# GASTROINTESTINAL STROMAL TUMORS: ABOUT 4 CASES AT THE ANGRE UNIVERSITY HOSPITAL (CÖTE D'IVOIRE)

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## ABSTRACT

### Background

Gastrointestinal stromal tumors are rare, sporadic connective tissue tumors. Very few cases have been reported in Africa, including Ivory Coast.

### Aim

To report 4 cases of GIST at the Angré University Hospital in Ivory Coast.

### Patients and method

It was a retrospective case series from April 2, 2020, to May 31, 2023, at the Hepato-gastroenterology Unit of the Angré University Hospital. GIST cases followed in consultation or hospitalization, confirmed by pathological examination and immunohistochemistry, were included. Data collection was based on consultation and hospitalization files, entered and processed anonymously. The variables studied were sociodemographic, clinical, paraclinical, and therapeutic data.

### Results

We reported four cases of GIST. The patients had an average age of 61.7 years with a sex ratio of 1. The circumstances of discovery were a digestive hemorrhage, an epigastric mass, epigastric pain, and anorexia. The most common area was the stomach (3), and there was 1 case of mesentery GIST. Immunohistochemistry found three moderate to intense cytoplasmic and membrane markings by the anti-CD117 antibody, four markings for the anti-DOG1 antibody, three markings by the anti-CD34 antibody, and two membrane markings of the endothelial cell by the antibody anti-CD31. Treatment was surgical in 2 patients, followed by adjuvant treatment with Imatinib. The other two patients were treated with Imatinib alone for one and as neoadjuvant for the other, which will be followed by surgery if the tumor size regressed.

### Conclusion

Gastrointestinal stromal tumors are rare pathologies with non-specific symptoms. For optimal management, the diagnosis must be confirmed by immunohistochemistry.


***Keywords:*** *GIST – Stromal tumors - Immunohistochemistry - Molecular biology - Imatinib – Africa- Mutation - Gastrointestinal bleeding - Abdominal mass – C-Kit.*

## Introduction

Gastrointestinal stromal tumors (GIST) are rare, usually sporadic, connective tissue tumors traditionally located in the stomach or small intestine. These are the most common sarcomas [1, 2]. Clinically, it is essential to note that GISTs remain undiscovered for a long time until they reach a large size [3]. However, they are often found incidentally during radiological imaging or intraoperatively [4, 5]. Due to the development and advancement of immunohistochemical staining techniques and improvements in microscopic structural imaging, GISTs are becoming notable tumor entities with their specific markers and characteristics [6]. Although surgical resection is the potentially curative treatment for GIST, its management has been revolutionized by the approval of imatinib as an adjuvant and neoadjuvant treatment [7- 8]. In France, several studies have estimated their incidence at between 10 and 15 cases per year per million inhabitants, or approximately 600 to 900 new cases per year [9]. In Morocco, eight digestive stromal tumors were collected over six years [10]. In Ivory Coast, very few studies have been carried out with very few cases: the first study involved three cases of GIST, which were diagnosed after three acute gastrointestinal bleedings, and the second study concerns 1 case of GIST, which was discovered on abdominal computed tomography (CT), the objective of which was to describe the radiological semiology and management of this condition [11,12]. We report a case series of 4 GIST in a tertiary hospital in Abidjan, Côte d'Ivoire.

## MATERIAL AND METHOD

### Type, setting, and period of study

This retrospective case series study was conducted at the Hepato-Gastro-Enterology (HGE) Unit of the Internal Medicine and Geriatrics Department of the Angré University Hospital from April 2, 2020, to May 31, 2023.

### Selection criteria

### Inclusion criteria

Our study included cases of GIST followed in the HGE Unit of the Angré University Hospital and confirmed by pathological examination and immunohistochemistry.

### Exclusion criteria

Our study did not include cases of gastrointestinal tumors whose diagnosis was not confirmed by pathological examination or whose files were incomplete.

### The variables studied

- Socio-demographic characteristics: age, gender, profession, level of education, residence, marital status
- Clinical characteristics: reason for consultation or hospitalization, functional signs, history, physical signs
- Paraclinical characteristics: digestive endoscopy, pathological examination, immunohistochemical examination, thoracic and abdominopelvic scan
- Treatment: medical, surgical, targeted therapy
- Evolution: favorable, unfavorable, death

### Support and data collection

Data were collected from consultation and hospitalization records, entered and processed anonymously.

