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Case Report / Приказ болесника

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Malignant chondroid syringoma with calvarial invasion and intracranial extension

Малигни хондроидни сирингом са инвазијом калварије и интракранијалним ширењем

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SUMMARY

Introduction Malignant chondroid syringoma (MCS) is an exceptionally rare malignant adnexal tumor with aggressive biological behavior. This report describes a rare case of frontotemporal MCS with calvarial invasion and intracranial extension.

Case Outline A 65-year-old male presented with a recurrent ulcerated cutaneous tumor in the left frontotemporal region, with four previous surgical excisions that had been histopathologically diagnosed as malignant basal cell carcinoma. Preoperative computed tomography (CT) and magnetic resonance imaging (MRI) revealed calvarial osteolysis with intracranial tumor extension. Radical excision with craniectomy, dural resection, and duraplasty was performed, followed by reconstruction using a local transposition flap and a secondary free split-thickness (Thiersch) skin graft. Histopathological and immunohistochemical analyses confirmed MCS with bone and perineural invasion and tumor involvement of the deep surgical margin (R1). Adjuvant conformal radiotherapy was administered. No recurrence or metastasis was observed during a nine-month follow-up period.

Conclusion MCS may clinically mimic other cutaneous malignancies, which can lead to delayed diagnosis. Wide surgical excision and long-term follow-up are essential for adequate disease control.

Keywords: sweat gland neoplasms; skin neoplasms; neoplasm invasiveness

САЖЕТАК

Увод Малигни хондроидни сиринго̀м (МЦС) представља изузетно редак малигни аднексални тумор са агресивним биолошким понашањем. Циљ овог рада је да се прикаже редак случај фронтотемпоралног МЦС са инвазијом калварије и интракранијалним ширењем.

Приказ болесника Мушкарац стар 65 година јавио се због рецидивантне улцерисане туморске лезије у левој фронтотемпоралној регији, уз податак о четири претходне хируршке ексцизије које су хистопатолошки биле дијагностиковане као малигни базоцелуларни карцином. Преоперативна компјутеризована томографија (ЦТ) и магнетна резонанца (МР) показале су остеолизу калварије са интракранијалним ширењем тумора. Изведена је радикална ексцизија тумора са краниектомијом, ресекцијом дуре и дурапластиком, након чега је урађена реконструкција локалним транспозиционим кожним режњем и секундарним слободним *split-thickness* (*Thiersch*) кожним графтом. Хистопатолошка и имунохистохемијска анализа потврдиле су МЦС са инвазијом кости и перинеуралном инвазијом, уз присуство тумора на дубокој ресекционој маргини (R1). Постоперативно је примењена адјувантна конформална радиотерапија. Током деветомесечног периода праћења није регистрован рецидив нити метастатска болест.

Закључак МЦС може клинички имитирати друге кожне малигнитете, што може довести до одложене дијагнозе. Широка хируршка ексцизија и дуготрајно праћење болесника кључни су за адекватну контролу болести.

Кључне речи: неоплазме знојних жлезда; неоплазме коже; инвазивност тумора

INTRODUCTION

Malignant chondroid syringoma (MCS) is an exceptionally rare malignant tumor of the eccrine sweat glands, first described by Hirsch and Helwig in 1961 as a “mixed tumor of the skin” with chondroid stroma [1]. Benign chondroid syringoma accounts for less than 0.1% of primary adnexal tumors and typically presents as a slow-growing, painless subcutaneous nodule in the head and neck region of middle-aged men [2, 3]. Its malignant counterpart is even rarer. By the early 1980s, only isolated cases had been reported, with Gupta et al. [4] publishing a collective

review in 1982. Subsequent reports confirmed its aggressive behavior and metastatic potential [5]. Approximately 51 cases have been documented worldwide [3, 6]. Unlike the benign type, MCS more commonly affects the extremities and trunk and shows a female predominance [3]. It is a potentially aggressive tumor with a tendency for local recurrence after inadequate excision and has the capacity for distant metastasis [7].

We present a rare case of MCS in the left frontotemporal region of a 65-year-old male, with calvarial invasion and intracranial extension.

