# SEMINÁRIO DE DERMATOPATOLOGIA

Núcleo de Especialidades – SBP

23/06/2012

# SEMINÁRIO DE DERMATOPATOLOGIA

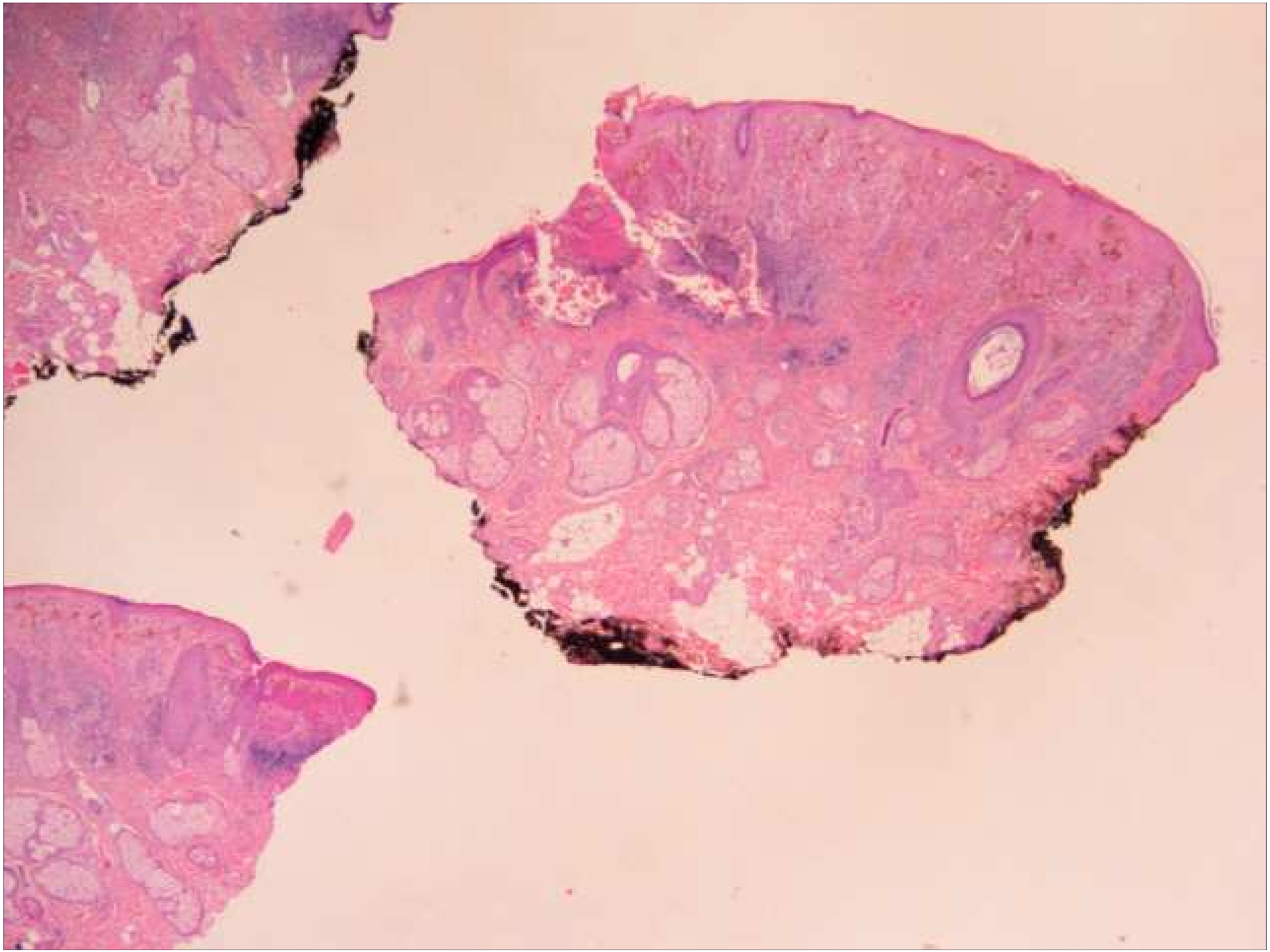
ANATOMED
INSTITUTO DE ANATOMIA PATOLÓGICA DE BAURU

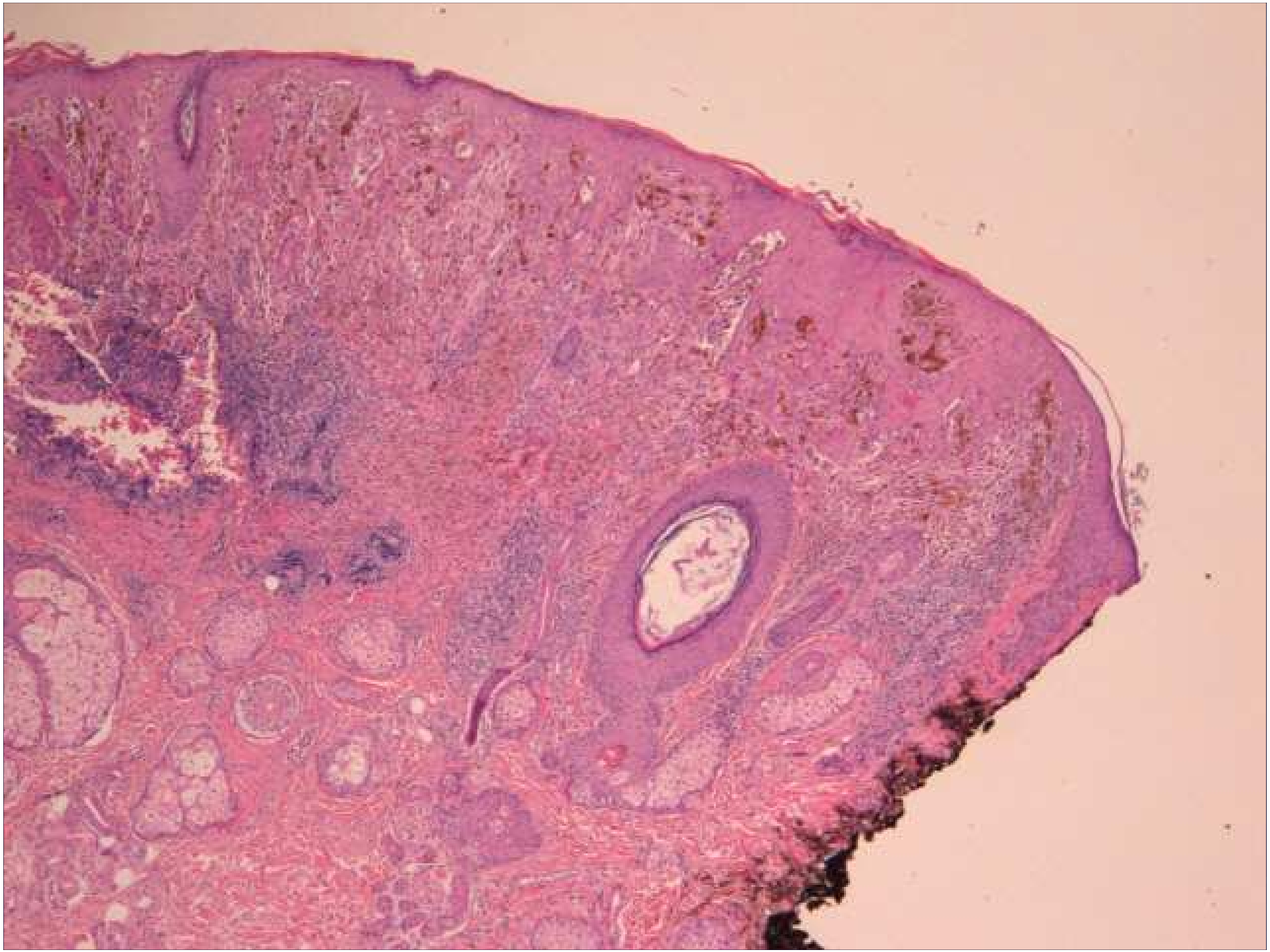
VERONESE
Patologia e Citologia

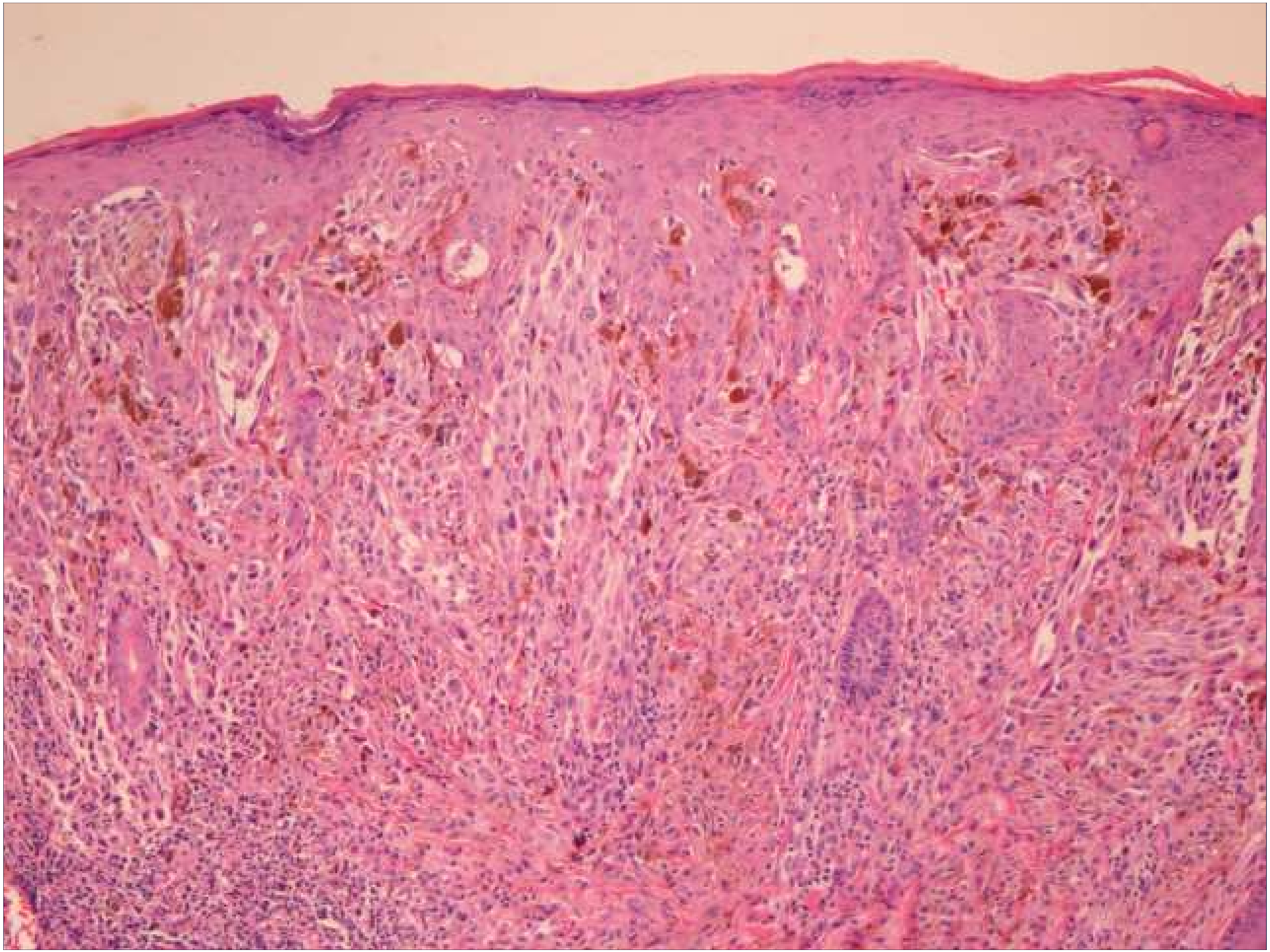
**ANATOMED - BAURU**

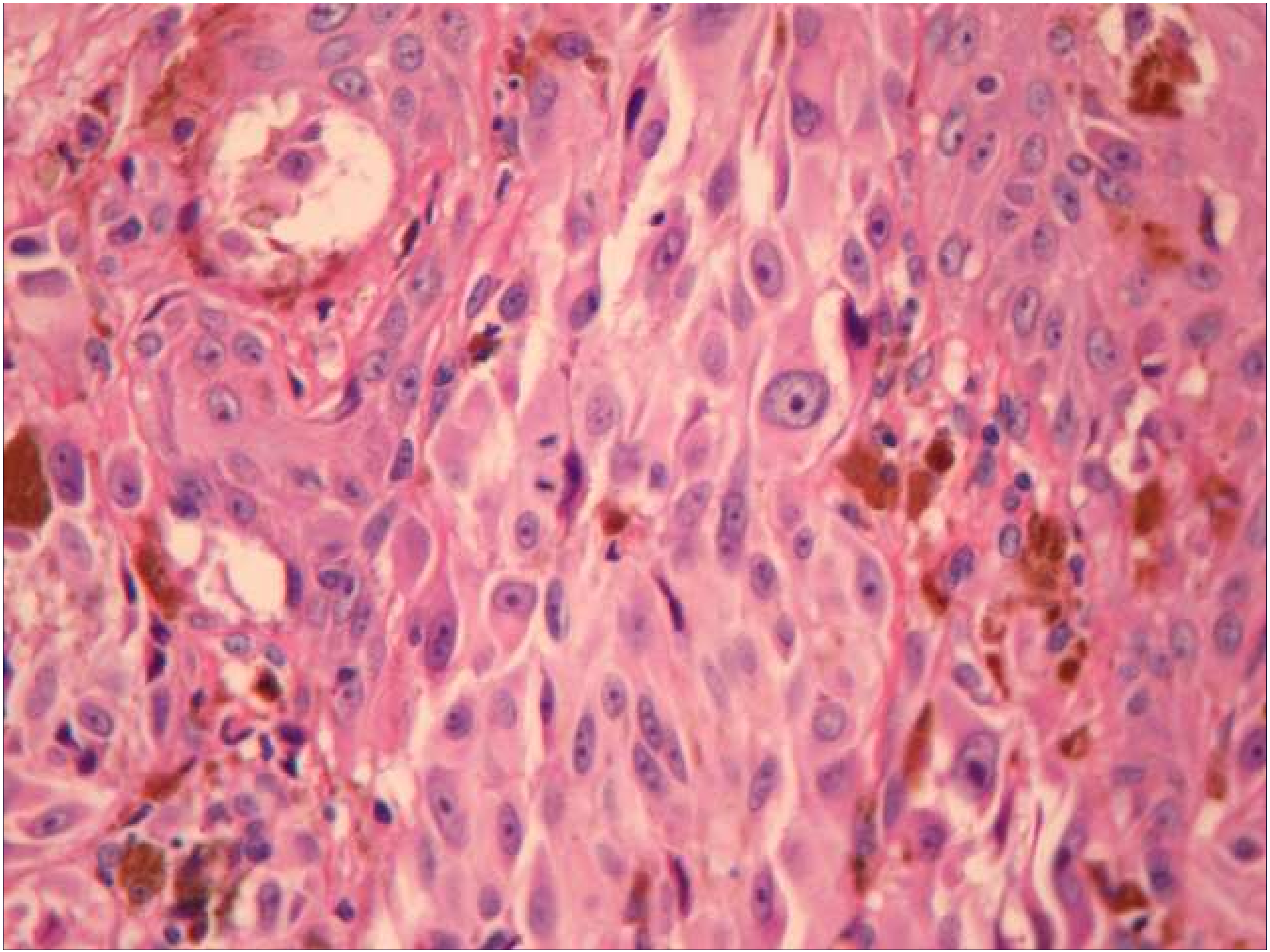
**VERONESE PATOLOGIA E CITOLOGIA – ARAÇATUBA**