### Data entry and analysis

To exploit these data, we established medical observations, including sociodemographic, clinical, paraclinical, and therapeutic data and the resulting evolution.

### Ethical aspect

Ethical aspects and professional conduct were respected. The data were collected, entered, and processed anonymously.

### Conflict of interest

No conflict of interest.

## RESULTS

We collected 4 cases of GIST during the study period, whose observations were reported.

### case #1

Patient aged 56, teacher, hospitalized from 04/12/2021 to 04/23/2021 for upper gastrointestinal bleeding (UGIB). The onset of the symptoms dates to approximately ten days before his hospitalization, with the sudden onset of a very abundant UGIB externalized in the form of hematemesis and hematochezia. There was a hemodynamic impact, such as dizziness and loss of consciousness. All preceded by diffuse abdominal pain without fever. She also reports a deterioration in her general condition, such as weight loss amounting to 7 kg in 4 months. The patient was evacuated to the medical emergency room, where the biological assessment showed a hemoglobin level of 3.9 g/dl and the hematocrit was 11.9%. The patient benefited from resuscitation measures with several packed blood transfusions. She has had a history of high blood pressure for three years on perindopril/amlodipine 8/10 mg, cardio aspirin 100 mg, and is a fan of traditional treatment based on decoctions. A physical examination found a hemodynamically stable patient with a soft, symmetric, and non-tender abdomen without distention and palpable masses or melena on rectal examination. There were no signs of portal hypertension or hepatocellular insufficiency. The performed EGD revealed a fundic polyp 60 mm in diameter, with a regular surface, inflammatory with a non-hemorrhagic ulcer at its apex (fig 1). The pathological study of the biopsies carried out was in favor of a low-grade GIST of Miettinen malignancy of the stomach. In the immunohistochemical analysis, the cells strongly expressed the anti-CD34 antibody and weakly the anti-DOG1 antibody, posing the diagnosis of a gastrointestinal stromal tumor of low malignancy. A resection was performed by removing the cancer and respecting 2 cm of healthy margin. A thoracic-abdominal-pelvic CT scan was performed three months after the operation and did not reveal any thoracic-abdominal-pelvic tumor. However, it revealed hetero-nodular hypertrophy of the right thyroid lobe; the pathological examination after the cyst puncture of the thyroid nodule revealed a suspicious malignancy aspect (category C5, according to the terminology of BETHESDA 2017). The patient underwent a thyroidectomy in June 2022 with simple post-operative outcomes. An EGD control performed 06 months later came back normal, and the pathological examination of systematic antral (3) and fundal (2) gastric biopsies revealed the presence of chronic antral

gastritis (3/3), non-atrophic., active (2/3), without intestinal metaplasia, not associated with follicular gastritis. Severe presence of *Helicobacter pylori* (3/3). Chronic fundic gastritis (3/3), non-atrophic, active (2/3), without intestinal metaplasia, not associated with follicular gastritis—average presence of *Helicobacter pylori* (2/3). There was no dysplasia and no histological sign of malignancy on the fragments examined. The patient received concomitant quadruple therapy (metronidazole 500 mg x 2/day + amoxicillin 1g x 2/day + clarithromycin 500 mg x 2/day + Rabeprazole 20 mg x 2/day) for 14 days for *Helicobacter pylori* eradication. The patient's clinical and paraclinical evolution was marked by good general condition.

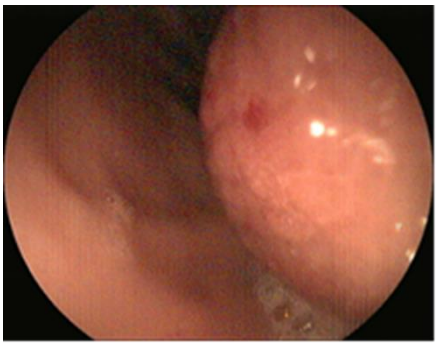

*Fig1. Endoscopic view of fundic polyp.*

**case #2**

A 45-year-old patient without any medical-surgical history was referred on 09/21/2021 to manage an epigastric mass. The onset of symptoms dates back approximately two months, with the gradual onset of a non-painful epigastric mass associated with a general condition deterioration such as unquantified weight loss without any notion of intestinal transit disorder. The physical examination revealed a patient with a WHO performance status score of 1, a large mass 15 cm in diameter located in the left hypochondrium. An abdominal CT scan showed a large tissue mass developed at the expense of the Celio-mesenteric region. Pathological examination after carrying out a transcutaneous biopsy of the mass revealed a histological appearance suggestive of a GIST of the mesentery. On immunohistochemical examination:

- The anti-CD117 antibody moderates cytoplasmic and membrane marking.
- intense cytoplasmic and membrane marking by the anti-DOG1 antibody.
- intense membrane marking by the anti-CD34 antibody.
- membrane marking of endothelial cells by the anti-CD31 antibody,

Confirming the morphological diagnosis of GIST of the mesentery. Remote extension assessment (EGD, colonoscopy, thoracic-abdominopelvic CT scan) found no metastases. Furthermore, the tumor was classified as locally advanced and inoperable. A multidisciplinary consultation meeting of surgeons, oncologists, radiologists, and anatomopathological decided:

- treatment with targeted therapy based on Imatinib 400 mg per day,

- a clinical and paraclinical evaluation every three months showed a satisfactory clinical condition and regression of the tumor, which went from 15 cm to 6 cm on the last abdominal CT scan carried out in April 2023.
- R0 surgery will be re-discussed if the tumor regression is more than 80% satisfactory.

**Case #3**

The patient, aged 90, is a retired nurse. She has been followed since April 2021 for anorexia. The onset of symptoms dates to approximately three months before his admission, with the progressive onset of deterioration in general conditions such as unquantified weight loss, asthenia, and anorexia. She has hypertension treated by amlodipine, diabetic on galvusmet. She has a history of hysterectomy in 1982 for uterine fibroids. The clinical examination showed a patient with WHO performance status 2 with a BMI = 22.89 kg/m2 without dehydration or malnutrition. There was no jaundice or anemia. She had painless bilateral lower extremity pitting edema. The abdomen was soft and painless, without hepatomegaly or splenomegaly. There was no Troisier lymph node. The EGD revealed a large polyp measuring 10 cm under the ulcerated heart (figure 2). The pathological examination of the biopsies concluded with a histological appearance suggestive of a GIST associated with reactive gastritis without *Helicobacter pylori*. The immunohistochemistry study showed at the level of tumor cells:

- moderate to intense cytoplasmic and membrane staining by the anti-CD117 antibody
- moderate to intense cytoplasmic and membrane labeling by the anti-DOG1 antibody
- intense membrane marking by the anti-CD34 antibody
- membrane marking of endothelial cells by the anti-CD31 antibody

Thus, the diagnosis of stomach GIST was confirmed. A thoracic-abdominopelvic CT scan showed a multicystic liver without secondary pleuropulmonary localization. Medical treatment with Imatinib 400 mg/day and regular monitoring every three months was prescribed. The quarterly paraclinical evaluation showed a discreet increase in the size of the hepatic biliary cyst of segment VI and bilateral basal lung disease. Furthermore, the general condition was good after two years.

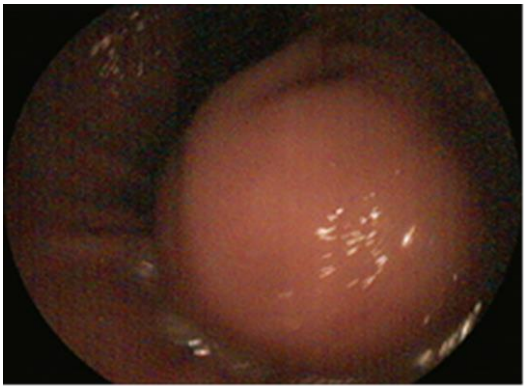

*Fig 2. Endoscopic view: Subcardiac polyp in retroversion position.*

**Case #4**

A 56-year-old patient, Steward, is followed in consultation for the management of a digestive tumor. The history of the disease dates to March 2017, with the occurrence of chronic epigastric pain radiating to the back and not calmed by PPI treatments. Physical examination was unremarkable. EGD revealed a Siewert II circumferential esophagogastric junction tumor. The histological study suggested a GIST of low malignancy. The immunohistochemistry study showed:

- the anti-CD117 antibody gives an obvious positive marking on the entire tumor proliferation
- the anti-DOG1 antibody gives a more discreet and more focal positive marking
- there was no staining with the anti-desmin antibody
- the ant-Ki67 antibody reveals a shallow proliferation index (less than five mitoses on high power fields).