CASE REPORT

A 65-year-old male patient was admitted to the University Clinic for Maxillofacial Surgery in Skopje due to a recurrent cutaneous tumor in the left frontotemporal region. The patient reported four previous surgical excisions in the same region in another hospital in 2018, 2019, 2021, and 2022, with repeated histomorphologic diagnoses of basal cell carcinoma, without immunohistochemical confirmation of the tumor cell origin. These pathohistological reports were issued by a non-reference pathology laboratory in a regional center. Clinically, the lesion presented as a nodular mass with central ulceration and a peripheral telangiectatic vessels, elevated above the base, firm and painless on palpation, with scar tissue from previous surgeries (Figure 1). An incisional biopsy was performed. Preoperative computed tomography (CT) and magnetic resonance imaging (MRI) of the head and neck revealed bone invasion and osteolysis in the left frontotemporal region, with intracranial tumor extension (Figure 2). Due to confirmed intracranial extension, multidisciplinary surgical treatment was indicated.

The patient underwent surgery at the Neurosurgery Clinic in Skopje, performed by a team consisting of a neurosurgeon, plastic surgeon, and maxillofacial surgeon under general

endotracheal anesthesia. Radical tumor excision, craniectomy, and excision of the dura mater followed by duraplasty were performed (Figure 3). The primary surgical defect was reconstructed using a local transposition skin flap, while the secondary defect was reconstructed with a free split-thickness skin graft according to Thiersch from the anterior thigh (Figure 4).

The surgical specimen was submitted to the Institute of pathology at the Medical Faculty in Skopje, which is the central reference pathohistological laboratory in the country. Macroscopic examination of the surgical specimen revealed lobulated tumor tissue with a maximum dimension of 3.5 cm. Microscopically, tissue sections demonstrated skin covered by a thin epidermis showing central ulceration. At this level, a malignant neoplasm composed of round to oval tumor cells arranged in nests, cribriform, and trabecular structures was observed (Figure 5). The peripheral cells of the nests had a cuboidal appearance (Figure 6). The tumor cells exhibited moderate cellular and nuclear atypia. The stroma was fibro-collagenous, focally thickened, with areas showing a chondroid appearance (Figure 7). A moderate lymphocytic inflammatory infiltrate was present within the stroma. The tumor diffusely infiltrated into deeper tissues, involving subcutaneous adipose tissue and underlying striated muscle. Tumor involvement was present at the deep resection margin, while peripheral resection margins were free of tumor. Lymphovascular invasion was not identified; however, perineural invasion was present.

Additionally, tumor infiltration into fragments of bone tissue was confirmed. Immunohistochemical analysis demonstrated expression of high-molecular-weight cytokeratin (CKHMW) in tumor cells (Figure 8), as well as focal weak expression of smooth muscle actin (SMA) (Figure 9). In contrast, there was no expression of epithelial membrane antigen (EMA), epithelial-specific antigen (ESA), cytokeratin 7 (CK7), cytokeratin 8/18, cytokeratin 20

(CK20), c-kit (CD117), CD34, or carcinoembryonic antigen (CEA). The proliferative index Ki-67 was high, approximately 40–50% (Figure 10). The histomorphologic and immunophenotypic findings were consistent with MCS. According to the UICC classification, the tumor was staged as pT4a, N0, M0, G2, L0, V0, R1, corresponding to stage IVA. Following surgical treatment, due to high-risk pathological features—including tumor infiltration of the deep resection margin (R1) and confirmed perineural invasion (Pn1) – adjuvant conformal radiotherapy was administered, with a total tumor dose (TTD) of 60 Gy delivered in 30 daily fractions of 2 Gy each. At 9 months after surgery, there was no evidence of local, locoregional, or distant recurrence.

Ethics: Written informed consent was obtained from the patient for publication of this case report and any accompanying images. All identifying details have been removed or anonymized to ensure patient privacy.

DISCUSSION

MCS, also known as malignant cutaneous mixed tumor (CMT), represents an exceptionally rare malignant tumor of the skin adnexa [8]. Four mechanisms of malignant transformation in cutaneous mixed tumors have been described in the literature [9]: *De novo* malignant development, malignant transformation of a long-standing benign CMT that begins to grow rapidly, secondary skin infiltration by a malignant mixed tumor originating from another organ such as the salivary glands, and in extremely rare cases development from a pre-existing apocrine or eccrine adnexal tumor, such as spiradenoma. Clinically, MCS presents as a firm, painless dermal or subcutaneous nodule with slow growth, often mimicking benign lesions [6]. However, rapid enlargement, ulceration, and deep invasion may occur [7]. Lesions exceeding 3 cm in size are typically indicative of malignancy, although benign lesions over 10 cm have