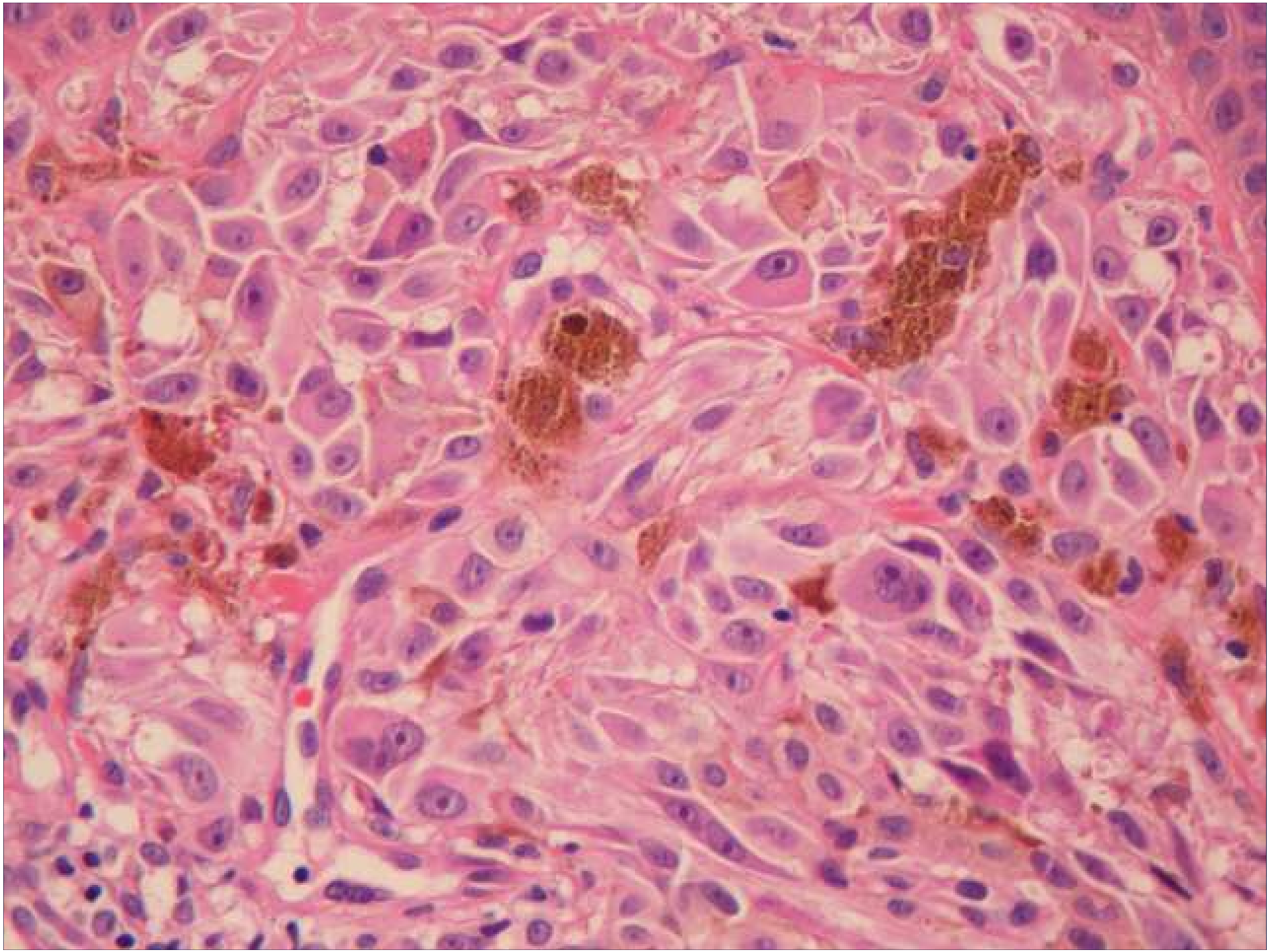
- Paciente feminina, 37 anos
- Lesão de pele da face com cerca de 0,5 cm
- Evolução desconhecida

