

A comprehensive review of the “tigroid” background cytological concept: what, when, where and why?

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Summary

The concept of “tigroid” background is used in cytology to describe a peculiar smear background characterized by the presence of a relatively granular, reticulated material that was described as “foamy, lazy, tiger-striped or astrakhan”. It was used to describe the background seen in smears obtained from seminoma. In addition to seminoma, we now know that it can be present in different tumours, mostly carcinomas and round cell sarcomas. These share with seminoma a cytoplasm with high glycogen content and many times clear cell morphology. The “tigroid” background is seen when smears are air-dried and Romanowsky-based stains are used (May-Grunwald-Giemsa and Diff-Quik stains). It is only seen in fine needle aspiration or intraoperative squashing or scrapping samples, but not in specimens obtained from effusions or liquid-based cytology. Wet-fixed cytologic samples with alcohol or with formaldehyde tend to dissolve the background so it is not usually present in Papanicolaou stained smears. In this review, we discuss tumours in which the “tigroid” background is observed and its potential diagnostic utility and aetiology. It is interesting to remark that except for parathyroid adenoma and adenomatoid tumour all the neoplasms in which this background has been observed are malignant.

Key words: cytology, fine needle aspiration, seminoma, “Tigroid” background

Introduction

It is common in Pathology to use analogies to compare morphologic findings with objects of our normal life. One example is the concept of “tigroid” background (TB) that we use in cytology to describe a peculiar morphologic finding that has diagnostic utility. The term was first used in 1976 by a pioneer of cytopathology, Dr. Paul Lopes-Cardozo (1913-2012) ¹. He used it to describe a characteristic background seen in cytological smears obtained from seminoma. Although it still is classically associated with seminoma (dysgerminoma and germinoma), we now know that the TB can be present in different tumours. Most share with seminoma a cytoplasm with high glycogen content and many times clear cell morphology. The purpose of this review is to highlight those non-seminomatous tumours in which cytological smears can show a TB. In addition to a helpful diagnostic element, its appearance in different tumours can permit better understanding of why such a background appears.

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The what and when of the “tigroid” background

It is a peculiar smear background (Fig. 1A, B) characterised by the presence of a relatively granular, reticulated material that Lopes-Cardozo described as “foamy, lazy, tiger-striped or astrakhan”¹. Astrakhan is the tightly curled fleece of the newborn Karakul lamb. As mentioned by Xie et al.² the most remarkable feature is the “alternating interwoven linear light-blue to purple and clear areas”. Eluri and Ali³ highlighted the tendency to uniformly coat the smears. This peculiar background appears a result of the disruption of the fragile cytoplasm of neoplastic cells during smearing. Part of the cytoplasmic content will form the confluent cytoplasmic stripes, which resemble those of a tiger. Moreover, this is a relevant concept that neoplasms showing a TB have in common: cytoplasmic fragility. Consequently, and regardless of the tumour type, their smears tend to show many “naked” nuclei.

When do we see a TB? When the appropriate tumours are sampled and air-dried, Romanowsky-based stains are used. The most commonly used in cytology routine are May-Grunwald-Giemsa and Diff-Quik stains. With these stains, the background shows a light blue colour and granular appearance. It is not metachromatic, which allows differentiation with the background granular material that sometimes is present in tumours containing myxoid substance or basement membrane material. We can see the background in fine needle aspiration (FNA) and intraoperative squashing and

scraping samples, but not in specimens obtained from effusions or liquid-based cytology. Although occasional reports have described it using alcohol-fixed Papanicolaou stained material⁴ this is the exception since the latter as well as formaldehyde-fixed, haematoxylin-eosin-stained specimens, tend to dissolve the glycogen-rich cytoplasmic material. Therefore, if a potential TB tumour is suspected (seminoma is the most common scenario), it is desirable to obtain air-dried smears for Romanowsky-based staining. Another requisite for its presence is a high cellular specimen with scarce blood or cystic content that can dissolve the delicate background^{2,5}. This is well illustrated in the report by Khunamornpong et al.⁵ that describes a TB in approximately half of the FNA and scraping samples of ovarian clear cell carcinomas, but in none of their respective positive peritoneal fluid specimens. A very important diagnostic consideration is that TB is not a constant cytomorphologic finding. For instance, in seminoma it can be absent in almost 50% of cases analyzed⁶. Thus, from a diagnostic perspective its utility depends on its presence rather than its absence, since the latter cannot rule out the diagnosis.

