



Case report

An extremely scarce incidence of primary Undifferentiated Pleomorphic Sarcoma of the Scalp of a 52-year-old female - A Case Report

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ABSTRACT

Introduction and importance: Sarcomas are malignant mesenchymal-cell tumors that comprise 1 % of all adult tumors. Undifferentiated Pleomorphic Sarcoma comprises a vastly rare subtype. It mostly occurs in males in their 6th decade of life. However, their exact incidence remains poorly demarcated, especially those occurring in the scalp. Since they lack any disease-specific presentations, we should maintain high clinical suspicion when presented with similar cases.

Case presentation: Herein, we demonstrate the clinical case of a 52-year-old Middle Eastern female, who presented to the outpatient clinic complaining of a one-year history of progressively growing protuberance in her right side of the scalp. It was painful and rapidly increased in size. Presurgical radiological assessment suspected a cystic formation. Utter resection of the mass was achieved, and histopathological analysis diagnosed it as a primary Undifferentiated Pleomorphic Sarcoma.

Clinical discussion: Meticulous surgical resection was the cornerstone treatment of our patient. Radiological imaging in addition to clinical suspicion was utilized for preoperative assessment. This patient has had a successful post-surgical recovery. She has been surveilled for 6 months so far with no evidence of tumor recurrence, metastasis, or clinical complications.

Conclusion: It is especially rare to see a primary Undifferentiated Pleomorphic Sarcoma in any patient population. It's even rarer that it occurs in such a patient demographic. Hence, it's vital that we document cases of this rare malignancy because that would lead the way in conducting informative clinical studies which enable physicians to select the proper treatment modality.

1. Introduction

Sarcomas are profoundly malignant tumors that have the capability to originate from any site within the body location and their annual global incidence ranges between 1.8 and 5 affected patients per 100,000 individuals. Most of the reported cases are of patients aging above 55 years of age [1]. Of all the neoplasia which affect the adult population groups, Sarcomas constitute almost 1 % of all those tumors [2,3].

With regards to the sites of tumor origin, almost 80 % of sarcomas arise from soft tissues, while the remaining 20 % originate from different bones and cartilage [4].

The most vulnerable age group is the adult population group, in which 80 % of sarcomas occur in such individuals [5].

From a pathophysiology standpoint, sarcomas are considered malignancies of mesenchymal tissue origin, and they include a wide variety of tumor subtypes with distinct histologic differences [6].

Abbreviations: BMI, Body Mass Index; IV, Intravenous; MRI, Magnetic Resonance Imaging; H&E, Hematoxylin and Eosin; IHC, Immunohistochemistry; CT, Computed Tomography; STS, Soft-Tissue Sarcomas; UPS, Undifferentiated Pleomorphic Sarcoma.

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The work has been reported in line with the SCARE criteria and the revised 2020 SCARE guidelines [7].

2. Presentation of case

2.1. Patient information

We present the case of a 52-year-old Middle Eastern female who is a known case of controlled Hypothyroidism for 5 years. She presented to the General Surgery clinic at our university hospital with the chief complaint of a chronic painful bulging underneath her scalp surface. Symptoms started as a gradually growing mass underneath the left parietal side of her scalp 1 year prior to her hospital admission. The bulge was incidentally felt by the patient. It was hard, moving upon touch, and started eliciting pain which later became unbearable. The pain was localized to the site of the bulge, stabbing in nature, intermittent, was estimated to measure 06/10 on the pain scale according to the patient, and was vastly relieved by over-the-counter analgesic medications.

The patient ignored those symptoms for most of the previous year and that is why she did not report them to any physician until those symptoms increased in that the bulge began increasing rapidly in size and the pain has become unresponsive to analgesics and estimated to be 08/10 on the patient's pain scale.

The patient denied any visible changes in the skin that overlies the protuberance. Changes inquired about included hair loss, hotness, redness, skin ulceration, or hypo-/hyperpigmentation.

The patient also denied experiencing any headaches, blurry vision, photosensitivity, hearing deficits, drooling, changes in appetite, general fatigue, night sweats, or fever. She also denied the presence of genitourinary symptoms or discrepancies in her bowel habits.

The patient's surgical history solely consisted of an open appendectomy performed 14 years ago.

Her drug history only included Levothyroxine 100 µg for her Hypothyroidism situation.

Lastly, her family, allergic, and psychosocial histories were negative.

We inquired about any exposure to radio-/chemotherapy, but the patient denied their presence. Her Body Mass Index (BMI) was 23 kg/m².