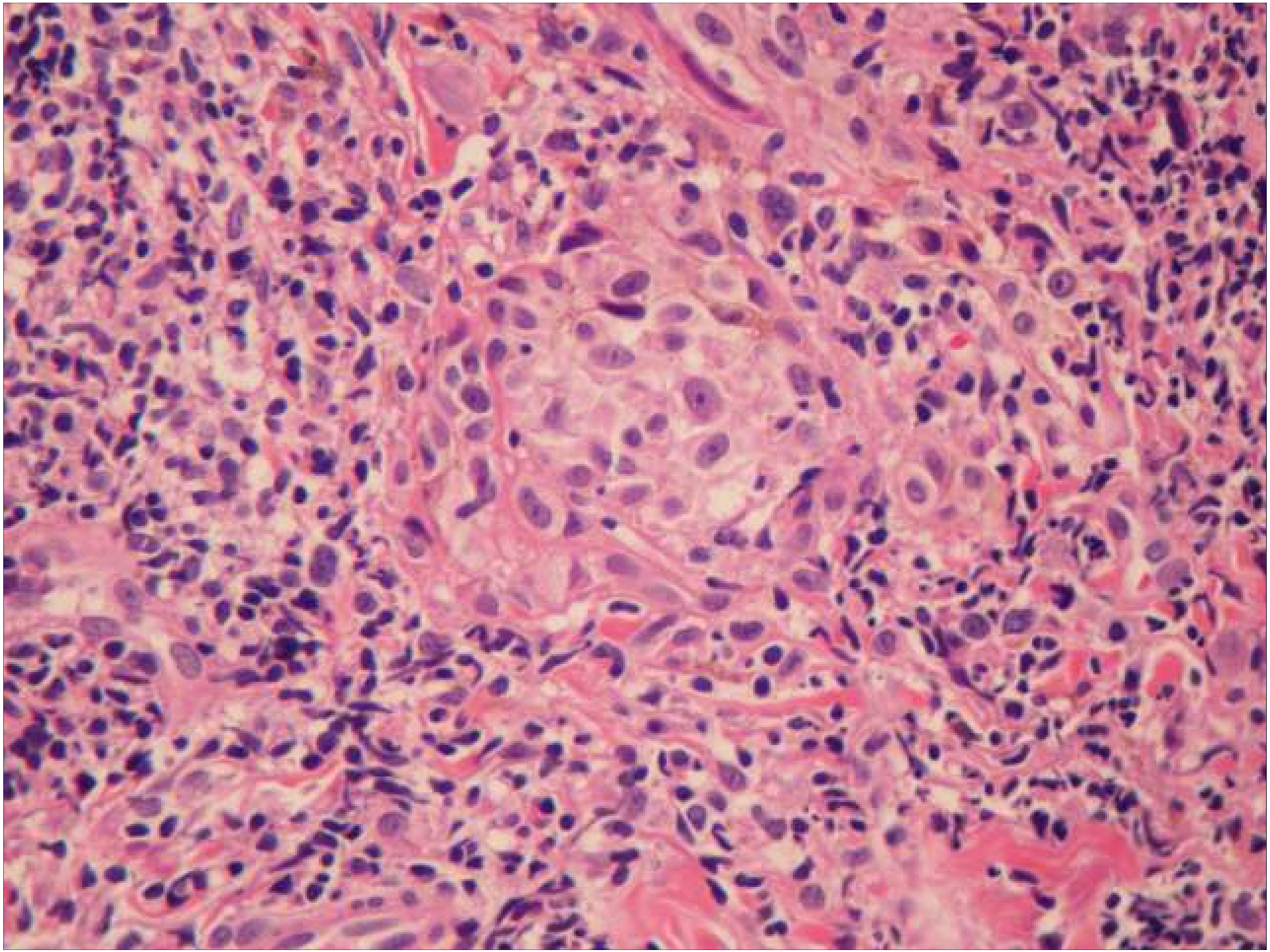


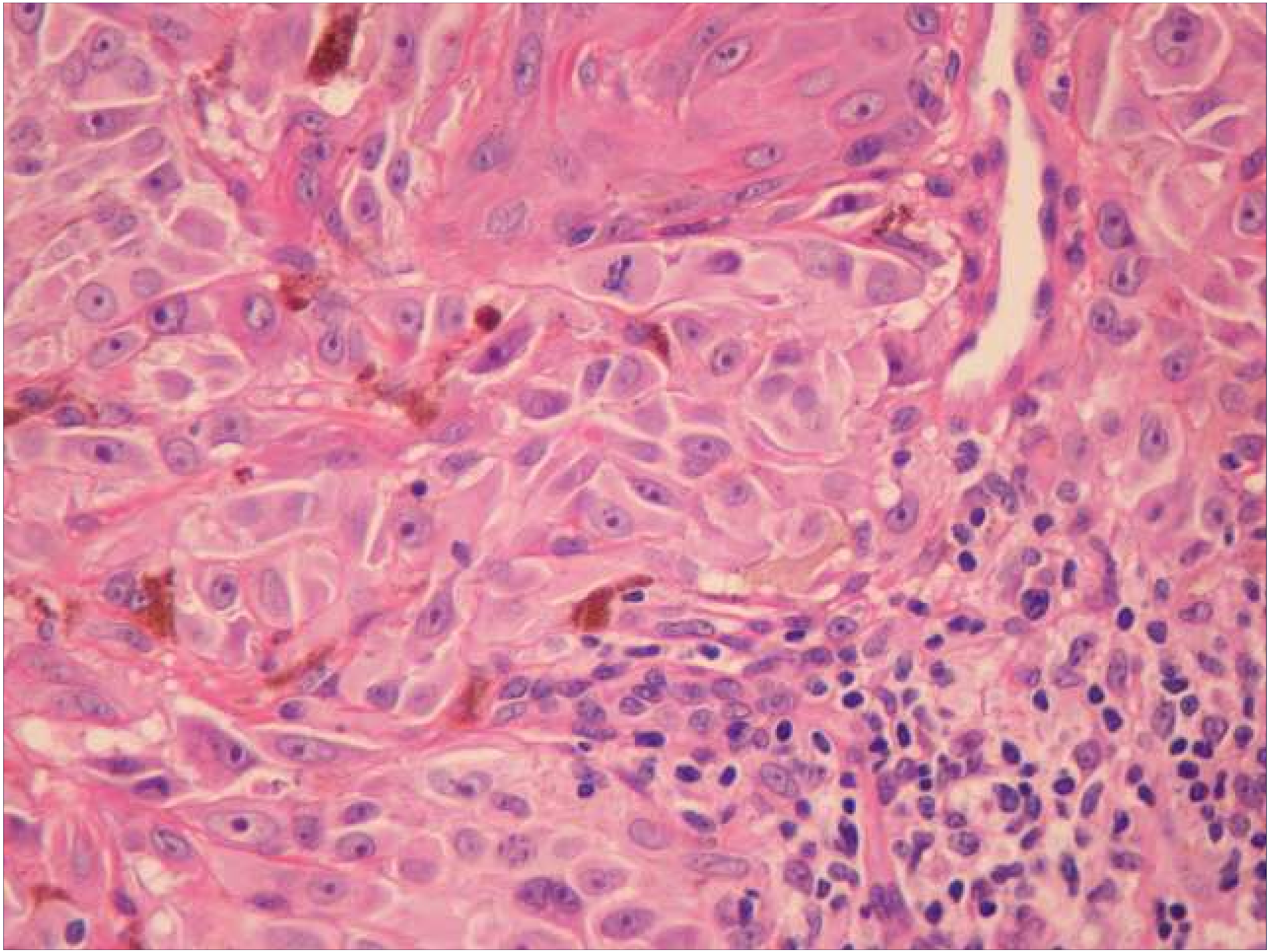


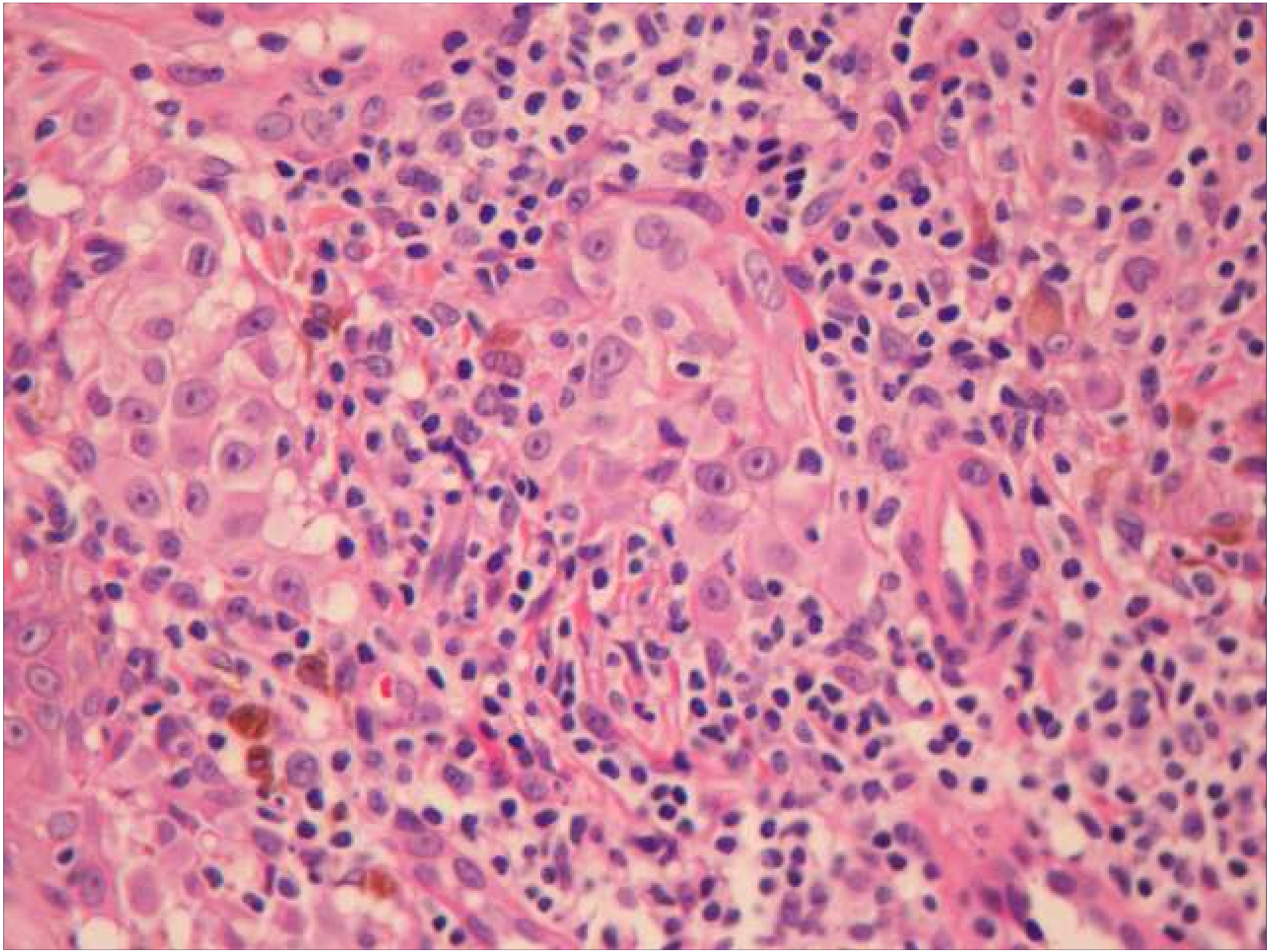


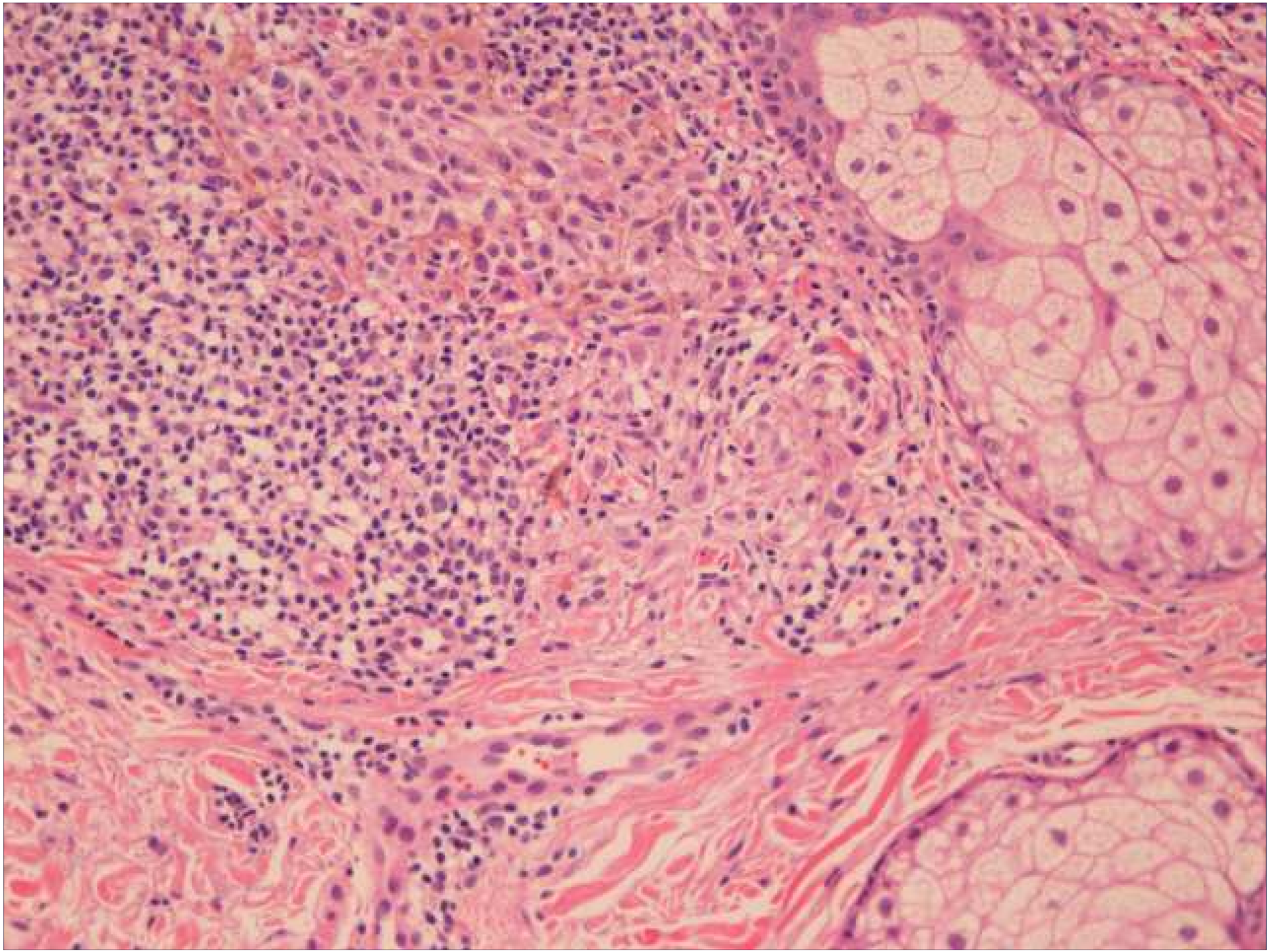


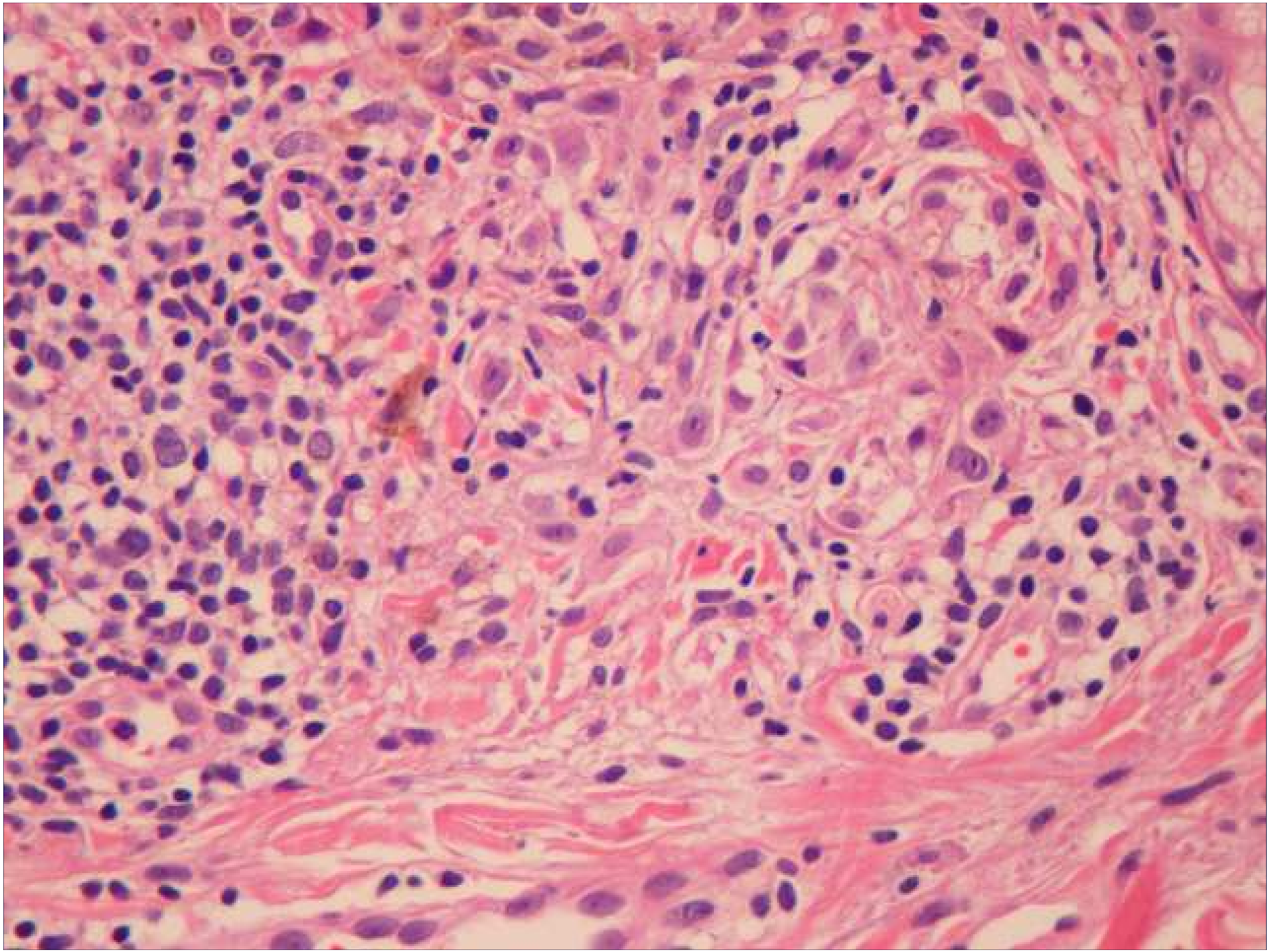


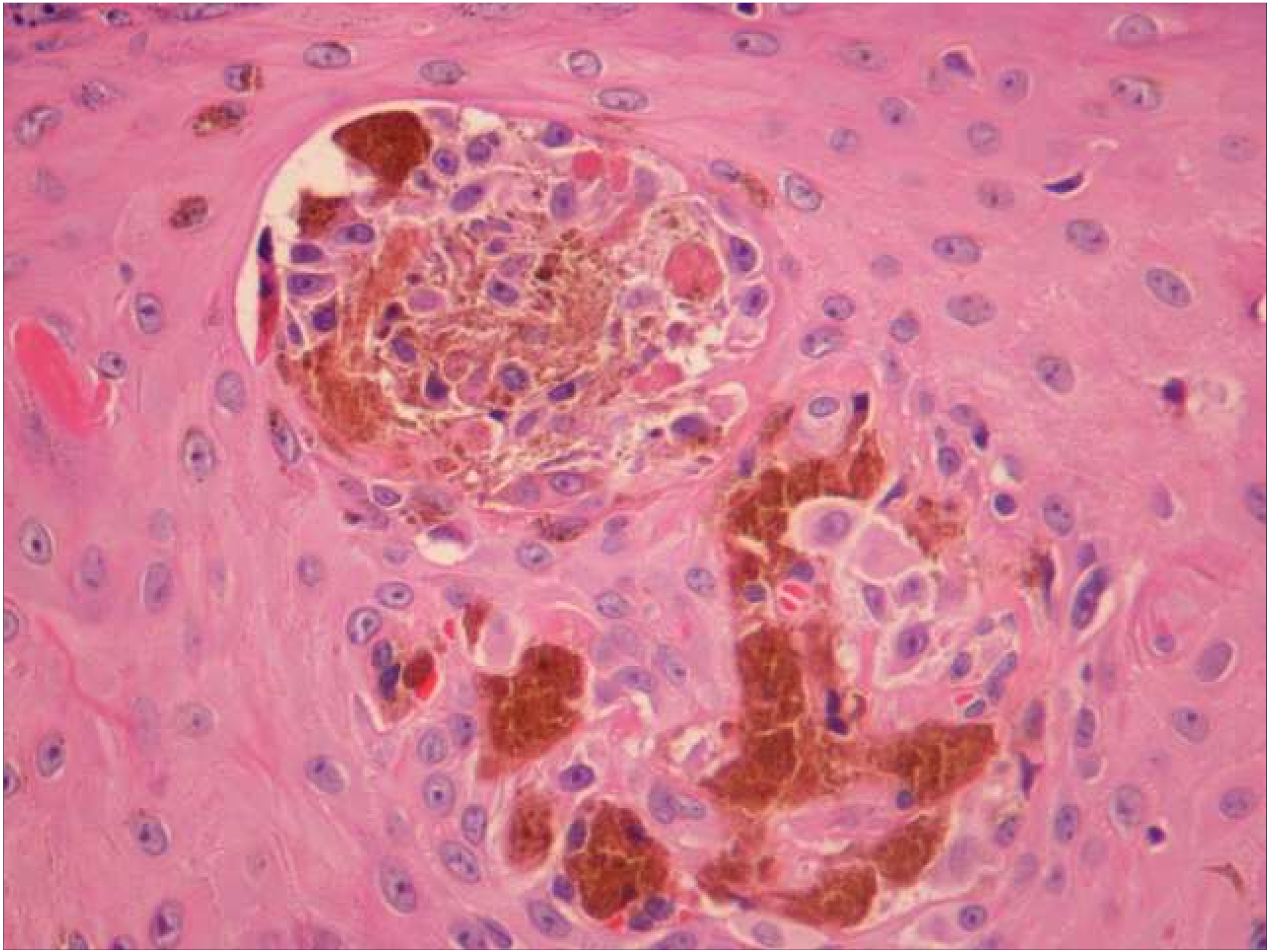


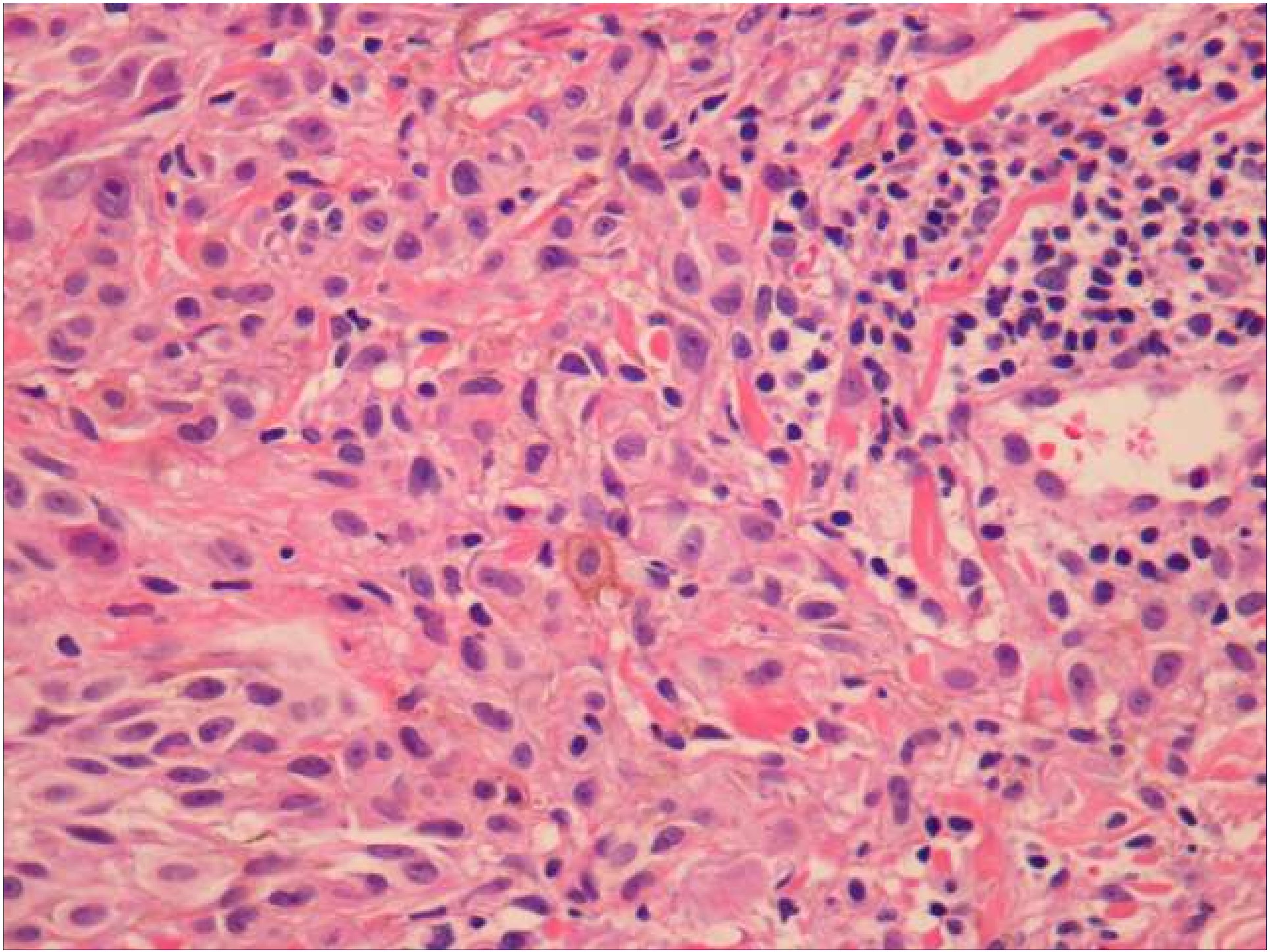












# LAUDO PROVISÓRIO

Minha opinião: **LESÃO SPITZÓIDE ATÍPICA DE COMPORTAMENTO BIOLÓGICO INDETERMINADO ("STUMP")** - caracterizada por epiderme irregularmente hiperplásica contendo ninhos juncionais de células muito atípicas, grandes, de citoplasma eosinofílico amplo e núcleos volumosos, com cromatina pouco grosseira e com nucléolo eosinofílico muito grande e irregular; estas células estão presentes também na derme superficial, formando massa sólida sem ninhos expansivos, atingindo a profundidade máxima de 1,05 mm (medida efetuada pelo método de Breslow), apresentando áreas com aspecto duvidoso