International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2025: 7.089

Advanced Gastric Adenocarcinoma with Bilateral Krukenberg Tumor and Cutaneous Metastasis in a Female Patient: A Case Report

Marianela Ascencio Paredes[1], Diana Montaño Orostico[2], Jose Sabino Montiel Castro[3], Ivan Melendez Garcia[4]

[1]Medical Intern at the Oncology Unit of the State of Puebla

[2]Medical Intern at the Autonomous University of the State of Hidalgo

[3]Attending Physician in the Medical Oncology Department of the Oncology Unit of the State of Puebla

[4]Attending Physician of the Department of Pathological Anatomy of the General Hospital of the South Eduardo Vazquez Navarro.

Abstract: ***Background: Cutaneous metastases and Krukenberg tumors are uncommon but clinically significant manifestations of gastric adenocarcinoma, often associated with advanced disease and poor prognosis. Patient: We report the case of a 48-year-old woman with no prior oncological history, diagnosed with diffuse gastric adenocarcinoma with signet-ring cells. Clinical Presentation: The patient presented with increased abdominal girth, diffuse abdominal and pelvic pain, fatigue, and a palpable lower abdominal mass. Subsequently, she developed multiple cutaneous lesions on the scalp, neck, breasts, back, and abdomen, which progressively increased in size. Key Diagnostic Findings: Gastroscopy confirmed diffuse gastric adenocarcinoma. Imaging studies revealed bilateral ovarian masses consistent with Krukenberg tumors. Cutaneous biopsy confirmed metastases of gastric origin. Laboratory findings showed elevated carcinoembryonic antigen (CEA) levels. Treatment and Intervention: Cytoreductive surgery was performed for the ovarian masses, and palliative management was indicated for cutaneous metastases. Systemic chemotherapy was initiated according to advanced gastric adenocarcinoma protocols. Results and Evolution: The patient experienced disease progression, with increased size and number of cutaneous lesions, persistent abdominal symptoms, and marked fatigue, reflecting a poor short-term prognosis. Conclusions: This case highlights the importance of early recognition of cutaneous metastases and Krukenberg tumors in patients with diffuse gastric adenocarcinoma due to their association with advanced disease and unfavorable outcomes.***

Keywords: Gastric adenocarcinoma; Krukenberg tumor; Cutaneous metastases; Signet-ring cell carcinoma; Advanced gastric cancer

1. Introduction

Gastric cancer is a leading cause of morbidity and mortality worldwide, ranking as the **fourth leading cause of cancer death** and the **fifth most frequently diagnosed cancer [1]. Its etiology is multifactorial, involving infectious, environmental, genetic, and host factors.** *Helicobacter pylori* infection is a well-established risk factor for gastric adenocarcinoma, while Epstein-Barr virus infection has also been implicated in specific subtypes of this neoplasm [2–3]. Dietary habits, such as high salt intake, nitrite consumption, smoked or cured foods, and contaminated drinking water, as well as a diet deficient in vitamins A and C, have been associated with an increased risk [2,4]. Other environmental and lifestyle factors include smoking, obesity (particularly in the proximal region and gastroduodenal junction), gastroesophageal reflux, and occupational exposure to substances such as rubber, tin, and coal [5–7]. Among the host factors, blood type A, pernicious anemia, and atrophic gastritis stand out, the latter increasing the risk of intestinal-type gastric cancer up to sixfold [6,7]. At the genetic level, hereditary syndromes such as adenomatous polyposis, Peutz-Jeghers syndrome, juvenile polyposis syndrome, hereditary breast and ovarian cancer, and Cowden disease have been associated with an increased risk of developing this neoplasm [7].

Gastric adenocarcinoma is primarily classified into two variants: intestinal type and diffuse type. The intestinal variant is the most common, while the diffuse type lacks adhesion molecules, lacks glandular formation, and is characterized by the presence of **signet ring cells** with eccentric nuclei and abundant cytoplasm [8–10]. This histological distinction not only has prognostic implications but also determines the therapeutic strategy. The molecular classification of gastric cancer, based on the Cancer Genome Atlas, incorporates clinical and histological features, including Epstein-Barr virus-associated mutations, microsatellite instability, chromosomal instability, genetic stability, and HER2 amplification [11–16].

