass (as shown by white arrow) along with calcifications and necrotic foci abutting psoas muscle and causing the displacement of inferior mesenteric artery (IMA) and vein (IMV).

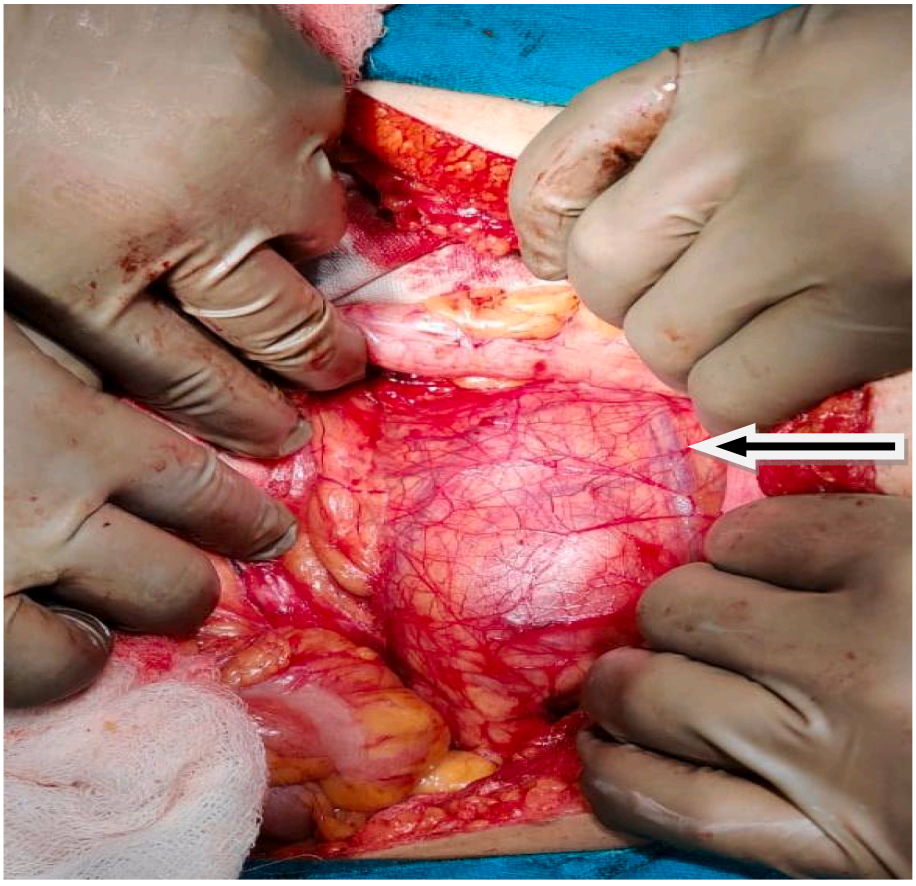

Fig. 3. Intraoperative picture showing left ureter (pointed by black arrow) draped over the retroperitoneal mass.

Discussion in multidisciplinary tumour board was done, no chemotherapy was advised and patient was kept under follow-up 3 monthly for 2 years and 6 monthly for next 3 years, annually thereafter along with annual MRI.

Patient is presently doing well without any evidence of recurrence.