de maturação, sem mitoses e com infiltrado linfocitário esparso na base da lesão. Nota-se a presença de pigmentos de melanina em toda a espessura da lesão, embora seja bastante menos frequente na profundidade. Na porção basal da epiderme e nos ninhos juncionais, foram encontrados vários corpos de Kamino.

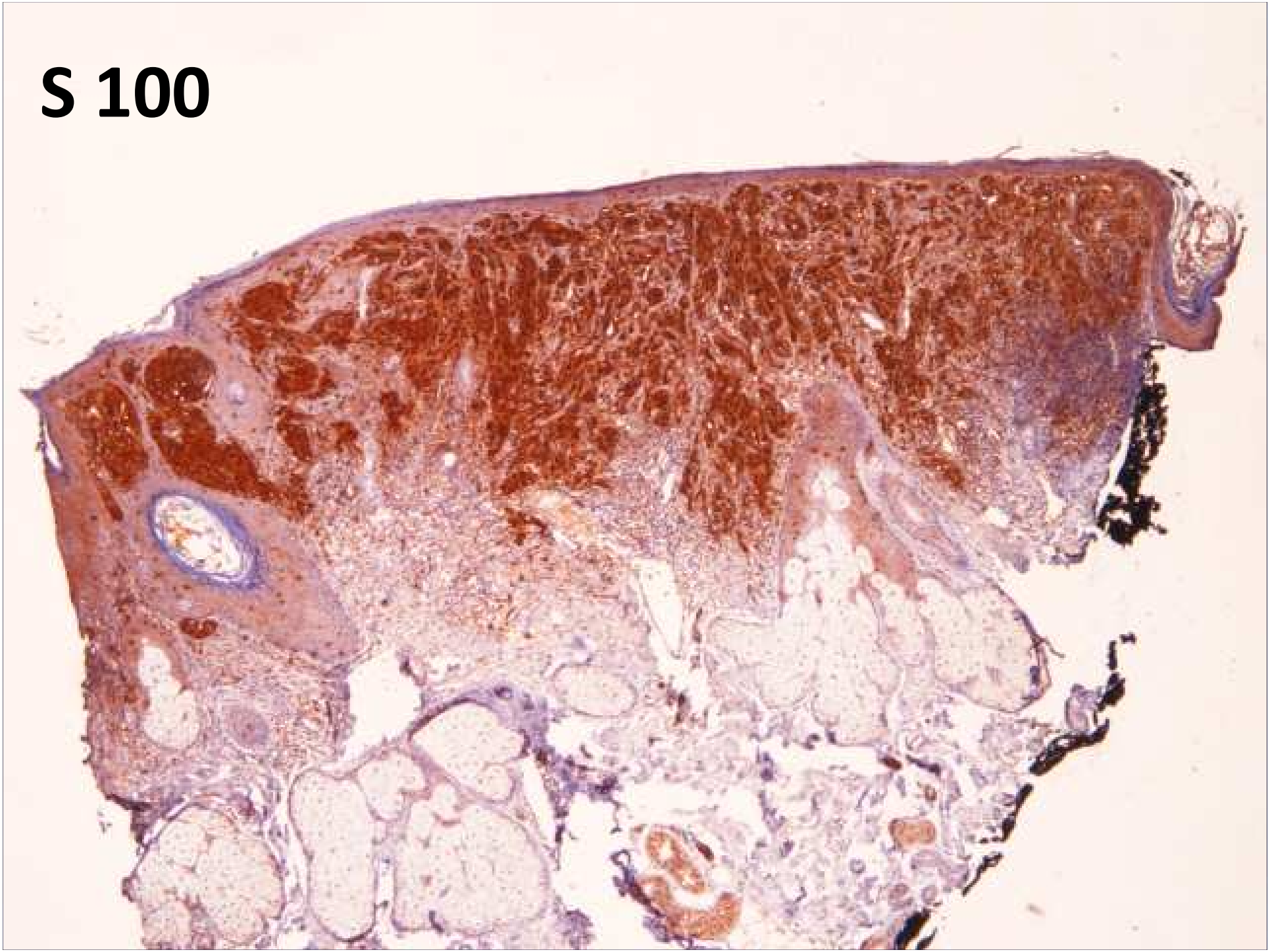
NOTAS: 1. Embora a lesão seja pequena (<5mm), não esteja ulcerada, não atinja a hipoderme e não contenha mitoses profundas, atípicas ou em grande número, as atipias nucleares são muito intensas e preocupantes.

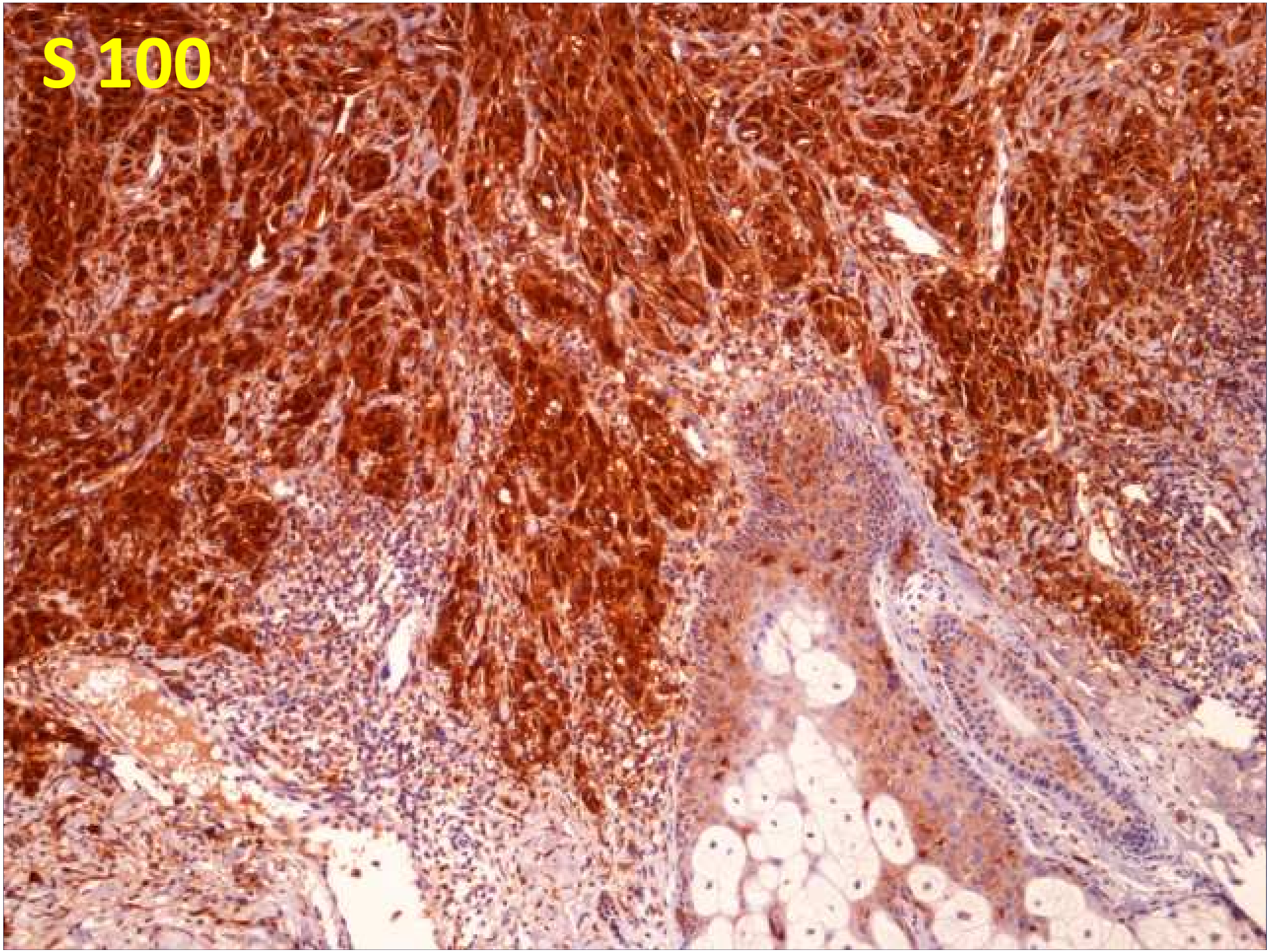
2. Na tentativa de definir onde esta lesão se situa no espectro das lesões spitzóides (benigna, borderline ou maligna), julgamos necessário o auxílio da imuno-histoquímica. Solicitamos a execução de exames com os seguintes anticorpos: S100, HMB45, MIB1, BCL2, Ciclina D1, e se possível, p21, CD40, CD44 e CD49.