also been documented [8, 10, 11]. Head and neck involvement is uncommon for the malignant variant, with only a limited number of reported cases [8]. Our case is notable for aggressive behavior with calvarial and dural invasion, a rare finding documented only sporadically [12]. Recent reports of chondroid syringoma with bone erosion support careful imaging and complete excision when deep invasion is suspected [13]. Osseous metaplasia in benign chondroid syringoma may mimic bone involvement and should be distinguished from true bone invasion in malignant cases [14]. Due to nonspecific clinical features, MCS is frequently misdiagnosed. The differential diagnosis of MCS includes a sebaceous cyst, dermoid cyst, neurofibroma, pilomatrixoma, amelanotic nevus, and basal cell carcinoma [15]. Excisional biopsy with histopathological and immunohistochemical analysis remains the diagnostic gold standard [6, 10]. Similar to previously reported cases [12], our lesion was repeatedly misinterpreted as basal cell carcinoma, likely contributing to delayed diagnosis. Histologically, our case demonstrates nests and trabeculae of atypical epithelial cells within a sparse chondromyxoid stroma [8]. Perineural invasion, present in our case, has also been documented in malignant forms [6]. Immunohistochemically, MCS typically shows biphasic expression. The epithelial component is positive for cytokeratins (including CK5/6), EMA, CEA, and p63. Areas of mesenchymal chondroid differentiation demonstrate S-100 and vimentin positivity [16]. In our case, positivity for CK5/6 and partial SMA expression, along with negativity for EMA, CEA, CK7, and other markers, and a high Ki-67 index (40–50%), support adnexal origin and the diagnosis of MCS, despite absence of all typical glandular markers. Fine-needle aspiration biopsy (FNAB) may aid in suspected cases [17]. Imaging modalities, including CT and MRI, are essential for assessing local extension and metastases [6]. Recurrence rates reach 50%, and distant metastases occur in up to 60% of cases [3,18]. Recent reports of pulmonary metastasis further emphasize the metastatic potential of MCS [19]. Wide surgical excision with tumor-free margins remains the cornerstone of treatment, often complemented by adjuvant

radiotherapy, with or without chemotherapy [20]. At 9 months after treatment, the patient remained disease-free. Given the high recurrence potential and reports of late metastases even decades after excision [8], long-term follow-up is mandatory.

MCS is a rare and aggressive adnexal tumor that frequently results in delayed or incorrect diagnosis due to its clinical and histomorphological variability. Our case, characterized by calvarial bone invasion and intracranial extension, highlights its potential for significant local destruction and underscores the necessity of early radical surgical excision. The high local recurrence and regional metastasis rates (50–60%) justify the use of adjuvant radiotherapy in patients with positive surgical margins or high-risk pathological features. Long-term and careful follow-up is essential, as recurrences have been documented even two decades after primary treatment.

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Conflict of interest: None declared.

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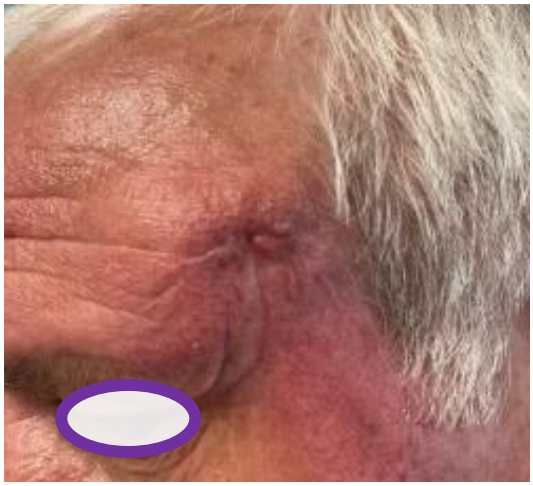