3. Clinical findings

Our physical examination commenced by taking the patient's vital signs. The results of which were normal. Inspection of the scalp took place, and we marked a visible vivid bulging underneath the patient's left posterior parietal lobe. No visible overlying scalp skin changes were elicited. Inspection of the remaining scalp skin was unremarkable. Upon palpation, a mass with ill-demarcated borders was felt. It was tender, rubbery, and mobile. Furthermore, there weren't any palpable regional lymph nodes. A complete laboratory panel was done, and yielded results were all normal.

3.1. Diagnostic assessment

We began our radiological assessment by performing an ultrasound. The results revealed a hypoechoic thin-walled cystic formation measuring approximately (3.2 × 3.5 cm). The contents of which were clear. The borders could not be accurately demarcated. However, the lesion appeared to be unattached to the underlying parietal bone. No calcifications, abnormal vascularization, or regional lymphadenopathy were seen.

Based on the previous findings, common lesions, and what could be appropriate to consider as a differential diagnosis, multiple differentials were considered. These included dermoid cysts, hemangioma, lipoma, angioma, and angiofibroma.

Preoperative patient nosocomial preparation included administration of appropriate preoperative antibiotics, the establishment of an

Intravenous (IV) access, and sampling of patient blood for crossmatching.

Marked preoperative obstacles were the unavailability of a Magnetic Resonance Imaging (MRI) machine in the medical facility at that period.

3.2. Therapeutic intervention

Surgical intervention was warranted based on the previous clinical situation. The surgery successfully took place at our university hospital. It was performed by a General Surgery specialist and a senior General Surgery resident with 13 and 4 years of experience, respectively. The operation was fully achieved under general anesthesia without any perioperative surgical or anesthetic complications.

An elliptical incision was done along the skin overlying the mass. This was chosen to facilitate the complete removal of the lesion. Intraoperatively, we found a cystic mass in the posterior parietal area of the Scalp. It was rubbery, attached to the surrounding soft tissue, unattached to the bone, and measured approximately (4.2 × 4.5 cm). Its borders were irregular and displayed signs of necrosis. Careful isolation from the surrounding structures was done and the mass was completely resected with a 2 cm free margin.

The resected specimens were immediately sent for thorough histopathological analysis.

The final diagnosis was postoperatively established through meticulous histopathological analysis of the excised mass. The histopathology report stated that the lesion had been grossly measured (4 × 4 × 1.5 cm). Microscopic analysis via Hematoxylin and Eosin (H&E) staining revealed the lesion's high cellularity. It was characterized by marked pleomorphism and bizarre nuclei. Furthermore, several mitotic figures and pleomorphic cells with remarkable cellular atypia were demonstrated (Fig. 1A–B–C).

Additionally, the surgical margins were free of tumor involvement.

Analysis via Immunohistochemistry (IHC) was warranted. The lesion only stained positive for Vimentin, while negatively staining for CD30, CD68, CK, S100, LCA, and Desmin. Furthermore, the cellular proliferation mitotic index Ki-67 was high and was >20 % (Fig. 2A–B–C–D–E–F–G–H–I). In conclusion, the diagnosis of a primary Undifferentiated Pleomorphic Sarcoma was made.

The patient underwent promising postoperative clinical recovery. She was later discharged to the outpatient setting within 6 days of the surgery. We fully explained to her the particulars of the uncovered microscopic analysis. Regular wound dressings were done in the clinic by a medical professional.

Finally, she was referred to an oncologist who is specialized in soft tissue sarcomas for the purpose of postoperative surveillance as indicated. Additionally, he was referred to a Reconstructive Surgery consultant for the performance of reconstructive surgery for the surgical site as necessary.

Our patient has been closely followed-up in our university hospital's clinic for 6 months thus far. During those visits, she has undergone physical examination, wound examination, clinical ultrasound, contrast-enhanced Computed Tomography (CT) scanning, and MRI imaging to ensure the lack of recurrence and/or metastasis of her condition. Those radiological and clinical examinations, fortunately, yielded normal results.

4. Discussion

One of the extremely rare subtypes of Soft-Tissue Sarcomas (STS) is the Undifferentiated Pleomorphic Sarcoma (UPS). It is widely perceived that mesenchymal stem cells are the progenitors responsible for this tumor origin [8]. There are multiple subtypes of UPS, these include pleomorphic, storiform, giant cell, myxoid, and angiomatoid. There is considerable controversy regarding the exact definition of this tumor subtype. Therefore, the previously published research can be extremely hindered because only the contemporary documented articles can