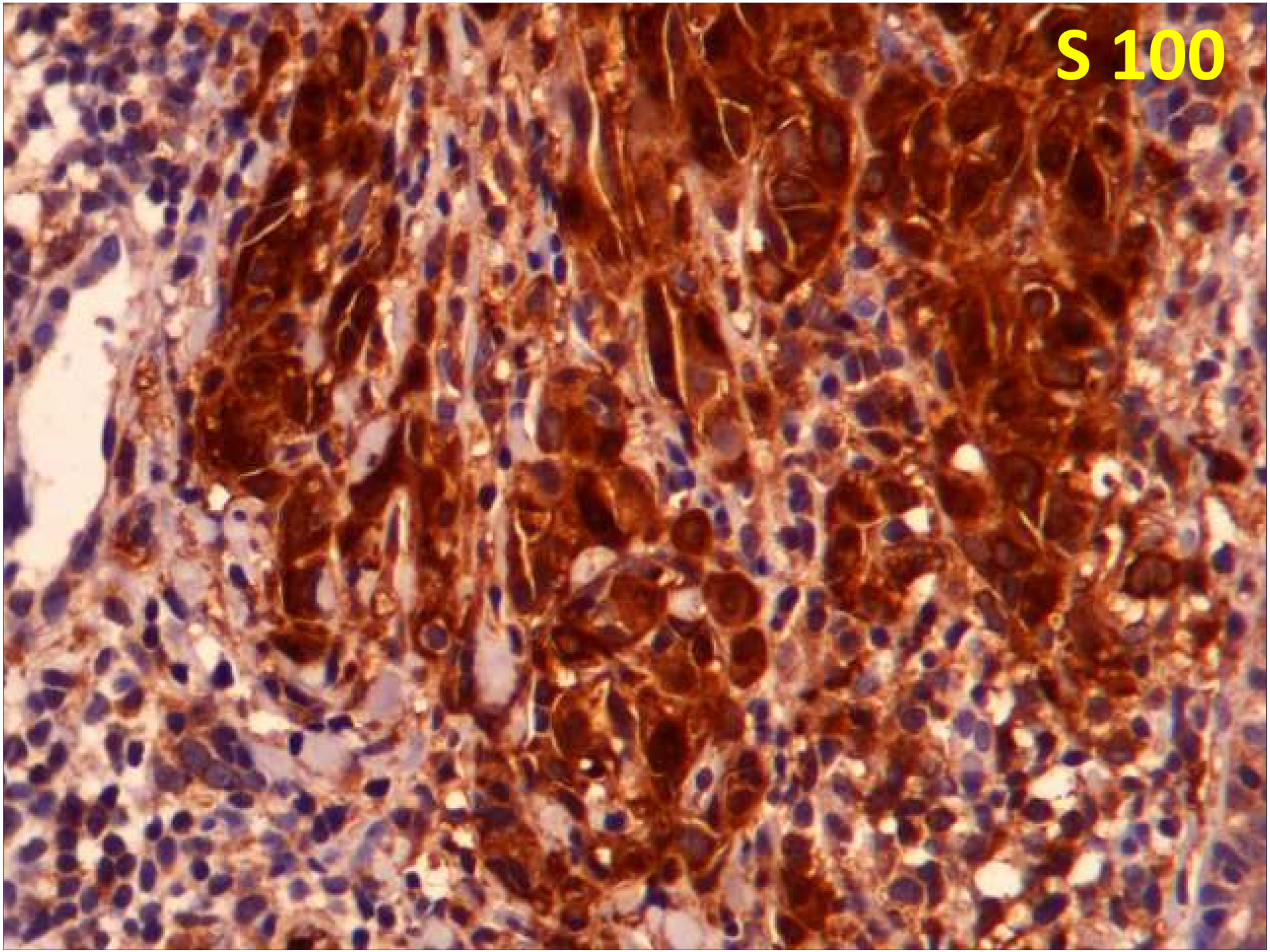
- MIB-1 expression is usually limited to small numbers (less than 5%) of cells in the superficial part of the dermal component of Spitz nevus compared with melanoma in which positive cells are often identified throughout the lesion.[78–80]
- Bcl-2 is frequently negative or only weakly positive in Spitz nevus, whereas in melanoma the majority of tumors are strongly positive.[81]
- Cyclin D1 is overexpressed in melanoma throughout the tumor. Contrariwise, in Spitz nevus, although the superficial aspect may be strongly positive, there is a progressive diminution in labeling with depth, mirroring the histological feature of maturation.[82,83]
- p53 is typically absent in Spitz nevus but is positive in many nodular melanomas.[82]
- p21 has been found to be overexpressed in Spitz nevus compared to melanoma, while survivin and topoisomerase II alpha, in contrast, are overexpressed in melanoma.[80,84]
- Decreased nuclear immunoreactivity for p16 in the dermal melanocytic component is present in melanoma as compared with Spitz nevus.[85] Loss of both cytoplasmic and nuclear p16 immunoreactivity seems to be more specific for melanoma than loss of nuclear reactivity alone.[85] Such tumors have shown increased desmoplasia and pleomorphism with a distinct infiltrating lower border but these features do not, however, appear to correlate with worsening biological behavior.
- CD40 is not expressed by Spitz nevus but is present in the dermal component of up to 40% of melanomas.[86]
- CD44 expression is maintained in Spitz nevus, in contrast to melanoma in which it is decreased.[87]
- Cdc7, a serine-threonine kinase is overexpressed in atypical Spitz nevus and melanoma, as compared to Spitz nevi.[88]
- No differences in the expression of c-kit (CD117) between Spitz nevus and melanoma has been detected by immunohistochemistry in one study.[89]
- CD99 staining has been detected in 56% of spitzoid melanomas and only 5% of Spitz nevi. While staining in melanomas is frequently diffuse and strong, such a pattern is not observed in Spitz nevi.[90]

None of these immunohistochemical stains is entirely reliable, and challenging lesions often produce equivocal results. The final diagnosis as always will depend on close clinicopathologic correlation and interpretation of the sections stained with hematoxylin and eosin remains the gold

# S 100




S 100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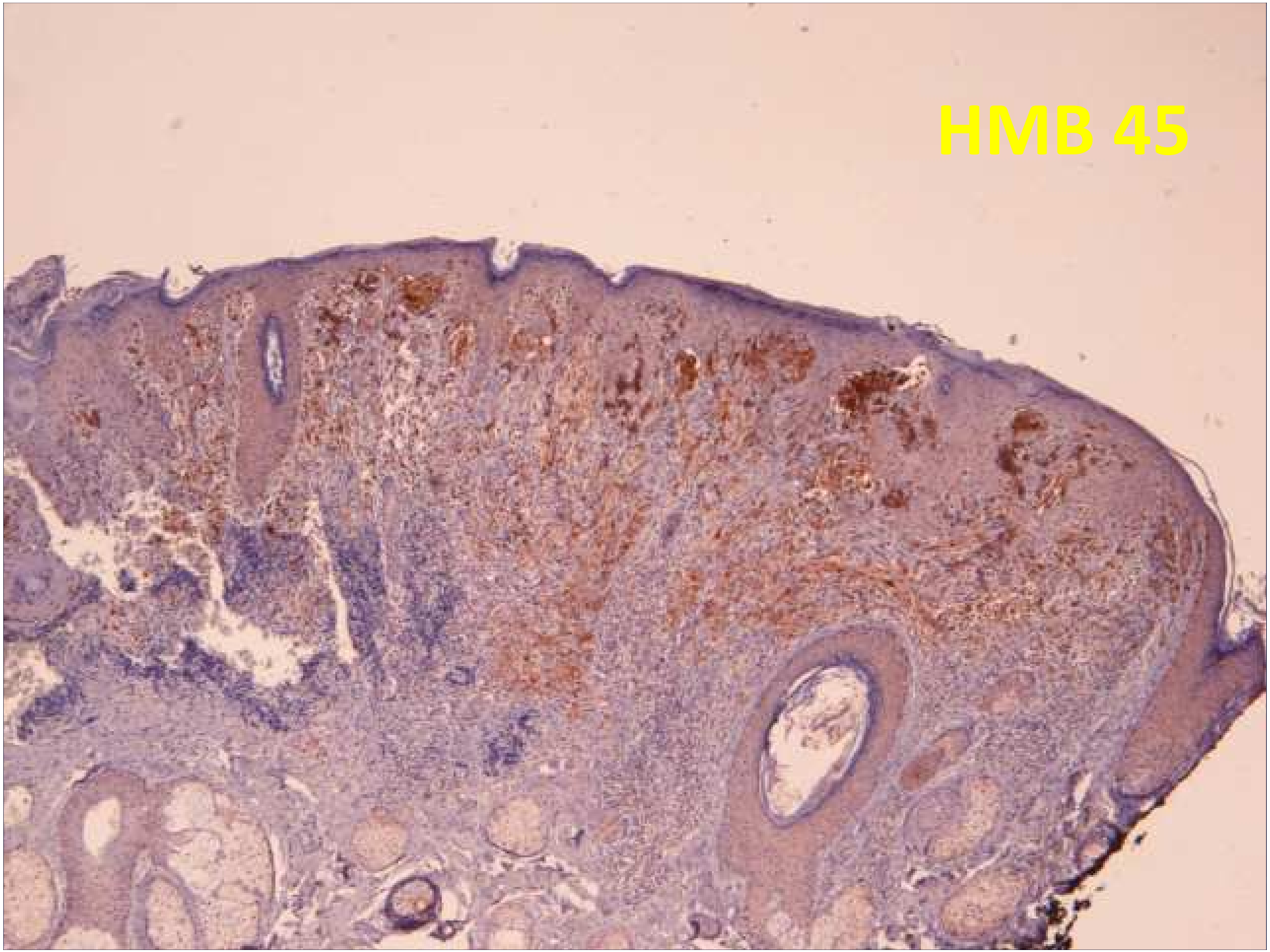
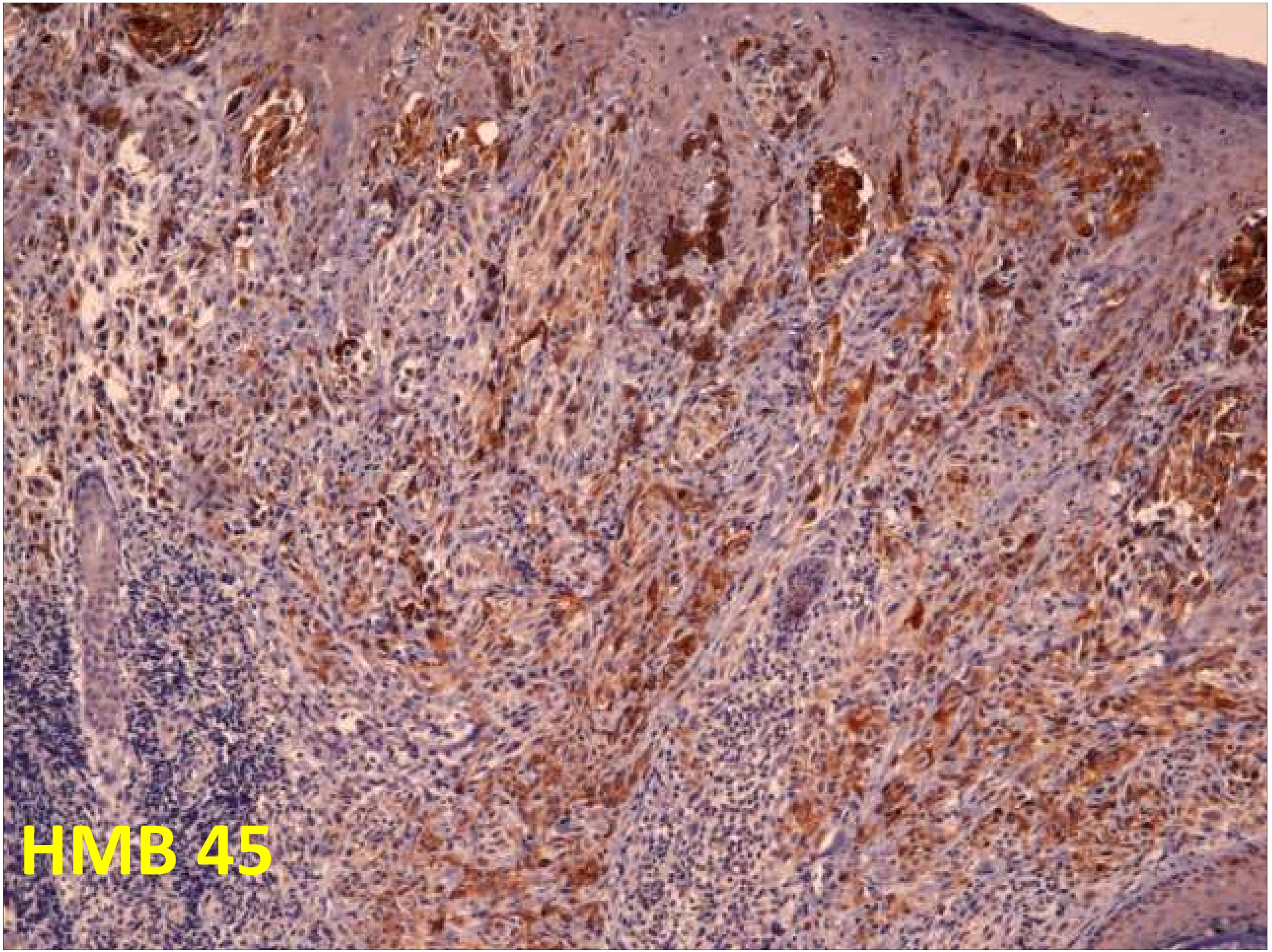