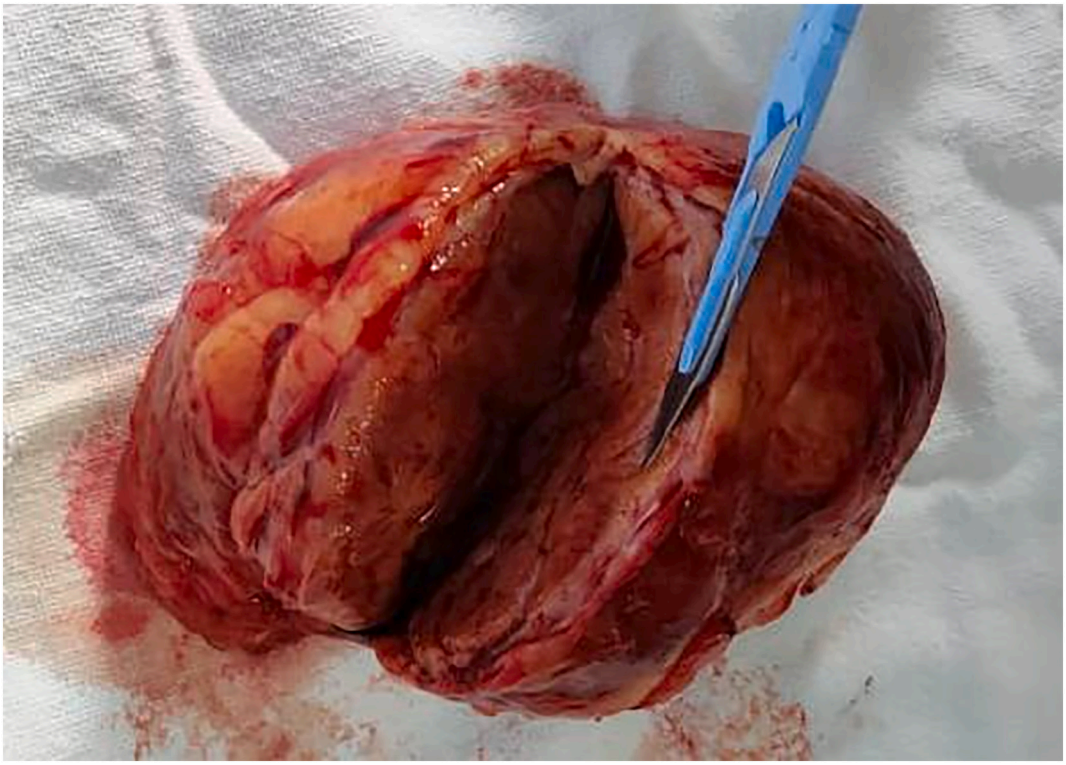

Fig. 4. Whole mass removed en bloc and on cut section showing orange-tan appearance.

3. Discussion

As per literature (pubMed, MeSH) there are 230 cases of retroperitoneal Castleman's disease have been reported before this case worldwide.

Prognosis of the disease is good if R0 resection is achieved (nearly 100%, 5 year survival).

It is a rare disease and having an equal distribution in both males as well as females. The age distribution is not confined to one particular group as it can found in young children to old age person (8–65 years) [5]. The incidence of this disease is not known exactly, but it has more inclination towards Asian population [9].

Location of Castleman disease is not fixed, it can be found anywhere, along the location of the chain of lymphatic pathway depending upon the type of Castleman disease, whether it is unicentric or multicentric type, which can be differentiated by number of lymph nodes sites involved in the body. This classification depends on gross location or appearance of disease. If it is unicentric, it is mainly found in the thorax and mediastinum or chest (65–70%), abdomen (15%) and neck (15%) [4,5]. Another type of classification is histological or microscopic type which is of mainly of four types i.e. plasma cell type, hyaline vascular, HHV-8 (human herpes virus) associated and mixed type. Unicentric Castleman disease (CD) is generally of hyaline vascular type, however multicentric Castleman disease (CD) doesn't have any specific or fixed type variant microscopically [10].

Grossly, both Hyaline vascular type and plasma cell type are rarely distinguishable as both can have well defined yellowish mass which is mostly encapsulated and uniform in appearance [11]. Microscopically, hyaline vascular type consist of prominent proliferation of small vessels which can be in the follicular region as well as in inter-follicular areas along with hyalinization along blood vessels. Presence of onion ring appearance and lollipop appearance in hyaline vascular type is generally a pathological identifiers on microscopical examination. Onion-ring appearance is due to a relative increase in dendritic cells as compared to lymphocytes, which ultimately leads to changes in the medullary portion of lymph nodes leading to its expansion in size.

Lollipop appearance is due to presence of prominent and increase hyalinization of small blood vessels in follicles. Plasma cell type of Castleman disease, microscopically doesn't have any prominent perivascular hyalinization leading to maintenance of the architecture of the lymph node follicular region and increasing the size of germinal centers of lymph nodes as compared to hyaline vascular type, presence of plasma cells are identified around cortical region of nodes [5,10]. Clinical spectrum of Castleman disease is variable, ranging from generalized lymphadenopathy to non-specific complaints. This heterogeneity of clinical features depends mainly on location, whether it is unicentric or multicentric and also on microscopic appearance i.e. Hyaline vascular or plasma cell type [12]. Unicentric type and hyaline vascular type of Castleman disease confined to the abdominal or retroperitoneal are mostly asymptomatic [13,14] clinical features are not per se due to Castleman disease, but mainly because of mass effect on adjacent organs. If it is present in the abdomen, there can be presence of pain, vomiting, obstructive features due to gut involvement or ureters leading to obstructive uropathy. Similarly, if present in the thorax or mediastinum, there can be breathing difficulty, chronic obstructive pulmonary disease (COPD) or pleural or pericardial effusion or hilar lymphadenopathy [15].