Figure 1. Clinical appearance of malignant chondroid syringoma

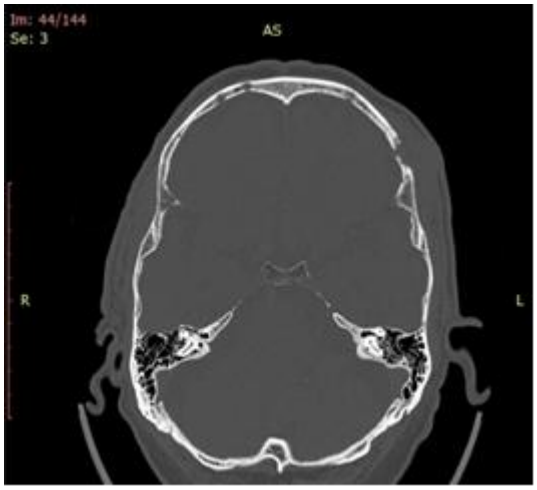

Figure 2. Preoperative computed tomography

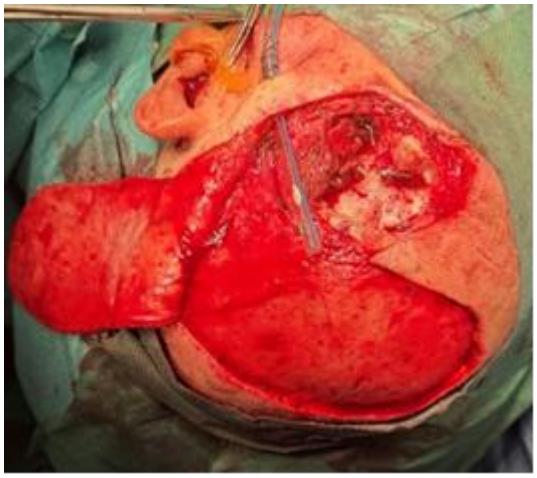

Figure 3. Surgical procedure: tumor excision, craniectomy, duraplasty and flap design

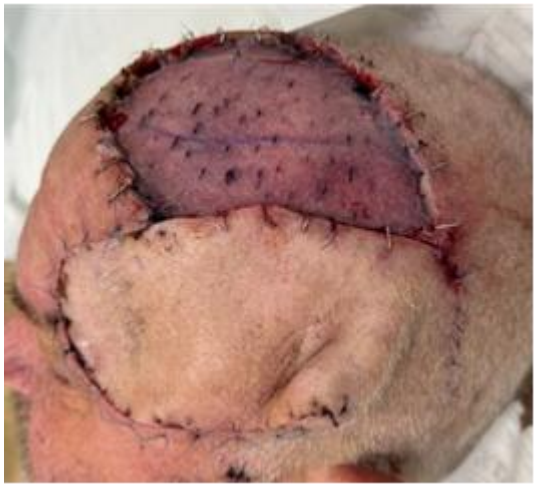

Figure 4. Postoperative appearance

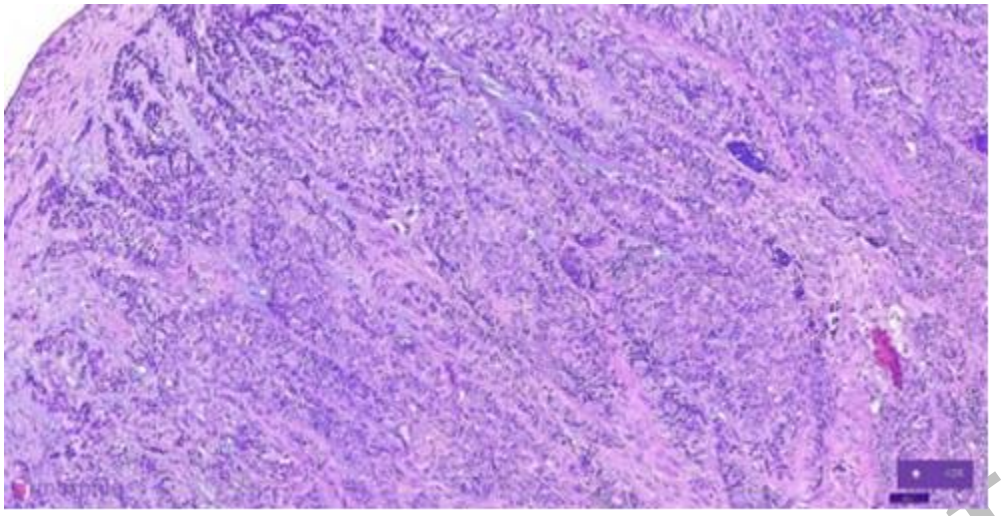

Figure 5. Digital micrography – Hematoxylin & Eosin (× 40)