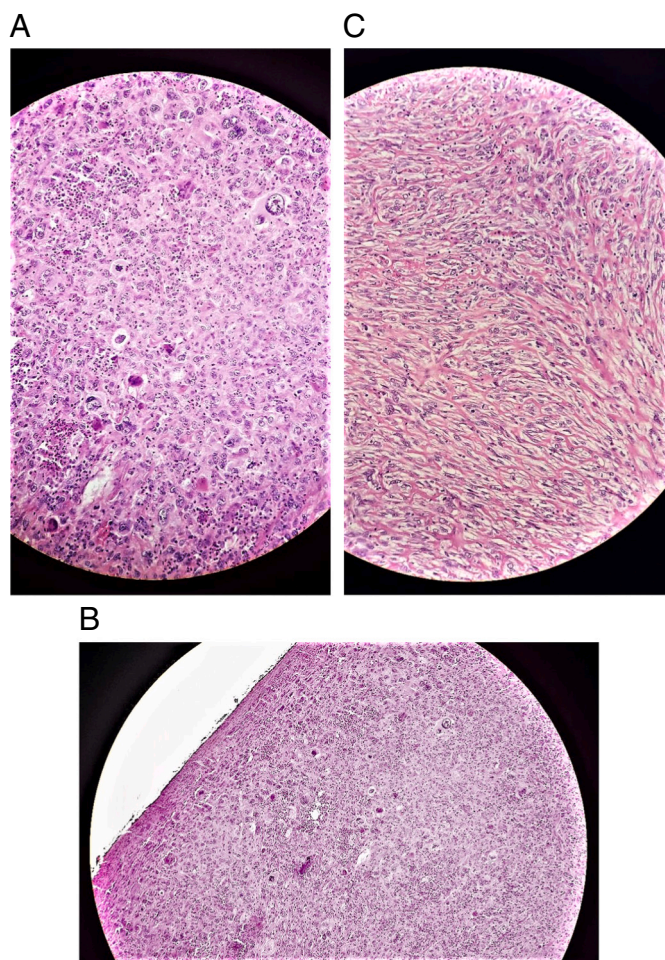


Fig. 1. A: Postoperative final histopathological analysis via H&E staining revealing the lesion's high cellularity, with marked pleomorphism and bizarre nuclei under high power field magnification.
 B: Postoperative final histopathological analysis via H&E staining revealing numerous mitotic figures with some bizarre forms.
 C: Postoperative final histopathological analysis via H&E staining revealing pleomorphic cells with marked cellular atypia under high power field magnification.

characterize this entity with confidence. As a result, UPS is a diagnosis of exclusion of other subtypes of STS [8].

There are multiple theories behind the etiological factors for UPS. Since STS are microscopically proven to consist of heterogeneous mesenchymal cell populations, it is thought of as mesenchymal-cell-derived tumor. However, there are also genetic factors considered, such as different genomic alterations [9].

With regards to the subclassification of STS, the World Health Organization in 2020 classified UPS under the category of malignant neoplasia of vague differentiation [10].

As for the epidemiological aspect, the Surveillance, Epidemiology, and End Results program conducted a study of 26,758 patients. 17.1 % of said patients had UPS. That put UPS as the second most prevalent neoplasia of STS after leiomyosarcoma. Furthermore, and with regards to gender-specific prevalence, UPS showed higher tendencies to occur in males rather than females. Ethnically, it favored the White rather than African race. The incidence of UPS proportionally increased with increasing age and predominantly occurs in the 6th decade of human life [11].

When it comes to the clinical presentation of patients, patients with UPS chiefly have an uneventful and asymptomatic clinical course, except for a rapidly proliferating bulge without obvious skin changes

[12].

In a contemporary research study of 100 cases of UPS patients, the limbs were more predominantly involved by the tumor with a 55 % rate, seconded by the trunk with a 35 % rate, the retroperitoneum with a 9 % rate, and the left atrium with a 1 % rate [13].

With regards to preoperative diagnosis modalities, non-contrast CT for the chest, abdomen, and pelvis is ought to be employed when the physician suspects lesion involvement in the internal organs or in the retroperitoneum. On the other hand, CT and/or MRI for the vertebral column, head, and neck are only considered for certain cases as there are no pathognomonic findings for Undifferentiated Pleomorphic Sarcoma. Furthermore, there aren't ample data that supports performing either a sentinel lymph node biopsy or Positron Emission Tomography in cases of Undifferentiated Pleomorphic Sarcoma [14].

The primary differential diagnoses for UPS are the multiple subtypes of STS. Those can be properly ruled out via means of clinical suspicion, thorough physical examination, and histopathological analysis especially when implementing suitable immunohistochemical markers [15,16].