Clinically, patients with gastric cancer often present with **nonspecific initial symptoms**, such as persistent indigestion, postprandial fullness, and abdominal discomfort, which can delay diagnosis [10]. As the disease progresses, weight loss, nausea, vomiting, dysphagia, asthenia, and adynamia are commonly observed. Key clinical findings include palpable abdominal masses, supraclavicular lymphadenopathy (Virchow's node), a periumbilical lymph node (Sister Mary Joseph's node), and a left axillary lymph node (Irish node). Peritoneal spread may manifest as Krukenberg tumors, ascites, masses in the pouch of Douglas, or hepatomegaly [10]. In addition, **paraneoplastic manifestations** may occur , such as acanthosis nigricans and diffuse seborrheic keratosis, hematological disorders (microangiopathic hemolytic anemia and Trousseau's syndrome), renal conditions (membranous nephropathy) and autoimmune diseases [17].
Krukenberg tumor is a metastatic neoplasm of the ovary

that accounts for approximately 10% of ovarian cancers [18–21]. Its origin is primarily associated with gastric cancer (70% of cases), followed by colon and other organs. Most cases are bilateral and consist of signet ring cells [22–29]. The route of dissemination is postulated to be lymphatic, hematogenous, and transcoelomic, with the proximity between gastric lymph nodes and ovarian ducts being a determining factor [25–29]. Clinically, patients may remain asymptomatic until the tumor reaches a significant size or causes hormonal changes, presenting with nonspecific symptoms such as increased abdominal girth, pelvic or abdominal pain, abnormal uterine bleeding, late ascites, bowel obstruction, hirsutism, virilization, and cachexia [30–31]. **Cytoreductive surgery** is the main therapeutic approach, given that these tumors are often chemoresistant, and the median reported survival does not exceed 14 months [32–36]. Unfavorable prognostic factors include peritoneal involvement, synchronous presentation, ascites, and elevated levels of carcinoembryonic antigen [33–36].

On the other hand, **cutaneous metastasis secondary to gastric cancer** is a rare finding, with an estimated incidence of less than 5.3%; the most frequent sites include the thoracoabdominal wall, head, neck, and extremities [37–38]. In a meta-analysis that included 71 reports with 72 patients, a male predominance was observed (72.2%), with nodular lesions being the most common clinical form (45.8%), followed by erysipeloid lesions (27.8%) and ulcerated lesions (9.7%). More than 60% of the patients presented with multiple lesions, and the coexistence of extracutaneous metastases was frequent (64.7%), indicating advanced disease [38].

This clinical case describes a patient with **diffuse gastric adenocarcinoma with signet ring cells**, evolution with **bilateral Krukenberg tumor** and development of **multiple cutaneous metastases**, highlighting the aggressiveness of this neoplasm and the therapeutic challenge it represents.

2. Case Presentation Identification data and background

The patient is a 35-year-old woman at the time of diagnosis, originally from and residing in Pienla. She is a homemaker with a high school education, in a common-law relationship, and Catholic. Her family history includes an aunt with a history of ovarian cancer.

Regarding her non-pathological personal history, the patient denies alcoholism, smoking, drug use, and exposure to zoonotic diseases. She received a complete three-dose COVID-19 vaccination series, though the pharmaceutical company is unspecified. Her medical history includes a cholecystectomy performed ten years prior and bilateral tubal ligation five years prior. Her gynecological and obstetric history includes menarche at age 12, four pregnancies, three deliveries, and one abortion, with permanent family planning achieved through bilateral tubal ligation.