Confirming GIST with low mitotic index. Furthermore, a thoracic-abdominopelvic CT scan did not reveal any secondary location of the tumor. Distal esophagectomy and total gastrectomy were performed with an esophagojejunal anastomosis. The postoperative course was marked by an esophagojejunal fistula, which dried up. The patient was discharged after 30 days of hospitalization. Histological examination of the surgical specimen suggested a low-grade malignancy GIST, which immunohistochemistry confirmed. The patient was subsequently referred to oncology and placed on adjuvant treatment with Imatinib, followed by regular clinical, CT scan, and biological monitoring. The progress report seven months after esophagogastrectomy and six months after medical treatment: EGD did not show any lesion on esophago-duodenal montage; the histological study suggested chronic follicular duodenitis without villous atrophy, non-specific chronic jejunitis and an absence of malignant tumor proliferation. Another EGD control carried out 12 months later did not show any macroscopic lesion of tumor recurrence but revealed a sub-centimeter sessile polyp on the anastomosis jejunal side. The histological typing showed a pseudo polyp chronic inflammatory disease of the jejunum. A thoracic-abdominal-pelvic CT scan showed segmental thickening of the small

intestine in the left hypochondrium, which prompted a CT enterography scan, which came back normal. The evolution was good, with treatment continuing after 06 years.

**Observations summaries**

In our study, the median age of the patients was 61.7, ranging from 45 to 90. The sex ratio was 1. The most common site was the stomach (75%), and there was 1 case of mesentery GIST (25%). Demographic and clinical data are summarized in Tab 1.

*Tab1. Demographic and clinical features.*

| | Patient 1 | Patient 2 | Patient 3 | Patient 4 |
|---|---|---|---|---|
| Age (year) | 56 | 45 | 90 | 56 |
| Gender | Male | Female | Female | Male |
| Primary symptom | Upper gastrointestinal bleeding | Epigastric mass | Anorexia | Epigastric pain |
| Location of GIST | Stomach | Mesentery | Stomach | Esophagogastric junction |

The pathological results are summarized in Tab 2.

*Table 2. GIST's pathological characteristics*

| | **case 1** | **case 2** | **case 3** | **case4** |
|---|---|---|---|---|
| **Histology** | Low-grade malignancy of gastric GIST *Helicobacter pylori infection* | GIST of the mesentery | GIST associated with reactive gastritis without *Helicobacter pylori* | Low-grade GIST |

| | | | | |
|---|---|---|---|---|
| **Immunohistochemistry** | The cells strongly expressed the anti-CD34 antibody, weakly the anti-DOG1 antibody | - Moderated cytoplasmic and membrane marking by the anti-CD117 antibody.<br><br>- Intense cytoplasmic and membrane marking by the anti-DOG1 antibody<br><br>- Intense membrane marking by the anti-CD34 antibody<br><br>-Membrane marking of endothelial cells by the anti-CD31 antibody | - Moderate to intense cytoplasmic and membrane marking by the anti-CD117 antibody<br><br>- Moderate to intense cytoplasmic and membrane marking by the anti-DOG1 antibody<br><br>- Intense membrane marking by the anti-CD34 antibody<br><br>- Membrane marking of endothelial cells by the anti-CD31 antibody | -The anti-CD117 antibody gives an obvious positive marking on the entire tumor proliferation<br><br>-The anti-DOG1 antibody gives a more discreet and more focal positive marking<br><br>-There was no marking with the anti-desmia antibody |
| **Mitotic index** | | | | The anti-Ki67 antibody reveals a shallow proliferation index (less than five mitoses on high magnification fields) |

The treatment was medico-surgical (Tab 3).

*Table 3.* ***GIST treatments***

| | **Case1** | **Case 2** | **Case 3** | **Case 4** |
|---|---|---|---|---|
| **treatment** | R0: tumor resection+ Imatinib 400mg | Imatinib 400mg | Imatinib 400mg | Esophagogastrectomy + Imatinib 400mg/J |

## DISCUSSION

Our work was a retrospective cross-sectional study, reporting a series of 4 cases in which the diagnosis of digestive stromal tumor had been retained.