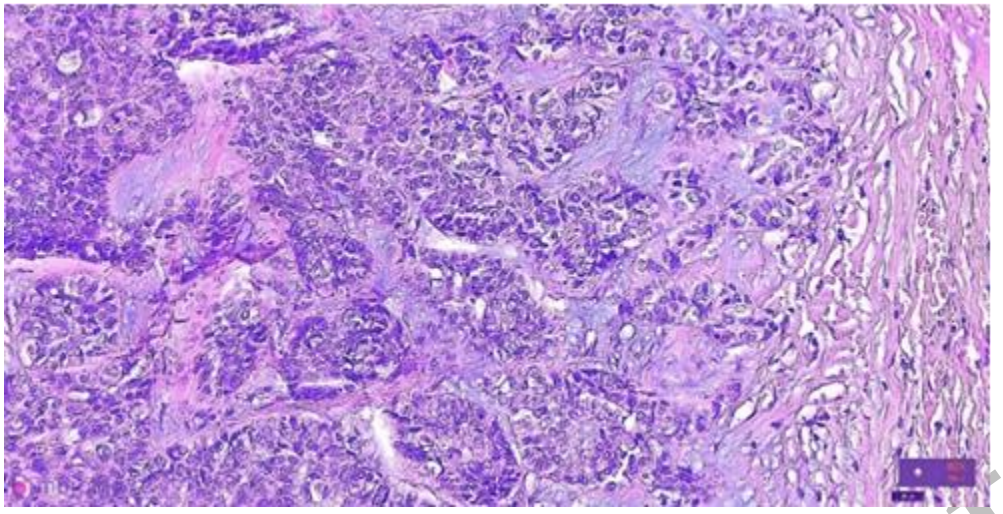

Figure 6. Digital micrography – Hematoxylin & Eosin (× 80)

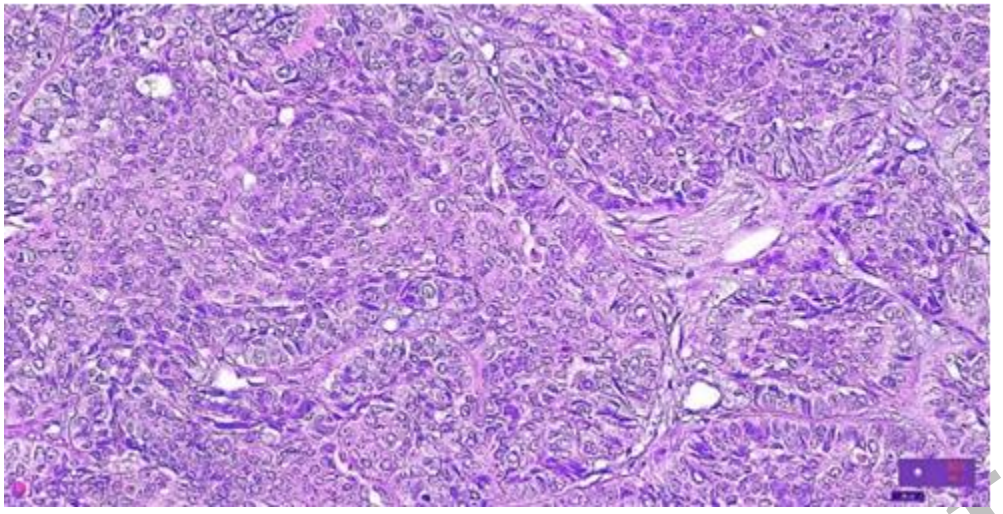

Figure 7. Digital micrography – Hematoxylin & Eosin (× 80)