HMB 45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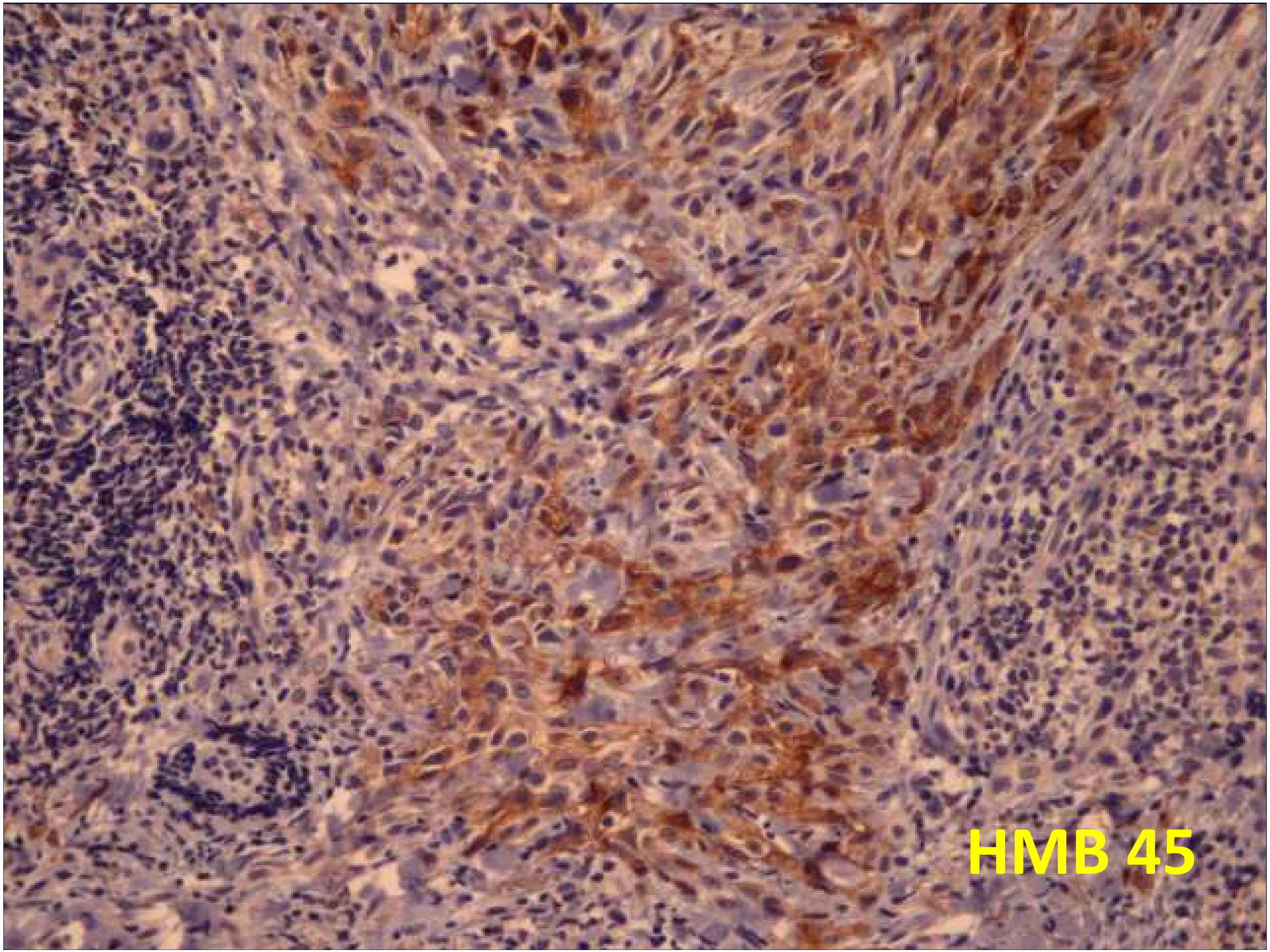
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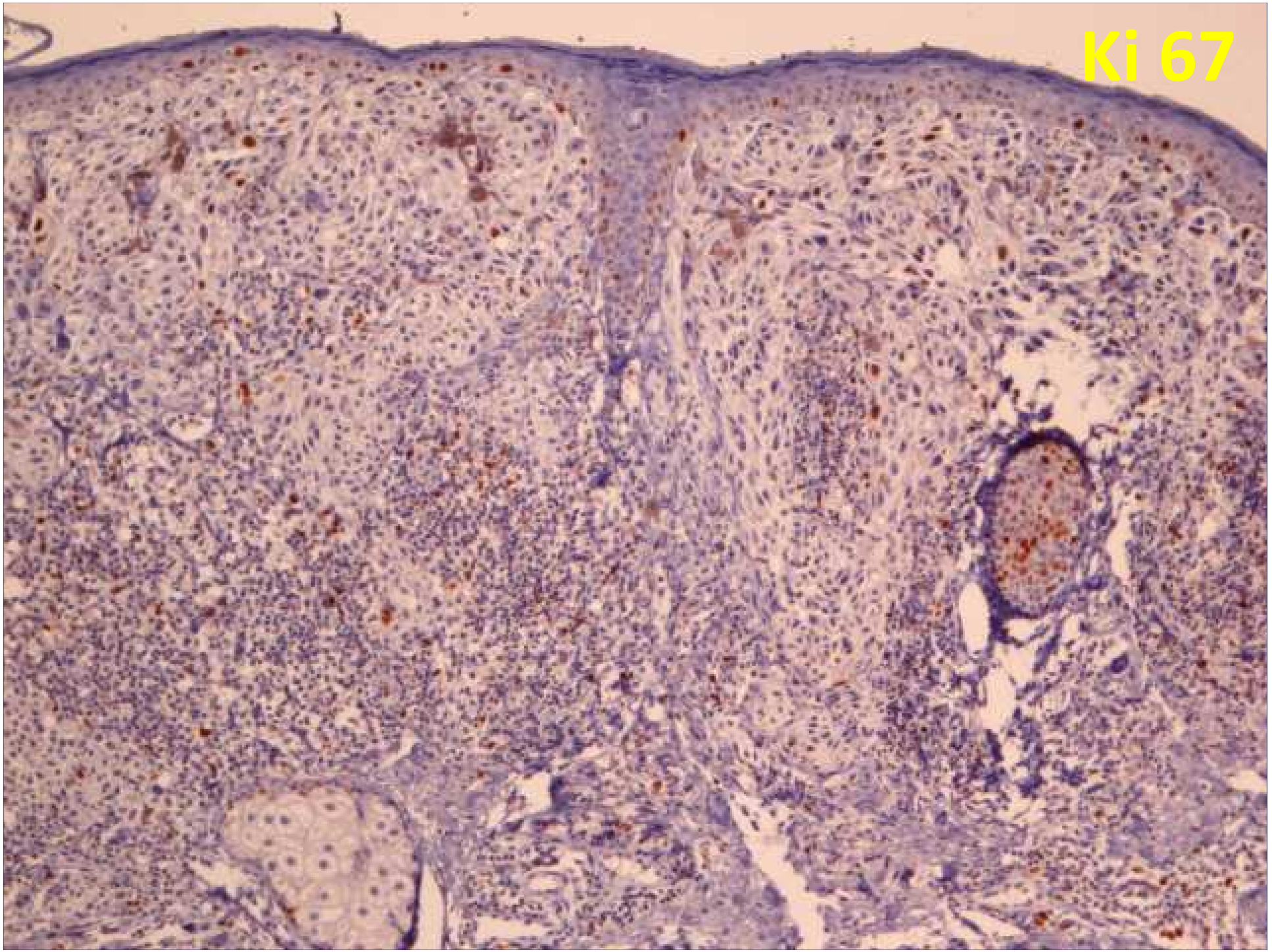
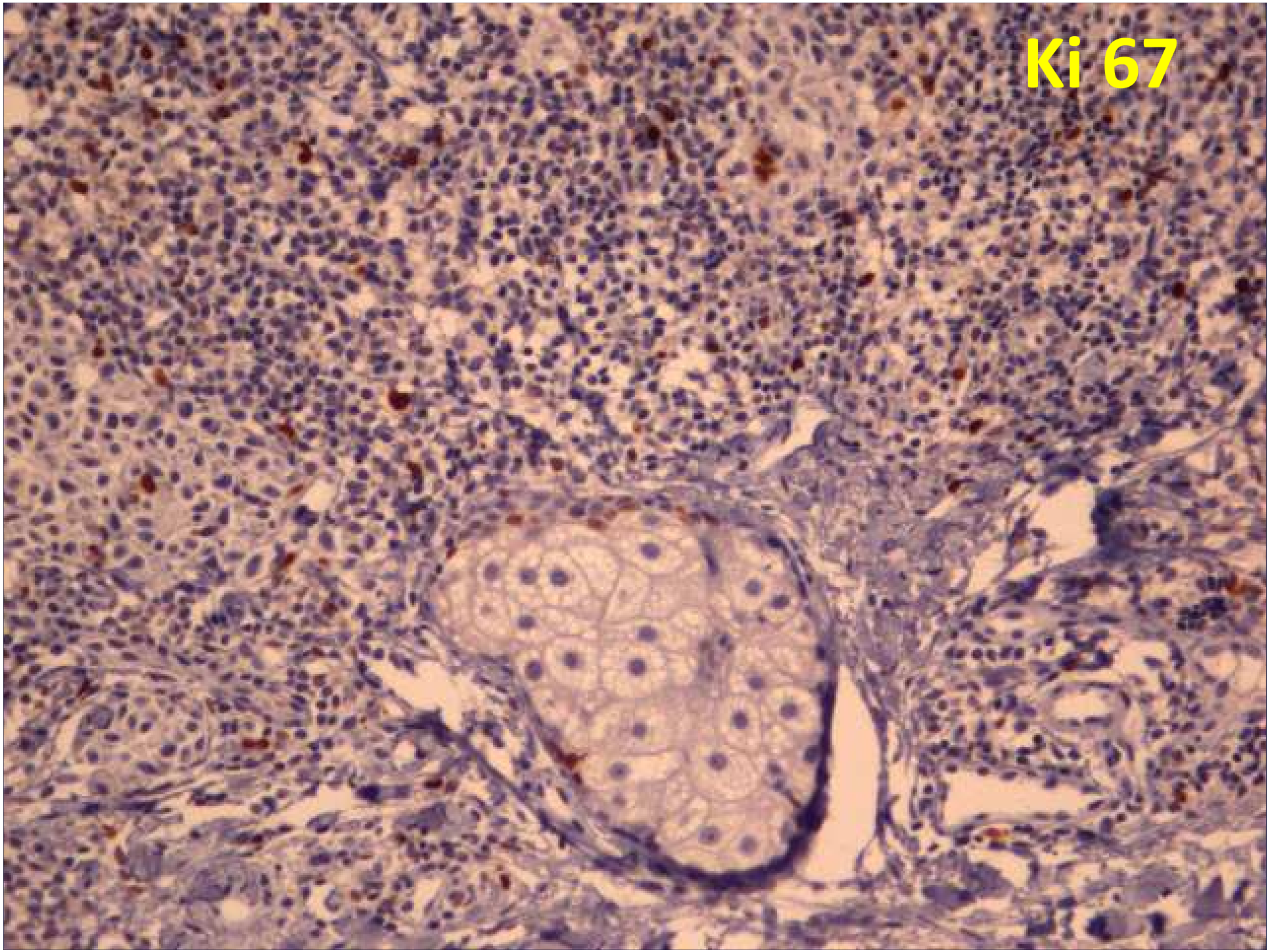