3. History of the present illness

The illness began in August 2023 with nonspecific gastrointestinal symptoms, characterized by postprandial fullness and increased appetite. Due to persistent symptoms, an upper gastrointestinal endoscopy with biopsy was performed on August 15, 2023, the histopathological report of which revealed **diffuse gastric adenocarcinoma with signet ring cells**.

3.1 Imaging studies and surgical management

The initial computed tomography scan (October 20, 2023) showed a distended stomach with contrast medium, irregular walls without significant enhancement, circumferential submucosal pyloric thickening of 46 mm with decreased gastric lumen, lymphadenopathy of 6 mm in short axis and bilateral ovarian cysts (approximate volume 37 cc right and 9 cc left)**, a distal gastrectomy with Roux-en-Y reconstruction** was performed. The definitive histopathological study showed poorly differentiated adenocarcinoma with signet ring cells, measuring 6 cm in its longest axis, surgical margins free of tumor, positive vascular permeation, and metastasis in 4 of 6 regional lymph nodes.

3.2 Cancer treatment

In her first evaluation by medical oncology (January 30, 2024), laboratory studies showed hemoglobin 11.9 g/dL, leukocytes 4.9 $\times 10^9$/L, platelets 164 $\times 10^9$/L, and neutrophils 3 $\times 10^9$/L. Adjuvant **chemotherapy with the XELOX regimen was indicated**, beginning on March 6, 2024. During the first administration, she experienced **hematotoxicity**, which was managed conservatively, allowing the regimen to continue until completing six cycles, ending on August 1, 2024.

3.3 Disease progression

A follow-up CT scan on August 19, 2024, revealed bilateral ovarian lesions of mixed component, interpreted as a probable **Krukenberg tumor**. The patient was referred to surgical oncology for oophorectomy, although the surgical protocol was not completed.

In March 2025, the patient presented with **multiple skin lesions**, consisting of well-defined, rounded, erythematous papules and nodules, 0.5 to 1.5 cm in diameter, **which progressively increased in size**. The lesions were extensive, affecting **the skull, neck, breast, back, and abdomen**. A skin biopsy confirmed dermal infiltration by signet ring cells, consistent with metastatic implants from diffuse gastric carcinoma. Immunohistochemistry showed positivity for CK AE1/AE3 and negativity for CD34, S100, actin, desmin, cyclin D1, and calretinin.

3.4 Recent studies and current status

The CT scan of April 7, 2025, revealed solid masses in the right (78 × 35 × 65 mm) and left (54 × 73 × 74 mm) ovarian stroma, consistent with bilateral Krukenberg tumor, in

addition to perisplenic free fluid, a Bosniak I simple renal cyst, and an umbilical hernia.

Recent laboratory results from July 7, 2025, reported: AFP 13.4 ng/mL, CA 19-9 19.4 U/mL, hemoglobin 14.7 g/dL, hematocrit 44.9%, leukocytes 10.8 ×10⁹/L, neutrophils 7.86 ×10⁹/L, platelets 298 ×10⁹/L, glucose 89 mg/dL, BUN 19 mg/dL, creatinine 0.8 mg/dL, total bilirubin 0.710 mg/dL (direct 0.25 mg/dL, indirect 0.456 mg/dL).

On May 29, 2025, she was re-evaluated in medical oncology; HER2 and PD-L1 were negative. Treatment was restarted with the XELOX regimen. At the last follow-up, the patient was **asymptomatic**, with an **ECOG performance status of 0**, and under active follow-up.

4. Discussion

We present the case of a 48-year-old woman diagnosed with diffuse signet ring cell gastric adenocarcinoma who developed bilateral Krukenberg tumors and multiple cutaneous metastases located on the skull, neck, breast, back, and abdomen, which progressively increased in size. She initially presented with postprandial fullness and increased hunger, which progressed to advanced disease despite cytoreductive surgery and systemic chemotherapy. Physical examination revealed multiple cutaneous nodules, some dome-shaped, firm, pink, and well-defined, as well as palpable abdominal masses and mild ascites. Biopsies confirmed the gastric origin of the metastases and the diffuse histological pattern of the primary tumor, and were negative for HER2 and PD-L1.