Our series of 04 cases found in 3 years was low, as were those reported in Tunisia [13], which found 25 cases in 20 years, or Morocco, which found 06 cases in 5 years [14]. Ahmadou in Mali [15] reported 25 cases in 10 years. This low number of cases reported in these studies reflects the rarity of this digestive tumor in our African countries, as described in Western literature [1, 2]. The median age of our case series was 61.7 years, which is without significant difference from that found in the Malian, Moroccan, Chinese, and Korean series, which ranged

from 54.9 to 61.1 years [13, 15- 17]. However, it is lower than that of Batcham et al. [ 12] in Ivory Coast and Hinz et al. [ 70 18] in Germany, who found respectively 65 years and 64 years, and higher than that found by Hassan in Qatar in 2014, whose age was 48.4 ± 13.7 [19]. GISTs can be found at any age, in young people but exceptionally in children [20 - 21]. Regarding gender, even if certain international studies show a slight male predominance, we note that the sex ratio is close to 1 [22 - 24]. It is like our research, which found an identical distribution between the two genders.

Although GISTs can remain asymptomatic for a long time, their discovery is often fortuitous. Clinical signs and complications generally appear when the tumor size is large. This method of revelation represents approximately 20 to 30% of diagnoses, and the discovery mainly takes place during a digestive endoscopy, a CT scan, or an abdominal surgical procedure [3-4, 9]. Great clinical diversity is noted; the symptoms differ depending on the location; they can manifest as digestive bleeding [25], abdominal pain, an abdominal mass, an obstructive syndrome, or, more rarely, hemoperitoneum [26 - 27]. Our series found a digestive hemorrhage, an abdominal mass, and a gastric tumor as the circumstances of discovery. We did not have any case of chance discovery circumstances, unlike Ahmadou in Mali [15], who noted 4 cases of chance discovery. Tumors increasingly develop from the stomach (60 to 70%), small intestine (20 to 30%), large intestine (10%), rectal and peri-anal region (<5%), esophagus, mesentery, appendix (<1%) [26]. In our series, the stomach represented the most frequent location (3 cases) and 1 case for the mesentery, a rare location.

The endoscopic appearance of GIST is not very specific, generally that of a regular nodule, with a submucosal appearance because it is covered by normal mucosa. Nevertheless, we must evoke this diagnosis in the stomach by argument of frequency. The tumor may also be ulcerated at its apex [9]. In our series, case no. 1 presented the same appearance of a fundic nodule 60 mm in diameter, with a regular surface, inflammatory ulcerated at its apex, probably having bled. Moreover, endophytic stromal tumors quickly form a mass bulging into the intestinal lumen, which can appear mobile or polypoid [28]. Confirmation of the diagnosis is made in most cases on analysis of the surgical specimen.

Ultrasound endoscopy is the best examination to characterize esophagi-gastroduodenal or rectal submucosal lesions [29]. In our series, none of the patients had performed an ultrasound endoscopy, which was unavailable in our country's public or private hospitals.

In our series, no patient performed an FDG Pet-Scan as it was unavailable in our country during the study period; however, the first nuclear medicine center was inaugurated on July 25, 2023, in Abidjan. The extension workup was limited to a thoracic-abdominopelvic CT scan, which found no pulmonary, hepatic, or peritoneal metastases. However, one patient presented with hetero-nodular enlargement of the right thyroid lobe, the pathological examination of which, after cyst puncture of the thyroid nodule, revealed an aspect suspicious of malignancy.

GISTs expressed CD 117 or c-Kit on immunohistochemistry in 90 to 95% of cases [30]. Other markers are recommended in case of CD 117 negativity (CD34, NSE, H caldesmon, anti-actin, protein S100, DOG 1, PKC theta) [30 - 32]. In our series, immunohistochemistry found three moderates to intense cytoplasmic and membrane markings by the anti-CD117 antibody, i.e., 75%, four markings for the anti-DOG1 antibody, i.e., 100%, three markings by the anti-CD34 antibody 75. % and two membrane markings of the endothelial cell by the anti-CD31 antibody,

i.e., 50%. In the Malian study, the marking was positive for CD117 in 100% of cases, CD34 in 8%, and DOG1 in 8% of cases [15].

Several prognostic classifications exist, but the most important ones are those of Joensuu [33] and Miettinen [34]. In our series, observation no. 4 reveals a shallow proliferation index by the ant-Ki67 antibody. Ahmadou in Mali [15] found a progressive risk according to the Miettinen classification: high (52%), intermediate (24%), low (8%), and deficient (16%).