Ki 67


Ki 67

Human PATHOLOGY

VOLUME 21 July 1990 NUMBER 7

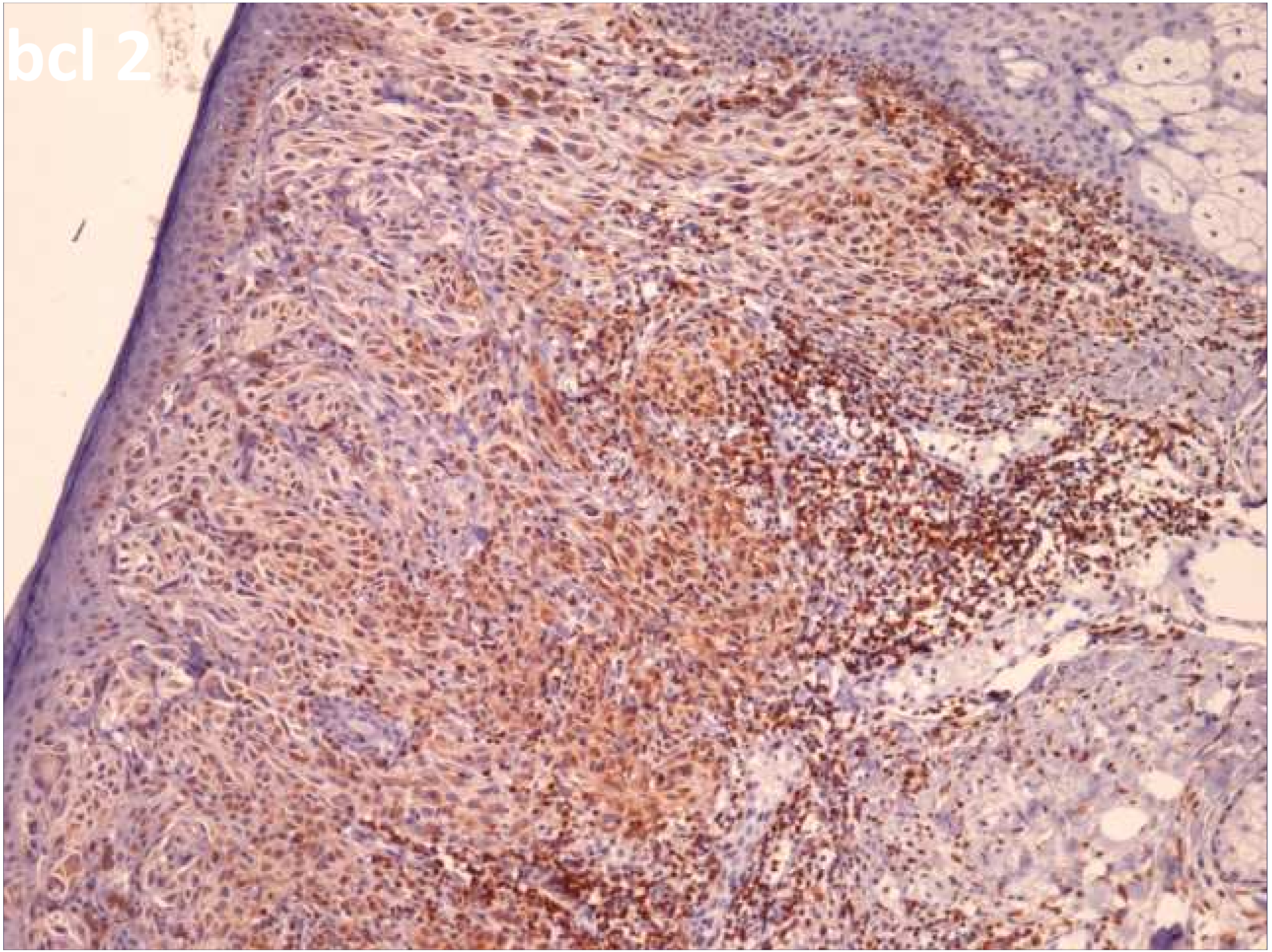
Editorial

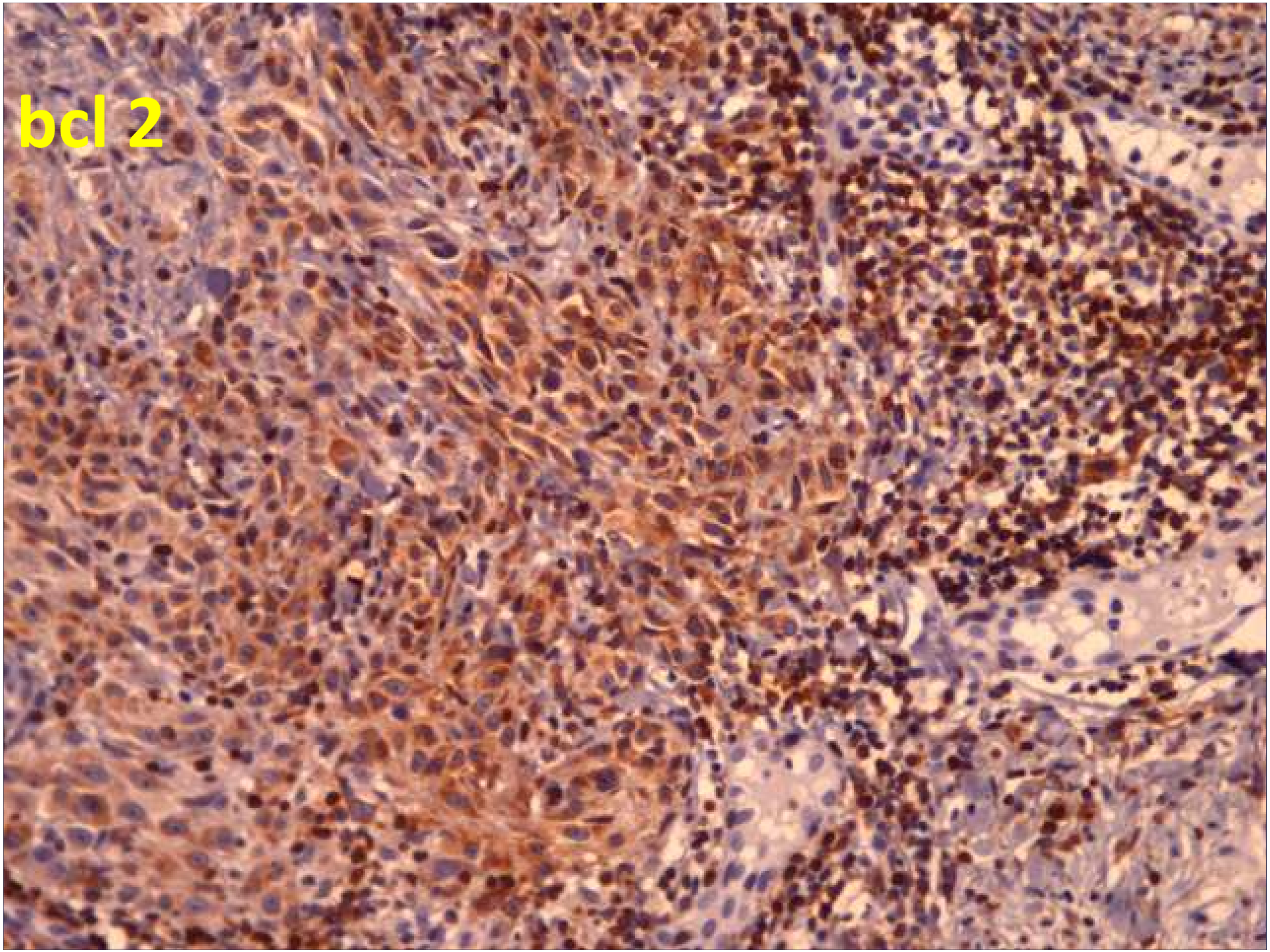
# Mitosis Counting in Tumors

For a long time the fixation delay in tumors after removal has been regarded as another important influencing factor, as mitoses were considered to complete their cycle in the absence of oxygen and thus disappear.[17,18] This disappearance rate was thought

A number of investigators have suggested a role for MIB-1 immunostaining as a diagnostic adjunct for distinguishing Spitz nevus from malignant melanoma.[16,17,22,41] Nagasaka *et al*[16] found that all Spitz nevi had a relatively low MIB-1 index (mean 3.2%), which was significantly lower than that of malignant melanoma (mean 15.3%). Similarly, Kanter-Lewensohn *et al*[17] found an average MIB-1 index of 4% in Spitz nevi and 29.7% in malignant melanoma and Bergman *et al*[22] reported 1.5% for Spitz nevi *vs* 14.9% for malignant melanoma.

Modern Pathology (2005) 18, 197–204


bcl 2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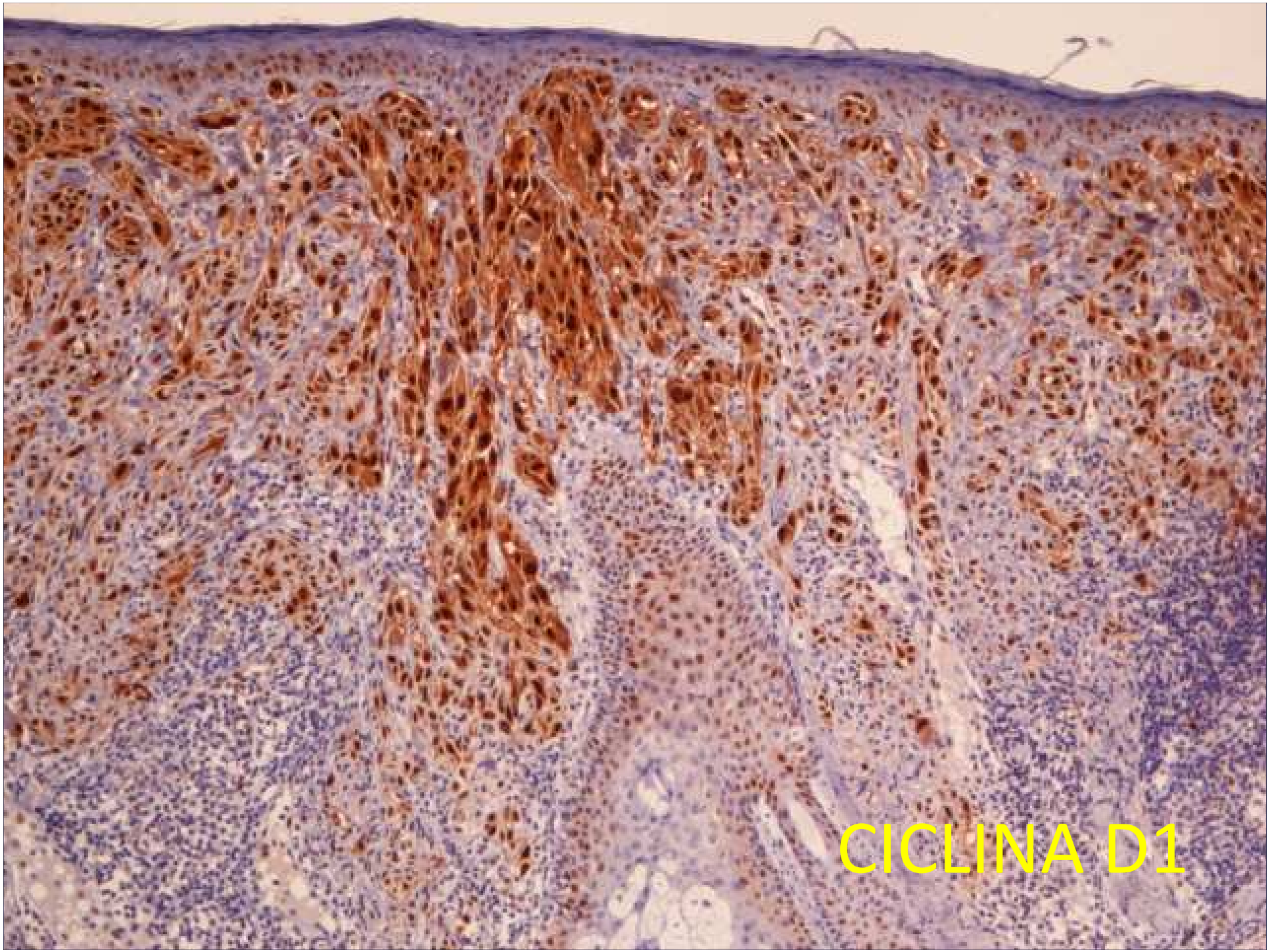
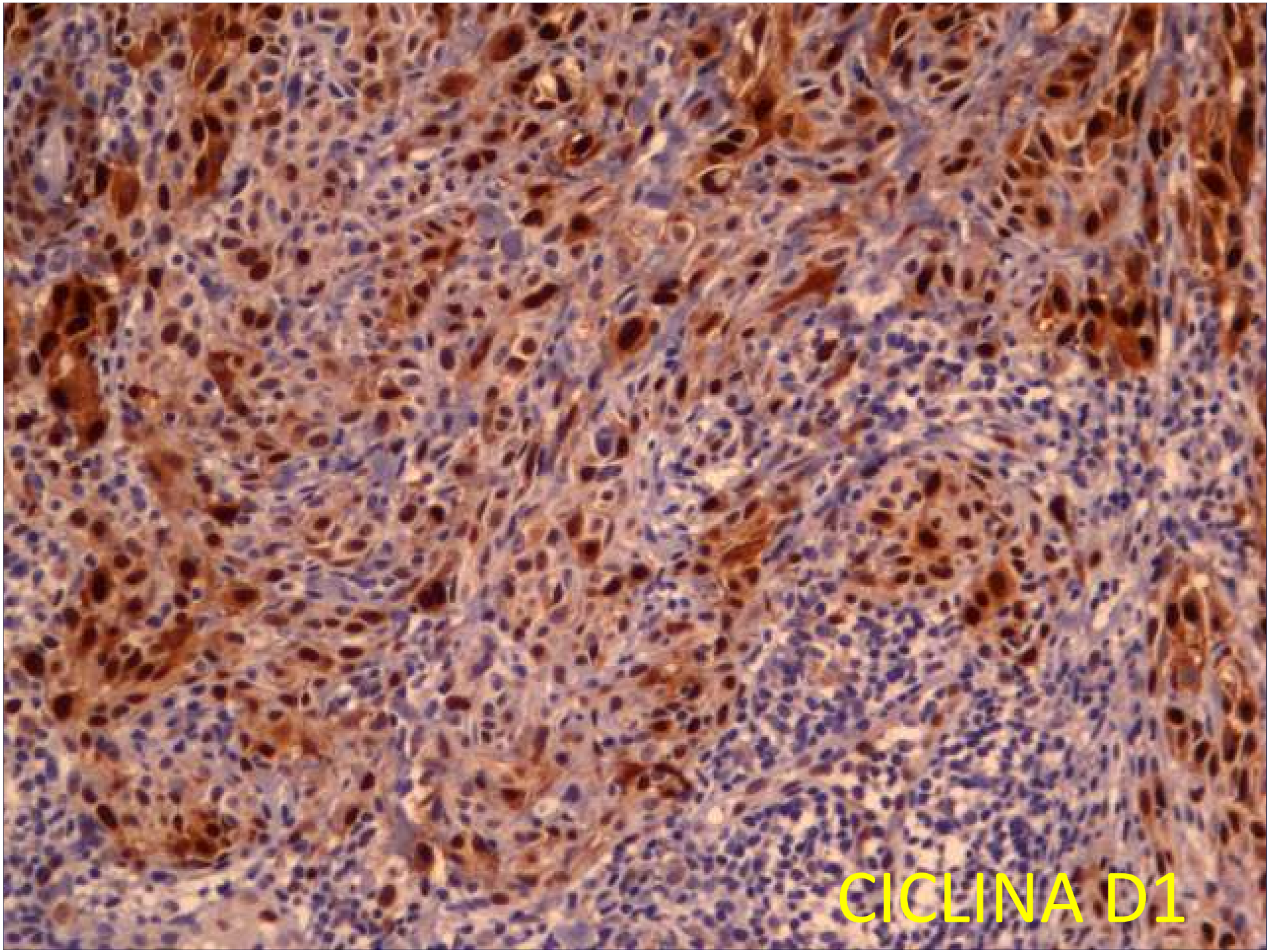

CICLINA D1


CICLINA D1

## Cyclin D1

Cyclin D1 regulates cell proliferation and progression from the G1 to S phase of the cell cycle (88–90). Cyclin D1 has potential in distinguishing benign nevi from Spitz nevi, dysplastic nevi, and melanoma. Benign nevi are reported to lack expression of cyclin D1 (91). Spitz nevi demonstrate a zonal distribution with a loss of expression with depth. Severely dysplastic nevi show increased expression compared with mildly dysplastic nevi, and melanomas show diffuse staining with cyclin D1 (92,93). Although one study reports only weak in situ cyclin D1 staining with no significant difference between nevi, primary melanomas, and metastatic melanomas (94), additional studies confirming the usefulness of cyclin D1 as a diagnostic melanocytic marker would strengthen the more promising findings.