Gastric cancer is the fourth leading cause of cancer-related death and the fifth most frequently diagnosed cancer worldwide [1–3]. Several risk factors have been identified, including Helicobacter pylori infection, Epstein-Barr virus, a diet high in salt and nitrites, consumption of smoked or unrefrigerated foods, obesity, smoking, gastroesophageal reflux disease (GERD), environmental exposure to rubber, tin, or coal, host factors such as blood type A, pernicious anemia, and atrophic gastritis, as well as genetic associations such as hereditary colorectal cancer syndromes, adenomatous polyposis, Peutz-Jeghers syndrome, and hereditary breast and ovarian cancer syndrome [4–7]. Gastric adenocarcinoma presents in intestinal and diffuse variants, the latter being characterized by signet ring cells and absence of glandular formation, with aggressive behavior and a poor prognosis [8–10]. The molecular classification based on the Cancer Genome Atlas incorporates histological and genetic features, including EBV, microsatellite instability, chromosomal instability, and amplified HER2, which influence prognosis and treatment [11–16].

Patients with diffuse gastric cancer may present with nonspecific initial symptoms such as indigestion, stomach upset, and postprandial fullness, progressing to weight loss, nausea, vomiting, dysphagia, asthenia, and signs of advanced disease such as Virchow's nodes, Sister Mary Joseph's nodes, ascites, hepatomegaly, or Krukenberg tumor [17]. The latter, named after Friedrich Ernst Krukenberg, is a metastatic ovarian tumor, usually of gastric origin, that accounts for approximately 10% of ovarian cancers [18–25]. It is generally bilateral, spreads via lymphatic, hematogenous, or transcoelomic routes, and may remain asymptomatic until reaching a large size [26–31]. Cytoreductive surgery is the primary treatment, although overall survival is often limited, with a reported median of 14 months [32–36].

Cutaneous metastases from gastric cancer are extremely rare, with a reported incidence of less than 1%, and are generally located in the thoracoabdominal wall, head, neck, and extremities [37,38]. The clinical presentation of this case is unusual not only due to the multiplicity of lesions but also their morphological heterogeneity (nodules, dome-shaped lesions) and their spread to uncommon areas such as the skull and breasts, reflecting advanced and aggressive systemic disease. The coexistence of cutaneous metastases with bilateral Krukenberg tumors emphasizes the rarity of this presentation and underscores the importance of considering early skin biopsy to confirm the gastric origin of atypical lesions.

Among the strengths of this report is the detailed documentation of the clinical course, including imaging studies, biopsies, and oncological follow-up, which allows for the correlation of clinical, histological, and therapeutic findings. Limitations include the absence of a complete molecular profile and a lack of information on quality of life and specific response to each chemotherapy cycle. This case highlights the need to maintain a high index of clinical suspicion when unusual skin lesions are present in patients with diffuse gastric cancer and underscores the importance of multidisciplinary management and personalized therapeutic strategies, as well as raising awareness of the potential for aggressive progression associated with extensive cutaneous metastasis.