The most common differential diagnoses considered for UPS are Lipoma, Liposarcoma, Angiosarcoma, Angioma, Leiomyosarcoma, Osteosarcoma, and Dermatofibrosarcoma Protuberans. Tumor metastases from other sites are also considered [12].

The cornerstone for the management of UPS occurring in the trunk, head, neck, and limbs is complete and utter surgical resection with adequate free margins. This can be successfully accomplished via wide local resection of a free margin of 2 cm. Radiotherapy implemented after surgical excision is applied either when the free margins are distanced <1 cm from the lesion, the lesion invaded the bony structures, or when there are significant vascular or nerve entities involved [15,17]. Furthermore, chemotherapy can also be considered for advanced UPS which has an advanced stage that hinders surgical resection or spread out in the body [17].

The gold standard for establishing a final diagnosis relies on competent histopathological analysis [17]. Upon examination of the UPS specimens under the light microscope, it portrays vivid cellular atypia, prominent mitotic structures, and pleomorphic cellular components. The malignant lesion of UPS could also demonstrate a sheet-like, storiform, or fascicular tissue organization inside a fibrous-based stroma [15].

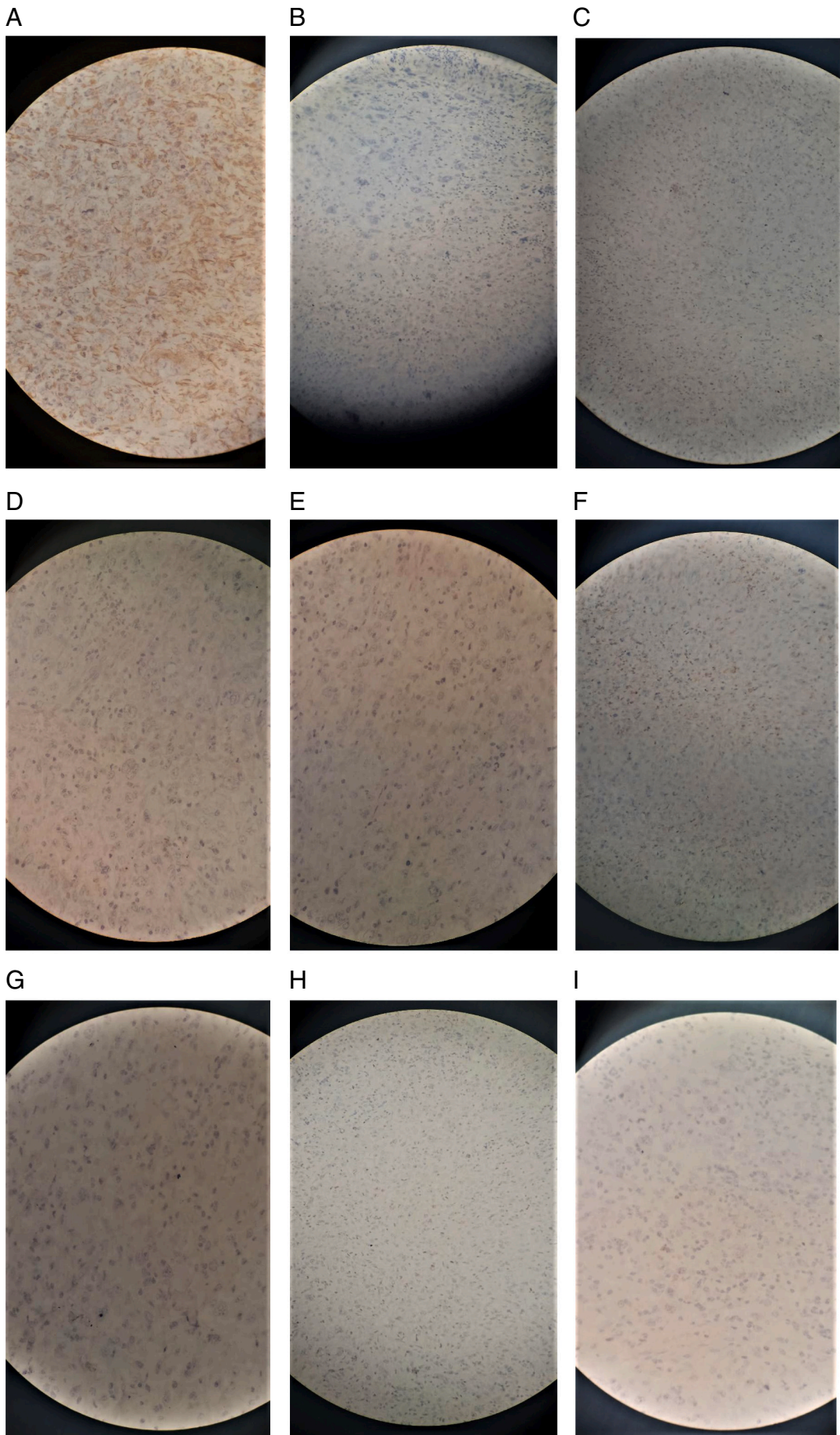
Nevertheless, the ultimate diagnosis is defined via thorough immunohistochemical analysis [18]. Some of the IHC markers used to differentiate UPS from other STS include CD68, CD30, S100, SMA, Kinases, Desmin, Vimentin, Ki-67 proliferation index, and p53 [12,19–22].