Multicentric and plasma cell types are generally having non-specific symptoms i.e. Fever, anaemia, weight loss, joint pains, rashes, etc. which are mainly attributed to role of inflammatory mediator mainly IL-6 in plasma cell types [16]. As a result of the role of interleukins (IL-6), there is advocacy about the role of steroids, immunosuppressant in its treatment [17]. Recurrence or relapse of plasma cell type is also attributed to the role of interleukins.

As in our patient, he was not having any specific symptoms except of only lower abdominal discomfort only.

Preoperative diagnosis of Castleman disease is very difficult as it can mimic many other diseases and there are no diagnostic clinical features and laboratory tests, tumour or bio-markers which can specifically indicate towards this disease. Radiological imaging ultrasound, contrast

enhanced Computed Tomography (CECT), contrast enhanced Magnetic Resonance Imaging (CE-MRI) or Positron Emission Tomography (PET-CT) do not show any specific diagnostic features apart from hypervascularity of mass suggesting unicentric Castleman's disease [18], homogeneous enhancement and presence of calcification occasionally and a feeder vessel presence [19]. Soft-tissue sarcomas account for 80% of retroperitoneal cancers. The most common is liposarcoma, followed by leiomyosarcoma and malignant fibrous histiocytoma [20]. But of course these imaging guide radiologist to keep possibility of this entity as a differential diagnosis among Gastrointestinal stromal tumour (GIST), Sarcoma, lymphoma, tuberculosis etc. Radiological imaging helps in guided tissue fine needle aspiration biopsy (FNAB) and helps in surgical planning, if required.

Similarly, in our case there was no hypervascularity of mass and the most probable diagnosis was GIST (gastrointestinal stromal tumour).

Role of tissue diagnosis preoperatively definitely helps in diagnosing, but it is not routinely practiced in view of high false negative rate associated with FNAB (Fine needle aspiration biopsy) and hypervascular nature of mass [21,22]. The risk of implantation metastases induced by fine-needle biopsy warrants consideration in patients with abdominal malignancies since it may compromise the outcome of radical surgery. It should only be performed when the result of the procedure has a direct impact on the choice of therapy [23].

En bloc surgical resection whether open or laparoscopically (depending upon the infrastructure or armamentarium) is the treatment of choice for unicentric Castleman disease. Achieving R0 resection margin translates into 100%, 5 year survival rate and 95% 10 year survival [21,24]. Unicentric disease had a significantly higher overall survival (95.3% vs 61.1%), 3 year DFS (89.7% vs 55.6%), and 5 year DFS (81.2% vs 34.4%) than multicentric disease [21]. Recurrence rates are high in cases where margin free resection is not achieved. Role of radiotherapy in adjuvant as well neoadjuvant settings is not clear cut established, but their role has been mentioned in the literature [25,26].

Multicentric Castleman disease can be treated by using single agent or combination chemotherapy agents R-CHOP based (rituximab, cyclophosphamide, doxorubicin, vincristine, and Prednisolone) [27] and by anti-interleukin 6 therapy [28].

4. Conclusion

Castleman disease is a real diagnostic challenge to all, for a clinician, radiologist or pathologist. As this disease comprises of a wide range of signs and symptoms and no leading signs on radiological imaging, all these features attribute to its difficulty in diagnosing. No specific blood investigations are currently present to help in diagnosing this disease. A tissue diagnosis is a good viable option whenever it is going to change the management of disease or suspecting medically treatable causes like lymphoma or tuberculosis. Hyaline vascular type is more common than plasma cell type and keeps a good prognosis as compared to plasma cell type. Surgery is the mainstay of treatment with less chance of recurrence if margin free surgery is performed. The role of other modalities like radiotherapy, steroids, immunosuppressant is yet to define and to be implemented from case to case basis after discussion in multidisciplinary tumour board.

Ethical approval

This case report was not necessary to obtain ethical approval.

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CRediT authorship contribution statement

Rashpal Singh-drafted the case report and the main operating surgeon

Rizul Prasher, Shivek Mohan and Bharat Thakur - assisted in searching literature and all were part of the surgical team.

Guarantor

Dr. Rashpal Singh, Assistant Professor, Surgical Oncology, Shimla, HP, India.
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Research registration
Not applicable

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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Not commissioned, externally peer-reviewed.

Declaration of competing interest

The authors have no conflicts of interest to declare.

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