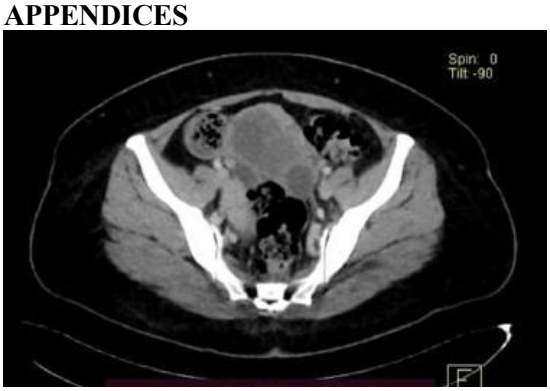
References

[1] Ilic M, Ilic I. Epidemiology of stomach cancer. World J Gastroenterol. 2022;28(12):1187–203.
[2] Thrift AP, El-Serag HB. Burden of gastric cancer. Clin Gastroenterol Hepatol. 2020;18(3):534–42.
[3] Yang WJ, Zhao HP, Yu Y, Wang JH, Guo L, Liu JY, Pu J, Lv J. Updates on global epidemiology, risk factors, and prognosis of gastric cancer. World J Gastroenterol. 2023;29(16):2452–68.
[4] Ajani JA, et al. Gastric Cancer, Version 2.2022, NCCN Clinical Practice Guidelines in Oncology. J Natl Compr Canc Netw. 2022;20(2):167–92.
[5] Lordick F, Carneiro F, Cascinu S, et al. Gastric cancer: ESMO Clinical Practice Guidelines. Ann Oncol. 2022;33(10):1005–20.
[6] Sun K, Jia K, Lv H, et al. EBV-positive gastric cancer: current knowledge and future perspectives. Front Oncol. 2020; 10: 583463.
[7] Machlowska J, Baj J, Sitarz M, et al. Gastric cancer: Epidemiology, risk factors, genomic characteristics and treatment strategies. Int J Mol Sci. 2020;21(11).
[8] Ning FL, Zhang NN, Wang J, et al. Prognostic value of modified Lauren classification in gastric cancer. World J Gastrointest Oncol. 2021;13(9):1184–

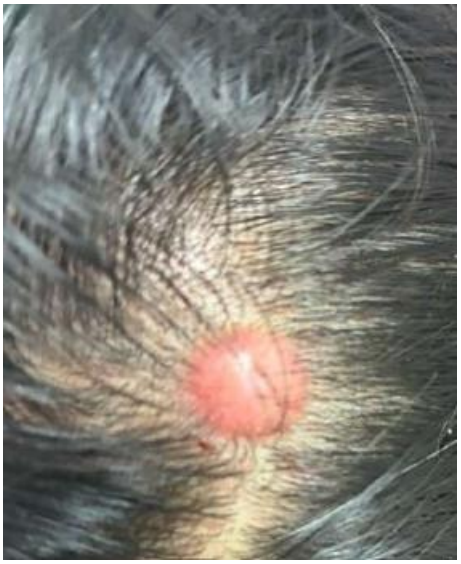
95.
[9] Hamid K, Hamza M, Rezac L. Linitis Plastica. SD Med. 2022;75(8):375.
[10] Smyth EC, Nilsson M, Grabsch HI, et al. Gastric cancer. Lancet. 2020;396(10251):635–48.
[11] Wang Q, Liu G, Hu C. Molecular classification of gastric adenocarcinoma. Gastroenterology Res 2019;12(6):275–82.
[12] Graham DY, Schwartz JT, Cain GD, et al. Prospective evaluation of the number of biopsies in the diagnosis of esophageal and gastric carcinoma. Gastroenterology. 1982;82(2):228–31.
[13] Sano T, Coit DG, Kim HH, et al. Proposal for a new gastric cancer TNM staging system. Gastric Cancer. 2017;20(2):217–25.
[14] Wakelin SJ, Deans C, Crofts TJ, et al. Comparison of CT, laparoscopic ultrasound and endoscopic ultrasound in preoperative staging of esophagogastric carcinoma. Eur J Radiol. 2002;41(2):161–7.
[15] Mihmanli M, Dilege E, Demir U, et al. Use of tumor markers as predictors of prognosis in gastric cancer. Hepatogastroenterology. 2004;51(59):1544–7.
[16] Simon M, Mal F, Perniceni T, et al. Accuracy of staging laparoscopy in detection of peritoneal spread in gastroesophageal adenocarcinoma. Dis Esophagus. 2016;29(3):236–40.
[17] Wanebo HJ, Kennedy BJ, Chmiel J, et al. Gastric cancer: patient care study by the American College of Surgeons. Ann Surg. 1993;218(5):583–92.
[18] Kubeček O, Laco J, Špaček J, et al. Pathogenesis, diagnosis and treatment of metastatic ovarian tumors: a comprehensive review. Metastasis Clin Exp 2017;34(5):295–307.
[19] Al-Agha OM, Nicastri AD. Krukenberg tumor: an overview. Arch Pathol Lab Med. 2006;130(11):1725–30.
[20] Bennett JA, Oliva E. Pathology of the adnexal mass. Clin Obstet Gynecol. 2015;58(1):3–27.
[21] Zulfiqar M, Koen J, Nougaret S, et al. Krukenberg tumors: imaging and clinical features update. AJR Am J Roentgenol. 2020;215(4):1020–29.
[22] Ma F, Li Y, Li W, et al. Metastasectomy improves survival of patients with gastric cancer and Krukenberg tumors: a retrospective analysis of 182 patients. Cancer Manag Res. 2019; 11: 10573–80.