With regards to UPS-related complications, the most frequently encountered ones include relapse, local recurrence, tumor metastases, and a high rate of patient mortality. There are also complications related to the sites involved in a UPS, such as extremity disability, amputation of an extremity, different levels of organ compromise, degeneration of neurovascular structures, and dangerous surgical wound adverse effects [17,23,24].

Timely diagnosis accompanied by clinical suspicion could aid in establishing suitable and time-saving therapeutic interventions. This will inevitably enhance the patient's prognosis. There's a contemporary retrospective study conducted in tertiary care medical facilities, which included 319 affected patients. It was deduced that recurrence rates accounted for 14.1 %, while metastatic rates equaled 7.8 % of patients involved [25].

It is perceived that tumor recurrence rates are directly proportional to tumor infiltration throughout the subcutaneous fatty layer and when a lesion measures a size >5 cm. Moreover, the rates of metastases amply increase when there's vascular infiltration by the malignant lesion. It is also increased with increasing patient age and insufficient resected free margins [26].

The UPS-specific 5-year-overall survival rate is estimated to reach 60 %, while it is 48 % for the 10-year-overall survival rate. It's worth noting



(caption on next page)

Fig. 2. A: IHC analysis reveals positive staining for Vimentin.
 B: IHC analysis reveals negative staining for CD30.
 C: IHC analysis reveals negative staining for CD68.
 D: IHC analysis reveals negative staining for CK.
 E: IHC analysis reveals negative staining for Desmin.
 F: IHC analysis reveals negative staining for LCA.
 G: IHC analysis reveals negative staining for S100.
 (H-I): IHC analysis reveals high mitotic index Ki-67 > 20 %.

that these predictive markers are negatively affected when radiation is the underlying cause of UPS [27].

Regular surveillance for affected patients should be conducted thoroughly to ensure that there aren't any relapses, recurrences, or metastases. With regards to clinical examination, it must be carried out at three-to-six-month intervals for the first 2 years postoperatively and then performed at an annual rate [17].

5. Conclusion

It's genuinely rare to diagnose a primary Undifferentiated Pleomorphic Sarcoma in the Scalp in any patient population. It is even rarer to see such a malignant lesion in a female, particularly in a Middle Eastern female. Symptoms and clinical presentations are non-specific and could be hugely misleading. This results in misdiagnoses and possible delays in effective management. This could harbor morbid consequences for patients. It is profoundly challenging to find adequate data about such a malignant disease subtype due to its extreme rarity. Moreover, the epidemiological percentages aren't clearly known. This warrants further studying of this malignancy and documentation so that we can establish informative epidemiological results. This will aid us in setting up research scenarios and treatment protocols to enable medical providers to choose the proper treatment modality.

Abbreviations

| | |
|-----|--------------------------------------|
| BMI | Body mass index |
| IV | Intravenous |
| MRI | Magnetic resonance imaging |
| H&E | Hematoxylin and eosin |
| IHC | Immunohistochemistry |
| CT | Computed tomography |
| STS | Soft-tissue sarcomas |
| UPS | Undifferentiated pleomorphic sarcoma |

Consent of patient

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.

Availability of data and materials

The datasets generated during and/or analyzed during the current study are not publicly available because the Data were obtained from the hospital computer-based in-house system. Data are available from the corresponding author upon reasonable request.

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This study is exempt from ethical approval in our institution.

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CRediT authorship contribution statement

OA: Conceptualization, resources, who wrote, original drafted, edited, visualized, validated, and literature reviewed the manuscript.

GA, AM: Supervision, visualization, resources, literature review, and review of the manuscript.

HA: Validation, resources, review of the manuscript, and histopathological analysis of the specimens.

MA: 1st surgical assistant in the General Surgery operation, supervision, project administration, validation, resources, and review of the manuscript.

AA: General Surgery specialist who performed and supervised the General Surgery operation, in addition to supervision, project administration, and review of the manuscript.

OA: The corresponding author who submitted the paper for publication.

All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no competing interests.

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