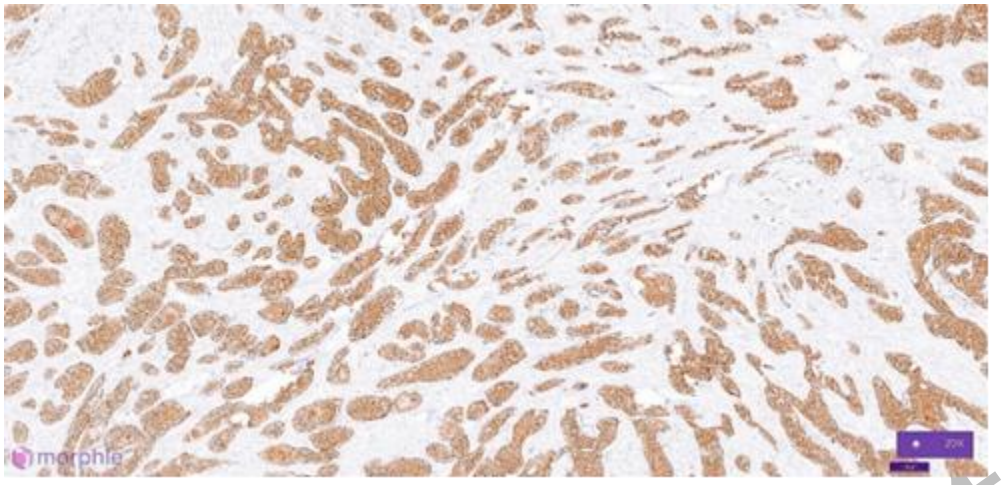

Figure 5. Digital micrography – high molecular weight cytokeratin (CKHMW) (× 20)

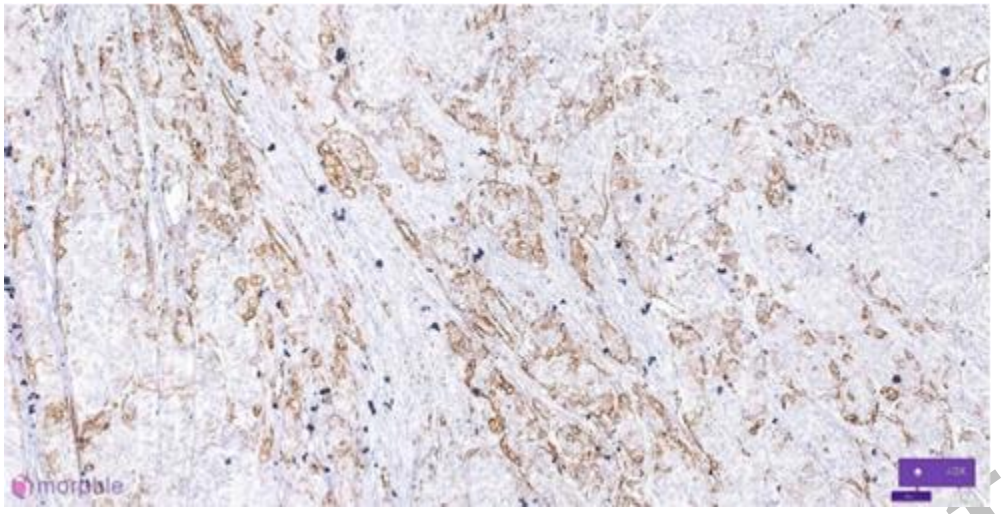

Figure 9. Digital micrography – smooth muscle actin (SMA) (× 40)

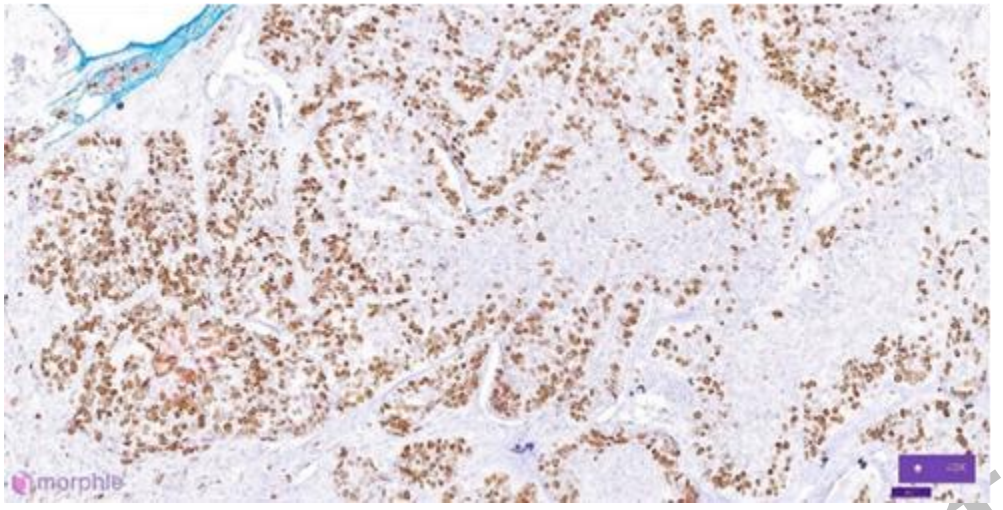

Figure 6. Digital micrography – Ki-67 (× 40)