1. Seow-En I, Hwarng G, Tan GHC, et al. Palliative surgery for Krukenberg tumors: 12-year experience and literature review. World J Clin Oncol. 2018;9(1):13–19.
2. Gaur NK, Shaikh O, Vijayakumar C, et al. Intestinal obstruction due to giant bilateral synchronous Krukenberg tumors of colorectal origin. Cureus. 2021;13(3):e14176.
3. Lin X, Han T, Zhuo M, et al. Retrospective study of clinicopathological characteristics and prognostic factors of Krukenberg tumor of gastric origin. J Gastrointest Oncol. 2022;13(3):1022–34.
4. Lionetti R, De Luca M, Travaglino A, et al. Clinical and pathology of Krukenberg tumor: systematic review and meta-analysis. Minerva Obstet Gynecol. 2022;74(4):356–63.
5. Jha S, Mitra S, Patra S, et al. Krukenberg tumor of ovary during pregnancy: learning from a mistake. Int J Gynecol Pathol. 2021;40(6):617–20.
6. Shi J, Huang A, Song C, et al. Effect of metastasectomy on prognosis of patients with ovarian metastasis from colorectal cancer: systematic review and meta-analysis. Eur J Surg Oncol. 2023;49(9):106961.
7. Tuzcu B, Sütcüoğlu O, Bayram EK, et al. Krukenberg presentation of recurrent gallbladder cancer tumor after a decade. J Gastrointest Cancer. 2023;54(1):264–7.
8. Sandhu S, Arafat O, Patel H, et al. Krukenberg tumor: a rare cause of ovarian torsion. J Clin Imaging Sci. 2012;2:6.
9. Shah B, Tang WH, Karn S. Transcoelomic dissemination and ovarian seeding during ovulation: a possible pathogenesis of Krukenberg tumor. J Cancer Res Ther. 2017;13(1):152–3.
10. Agnes A, Biondi A, Ricci R, et al. Krukenberg tumors: Seed, pathway, and soil. Surg Oncol. 2017;26(4):438–45.
11. Goidescu IG, Nemeti G, Preda A, et al. Krukenberg tumor in pregnancy: a rare case and literature review. J Matern Fetal Neonatal Med. 2022;35(25):7290–5.
12. Mendoza-Rosado F, Núñez-Isaac O, Espinosa-Marrón A, et al. Krukenberg tumor as incidental finding in term pregnancy: case report. J Med Case Rep. 2021;15(1):304.
13. Jeung YJ, Ok HJ, Kim WG, et al. Krukenberg tumors of gastric vs colorectal origin. Obstet Gynecol Sci. 2015;58(1):32–9.
14. Lionetti R, De Luca M, Travaglino A, et al. Prognostic factors in Krukenberg tumor. Arch Gynecol Obstet. 2019;300(5):1155–65.
15. Krathen RA, Orengo IF, Rosen T. Cutaneous metastasis: a meta-analysis of data. South Med J. 2003;96:164–7.
16. Yao GL, Tao YJ, Fan YG. Cutaneous metastasis from gastric cancer: manifestation, diagnosis, treatment and prognosis. Eur J Surg Oncol. 2024;50(2):107939.