Mod Pathol. 2005 Feb;18(2):197-204.

## Spitz nevi and atypical Spitz nevi/tumors: a histologic and immunohistochemical analysis.

Kapur P, Selim MA, Roy LC, Yegappan M, Weinberg AG, Hoang MP.

Clin Lab Med. 2011 Jun;31(2):311-20.

## Spitz nevi, atypical spitzoid neoplasms, and spitzoid melanoma.

Zedek DC, McCalmont TH.

Semin Cutan Med Surg. 2010 Sep;29(3):165-73.

## Spitz nevus and atypical spitzoid neoplasm.

Miteva M, Lazova R.

Department of Dermatology and Cutaneous Surgery, University of Miami, Miller School of Medicine, Miami, FL, USA.

# Immunohistochemistry of Melanocytic Proliferations

*Victor G. Prieto, MD, PhD; Christopher R. Shea, MD*

• *Context.*—Histologic analysis allows accurate classification of most melanocytic lesions as benign or malignant. Only in a minority of lesions is it necessary to use other techniques as an aid in the diagnosis. Among them, most authors recommend immunohistochemistry.

*Objective.*—To describe how to apply immunohistochemistry to particular differential diagnoses and the potential pitfalls.

*Data Sources.*—Personal experience and review of literature.

*Conclusions.*—There is no single marker, or combination thereof, that establishes an unequivocal diagnosis of melanoma or nevus. Thus it is necessary to carefully analyze the pattern of expression (patchy versus diffuse) and localization (maturation) in the context of morphologic standard features.

(*Arch Pathol Lab Med.* 2011;135:853–859)

# Spitz nevi and atypical Spitz nevi/tumors: a histologic and immunohistochemical analysis

Payal Kapur[1], M Angelica Selim[2], Lonnie C Roy[3], Mani Yegappan[1], Arthur G Weinberg[1,3] and Mai P Hoang[1,3]

[1]*Department of Pathology, University of Texas Southwestern Medical Center, Dallas, TX, USA;* [2]*Duke University Medical Center, Durham, NC, USA and* [3]*Children's Medical Center, Dallas, TX, USA*

**A subset of Spitz nevi poses substantial diagnostic difficulty, even among experts, due to its resemblance to malignant melanoma. These lesions are termed atypical Spitz nevi/tumors and there is currently a lack of objective criteria for predicting their biologic behavior. We compared the expression of Ki-67, p21, and fatty acid synthase by immunohistochemistry in 10 atypical Spitz nevi, 28 typical Spitz nevi, 19 compound melanocytic nevi and 18 invasive malignant melanomas. There was a progressive increase in fatty acid synthase cytoplasmic expression with statistically significant differences observed between Spitz nevi and atypical Spitz nevi ($P=0.003$) and between atypical Spitz nevi and malignant melanoma ($P<0.050$). Ki-67 nuclear staining was lower in both typical and atypical forms of Spitz lesions than in malignant melanoma ($P<0.001$). The degree of P21 nuclear expression in atypical Spitz nevi was not significantly different than in Spitz nevi, but was significantly greater than expression in conventional nevi and approached significance after multiple comparisons corrections for malignant melanoma. Thus, a high level of P21 expression makes a tumor more likely to be a typical or atypical Spitz nevus than a malignant melanoma, especially when coupled with a low Ki-67 index and weak expression of fatty acid synthase. These immunohistochemical observations support the concept that atypical Spitz nevi are distinct lesions of borderline biologic behavior residing between Spitz nevi and malignant melanoma. The study also compared a large array of histologic features of 16 cases of typical Spitz nevi in children with 12 typical Spitz nevi in adults. The adult lesions were significantly more likely to be intradermal and to display dermal fibroplasia, but were histologically similar to their pediatric counterparts in all other respects.**

*Modern Pathology* (2005) **18,** 197–204, advance online publication, 1 October 2004; doi:10.1038/modpathol.3800281

**Keywords:** Spitz nevi; spindle and epithelioid cell nevus; atypical Spitz nevi/tumors; p21; Ki-67; fatty acid synthase; immunohistochemistry

# Problematic pigmented lesions: approach to diagnosis

S L Edwards, K Blessing

**Abstract**

**A number of pigmented lesions are difficult to classify and raise the possibility of a melanoma diagnosis. Care should be exercised to exclude non-melanocytic lesions, and benign melanocytic entities, both of which can mimic melanoma histologically. In addition, the possibility of the lesion being a melanoma variant or epidermotropic metastasis should be considered. There will still be some cases that are difficult to resolve. These usually fall into one of three categories: atypical junctional melanocytic lesion versus early melanoma; naevus versus naevoid melanoma; and atypical Spitz, cellular blue, and deep penetrating naevi versus thick melanoma. These will pose problems even for experts. The atypical Spitz lesions are perhaps the most important category because they tend to be from younger individuals, the differential diagnosis is thick melanoma, and there is no single discriminating histological feature.**

(*J Clin Pathol* 2000;53:409–418)

Keywords: difficult diagnosis; pigmented lesions; melanoma

## General guidelines

Before looking at a pigmented lesion it is vital to know certain clinical factors, particularly the age of the patient, the anatomical location of the lesion, and if there has been previous surgery or trauma. The age is important because melanomas are more common with increasing age and are extremely rare (although they do occur) in children.[2] Spitz naevi occur predominantly in children and young adults, and are increasingly uncommon in the older age groups.[3] Some features related to an actively growing lesion are more acceptable in children and adolescents than they would be in an adult. For example, a lentiginous junctional growth pattern in an adult would be a pointer to in situ melanoma, whereas it would not infer the same in a child.

It is also essential to know the site of the biopsy. This is important for two reasons. First, different anatomical locations have different qualities of skin, which cause both benign and malignant melanocytic lesions to grow in characteristic patterns. This is particularly pertinent to the in situ component of melanomas, which aids their recognition. For example, lentigo maligna occurs on sun exposed skin of older individuals and presents as a lentiginous proliferation of atypical melanocytes in an

**30/05/2012: LAUDO COMPLEMENTAR:** Foi realizado painel imuno-histoquímico e conseguimos os seguintes resultados:

**S100 -** fortemente positivo nas células tumorais superficiais e profundas, sem diminuição na densidade na profundidade, significando falta de maturação;
**HMB45 -** positivo nas células tumorais superficiais e profundas, sem sinais de estratificação;
**MIB 1 -** positivo em cerca de 12% das células tumorais, inclusive na profundidade da lesão;
**Bcl 2 -** positivo em toda a extensão da lesão;
**Ciclina D1 -** positivo em toda a extensão da lesão.

Baseado na descrição anterior (acima) e nestes achados imuno-histoquímicos, minha opinião é que esta lesão deva ser considerada como **MELANOMA CUTÂNEO DE PADRÃO SPITZÓIDE -** em fase vertical de crescimento, nível III de Clark, atingindo a profundidade máxima de 1,05 mm (método de Breslow), sem mitoses no componente dérmico, sem microsatélites, sem sinais de regressão, sem ulceração, sem neurotropismo, sem invasão angiolinfática, com moderado infiltrado linfocitário intra e peritumoral focal e sem lesão precursora associada. A neoplasia chega muito próximo às bordas de ressecção da peça cirúrgica.

# Tutorial on Melanocytic Lesions

Lorenzo Cerroni, M.D., and Helmut Kerl, M.D.

The American Journal of Dermatopathology 23(3): 237–241, 2001

During the 21st Symposium of the International Society of Dermatopathology, which was held in Graz, Austria, September 2000, an entire session was devoted to a Tutorial on melanocytic lesions. A panel of 6 experts in histopathologic diagnosis of melanocytic tumors (A. Bernard Ackerman, New York; David E. Elder, Philadelphia; Peter Heenan, Perth; Helmut Kerl, Graz; Philip E. LeBoit, San Francisco; and Juan Rosai, Milan) had the opportunity of studying 71 cases submitted by participants in the Symposium before the beginning of the meeting. All cases were then presented during the ses-

**TABLE 1.** *Diagnostic categories and level of agreement*

| Diagnostic category | 6–0 | 5–1 | 4–2 | 3–3 |
|---|---|---|---|---|
| Desmoplastic nevus (n = 3) | 3 | — | — | — |
| Recurrent (persistent) nevus (n = 2) | 2 | — | — | — |
| Pseudomelanoma in children (n = 6) | 5 | 1 | — | — |
| Spitz nevi and variants (n = 16) | 4 | 7 | 4 | 1 |
| Other variants of melanocytic nevi (n = 12) | 4 | 4 | 1 | 3 |
| *Total (melanocytic nevi, n = 39)* | *18* | *12* | *5* | *4* |
| Melanoma *in situ* (n = 3) | 2 | 1 | — | — |
| Desmoplastic melanoma (n = 5) | 5 | — | — | — |
| Recurrent (persistent) melanoma (n = 3) | 1 | 2 | — | — |
| Variants of melanoma (non-nevoid) (n = 7) | 4 | 3 | — | — |
| Nevoid/spitzoid melanoma (n = 10) | 3 | 3 | 2 | 2 |
| *Total (malignant melanoma, n = 28)* | *15* | *9* | *2* | *2* |
| ***Total*** | ***33*** | ***21*** | *7* | *6* |

A very high level of agreement was observed also in the diagnosis of so-called pseudomelanoma in children (Fig. 2). Again, this clearly shows that in this particular group of lesions diagnostic criteria were used in a consistent and repeatable way by all experts. It should be mentioned, however, that one of the patients died of metastatic disease. (Follow-up information, when available, was provided by case contributors during the discussion.) The sad history of this patient should remember us that agreement on a given diagnosis does not mean that that particular diagnosis is correct.

JOURNAL OF PATHOLOGY, VOL. 182: 247–249 (1997)

EDITORIAL

# DIAGNOSTIC DISCORD WITH MELANOMA


## SUMMARY

The study of the Pathology Panel of the Dutch Melanoma Working Party highlights the great difficulty in achieving uniform diagnostic assessment of melanoma. Their solution is to set up a national reference panel and to focus continuing medical education on identified areas of particular difficulty. This could be appropriate for other countries, although selection of referees and funding may be problematic. It may also be timely to consider whether melanoma terminology can be rationalized to make it more likely to be reported consistently by pathologists whilst still providing sufficient information for proper patient management. Alternatively the reporting of most melanocytic lesions could be confined to pathologists who specialise in this subject, a practice which has evolved for other areas of pathology. This would facilitate the maintenance of standards and uniformity among that smaller group, but it would not avoid the need for a continuing awareness among all pathologists of the diagnostic pitfalls which abound in the area of melanocytic lesions.



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realistic about our role. Our responsibility is to offer an interpretation of morphological changes and give an informed opinion as to the likely behaviour of an identified lesion. That opinion should be based on current knowledge and practice, but remains an opinion and not an absolute fact. There is no current way of establishing the '*right*' diagnosis, other than relying on the wisdom of those who are respected as authorities in their field. With melanoma, there are countless cases

Pediatric Dermatology Vol. 19, No. 2 99–102, 2002

# A Current Dilemma in Histopathology: Atypical Spitz Tumor or Spitzoid Melanoma?

**Yesim Gurbuz, M.D.,* Rebiay Apaydin, M.D.,† Bahar Muezzinoğlu, M.D.,* and Nesimi Buyukbabani, M.D.‡**

*Departments of *Pathology and †Dermatology, Kocaeli University Medical School, Kocaeli, Turkey, and ‡Department of Pathology, Istanbul University Medical School, Istanbul, Turkey*

**Abstract:** Both clinically and histopathologically, melanoma of childhood is a rarely encountered lesion. In addition, it has particular histopathologic diagnostic problems. Differential diagnosis of this lesion and Spitz nevus is at times very problematic, in that distant metastases and death of the patient may be the only diagnostic criteria for some cases. We present a 4-year-old girl with an atypical melanocytic neoplasm with Spitzoid features on the left subscapular region.


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