In our series, the treatment was surgical and medical, depending on the case. First, about localized tumors, treatment was initially surgical with R0 resection. Case No. 1 involved performing a lumpectomy, and case No. 4 performed an esophagogastrectomy with esophagojejunal anastomosis, then medical adjuvant treatment based on Imatinib 400 mg/day. According to Batcham et al. [12] study in Ivory Coast, the surgical treatment consisted of surgical removal of the mass and a partial gastrectomy followed by chemotherapy based on Imatinib. Ellara et al. [13] in Tunisia reported 25 cases of GIST, 16 of which were localized and all treated surgically. In Mali [15], tumor excision was carried out in 76% of cases, and Imatinib, available free of charge, was prescribed in 16% of cases.

The alternative of neoadjuvant treatment is reasonable when the resection seems important or uncertain preoperatively to limit the initial surgical procedure and increase the chances of complete resection. Surgery is considered when the maximum response is observed, generally after 6 to 12 months of treatment [2]. It was the case of observation no. 2 of our series; the patient was put under neoadjuvant treatment with Imatinib 400 mg/day for a large tumor of approximately 15 cm in diameter, which decreased to 6 cm at the last abdominal scan carried out in April 2023. This quarterly clinical and paraclinical evaluation will continue, and then R0 surgery will be discussed again in a multi-disciplinary consultation meeting if the evolution is more than 80% satisfactory.

According to Mosnier et al. [35], in almost half of the cases, stromal tumors are immediately clinically pejorative, either because there is a locoregional invasion or because there are metastases. Malignancy can become evident more than ten years after the initial resection. In 75% of cases, recurrences and death are marked by peritoneal implants and liver metastases, the two being often associated. Extra-abdominal metastases exist in 25% of cases. Lymph node metastases are rare. In our series, the patients were all in good health, with follow-ups ranging from 2 years for some to 6 years for others.

The study's limitations were the biases inherent in a retrospective study: selection bias and recall bias. The difficulties were the chronology of events to arrive at the diagnosis, the insufficiency of data found in specific files, and the insufficiency of the technical platform in hospitals: failure to carry out specific additional examinations such as echoendoscopy and 18F-fluoro-2-deoxy-D-glucose (FDG) PET-Scan.

## Conclusion

Gastrointestinal stromal tumors are rare in our unit. Our study shows that the median age of our patients is 61.7 years, and GIST occurs in both men and women. The symptoms are not very specific and are highlighted by gastrointestinal bleeding and abdominal mass with a predominant gastric location (75%). The definitive diagnosis is made by anatomopathological

examination combined with immunohistochemistry of biopsies and surgical specimens. Management is multidisciplinary and based on surgery, which constitutes the only potentially curative treatment and imatinib, a tyrosine kinase inhibitor. Due to the very often poor prognosis of this tumor, monitoring is an essential aspect of patient care.

**Footnotes.**

Ahmed Fathy (Assistant professor of internal medicine), Hayam Rashed (professor of pathology), Mohamed Emara (Professor of gastroenterology, hepatology, and infectious diseases), and Sara Salem (lecturer of internal medicine, gastroenterology, and hepatology unit) were the peer reviewers.

**E- Editor:** Salem Youssef Mohamed, Osama Ahmed Khalil, Amany Mohammed.



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**Consent for publication**: the patients in this research gave written informed permission to publish the data in this study.

**Data and materials availability:** The datasets used or analyzed during the current study are available from the corresponding author upon reasonable request.

**Competing interests**: The authors declare that they have no competing interests.

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**Authors' contributions**

Henriette Ya Kissi Anzouan-Kacou, Adjéka Stanislas Doffou were responsible for conception and revision. Aboubacar Demba Bangoura, Abdoulatif Yaogo, and Amoin Ange Christelle DegnonTou interpreted and analyzed data. Innocents Boa Brou and Alain Koffi Attia wrote the manuscript, which was revised and approved by all co-authors.

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This work was done according to the CARE guidelines.

**Ethical approval:** All procedures involving human participants followed the institutional and national research committee's moral standards, the 1964 Helsinki Declaration, and its later amendments or comparable ethical standards. All authors declare that consent was obtained from the patient (or other approved parties) to publish this case report and accompanying images.

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