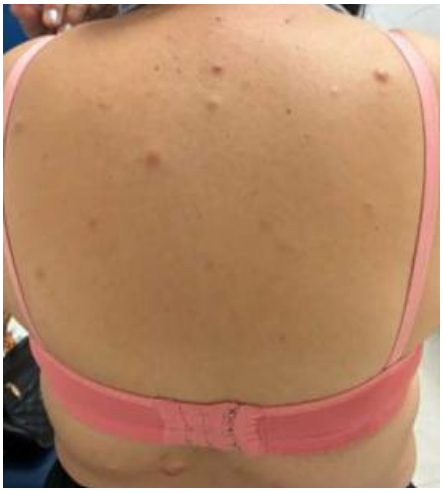
APPENDICES



Computed tomography revealed the presence of two solid masses of ovarian origin. The right lesion measured 78 × 35 × 65 mm and the left 54 × 73 × 74 mm. These characteristics are highly suggestive of bilateral ovarian metastases (Krukenberg tumor).
In addition, perisplenic ascites, a simple renal cyst (Bosniak I), and an umbilical hernia were observed as incidental findings.

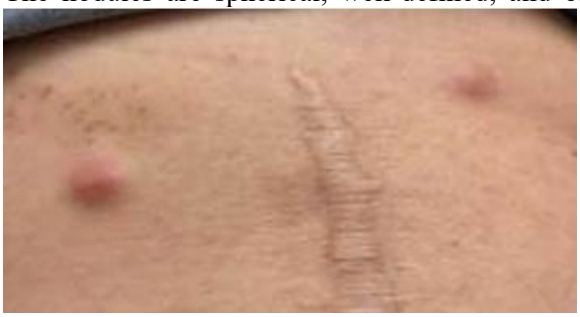


During the dermatological examination, multiple disseminated skin lesions were observed.
The lesion shown in the image is located on the scalp and is characterized as a nodular lesion with an erythematous appearance, a pinkish tone, and a smooth, shiny surface.
The lesion is semi-spherical in shape, with well-defined borders and a firm consistency upon palpation. Its size is estimated at approximately 1 cm in diameter.

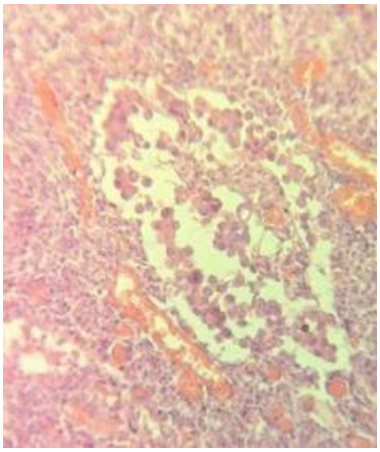


In the posterior thoracic region, the lesions are polymorphic, consisting of multiple erythematous-violaceous papules and nodular lesions. They are randomly distributed, vary in size, and range in diameter from 0.5 to 1.5 cm.
The lesions have a smooth surface, well-defined borders, and upon palpation they feel firm, mobile, and painless.

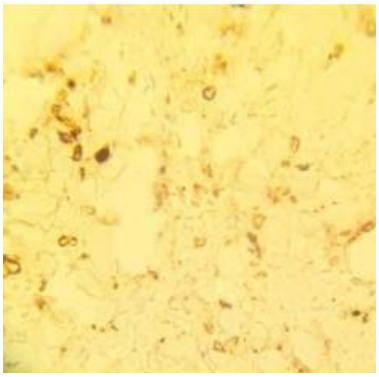
Erythematous subcutaneous nodules are evident in the abdominal wall.
These lesions are located in proximity to a midline surgical scar.
The nodules are spherical, well-defined, and of hard consistency.



Nests and cords of poorly differentiated carcinoma cells with "signet ring" morphology



Subcapsular lymph node metastasis by signet ring cell carcinoma



CK AE1/AE3 Positive cytoplasmic immunostaining in neoplastic cells