An interesting observation is that tissue-frozen sections obtained during intraoperative procedures may show the characteristic “tigroid” reticulated material (Fig. 2A, B). Since the image is lost after conventional tissue paraffin embedding (Fig. 2C), it seems that freezing permits its preservation even after fixation and staining. As opposed to cytology, in frozen sections it is usually observed as a focal finding. How-

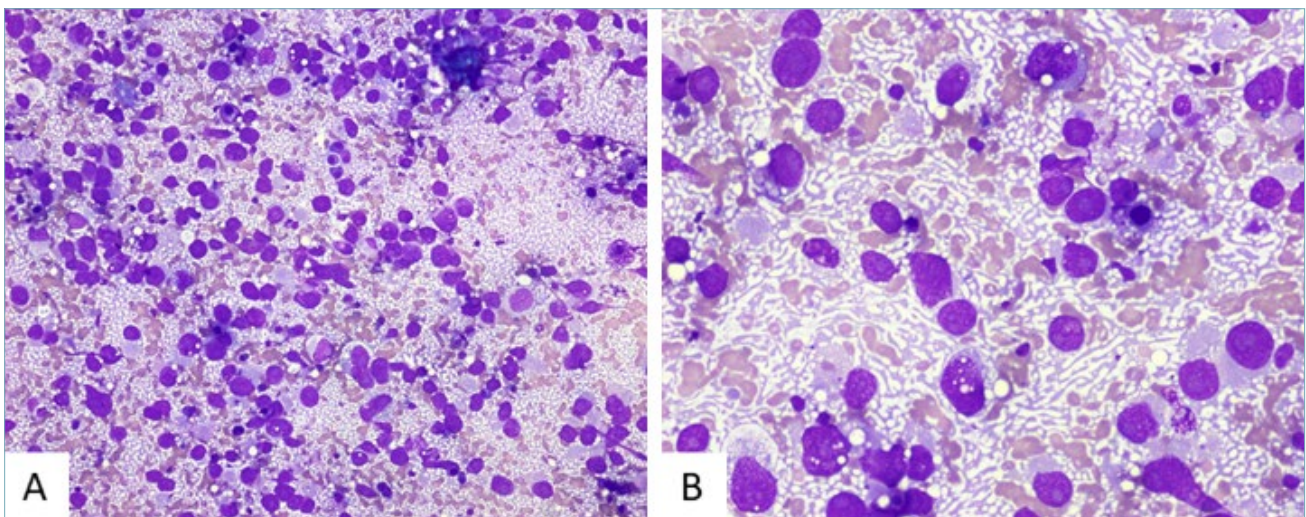


Figure 1. (A) A typical case of seminoma showing the foamy, lazy background that resembles astrakhan (Diff-Quik, x400). (B) Higher magnification reveals the typical alternating interwoven stripes that resemble those of a tiger. Seminoma tumour cells have cytoplasmic fragility and smears show numerous naked nuclei (Diff-Quik, x600)

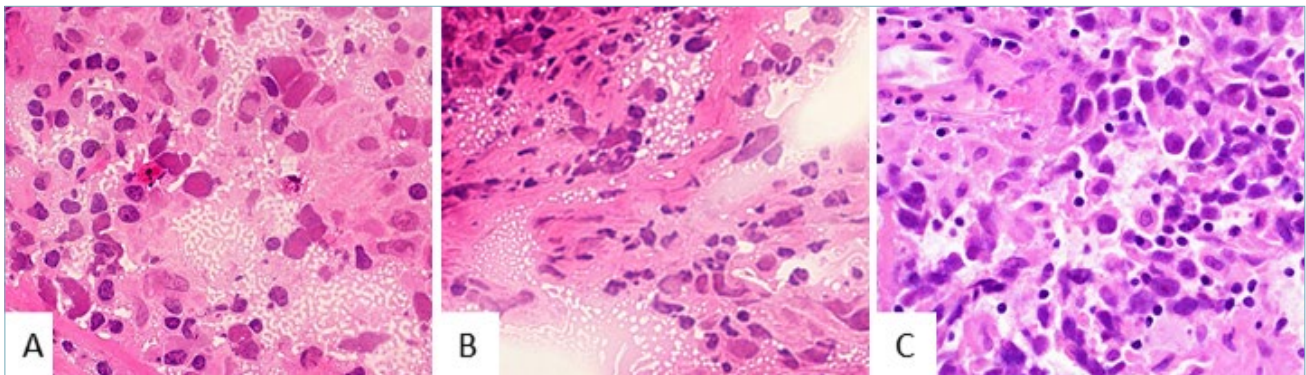


Figure 2. (A, B) Intraoperative frozen section assessment of a seminoma showing large cells with abundant cytoplasm, admixed lymphocytes and fibrous bands together with evident “tigroid” material (Haematoxylin-Eosin, x400). (C) The corresponding permanent section shows the same histopathological features except for the “tigroid” substance which is lost (Haematoxylin-Eosin, x400).

ever, it is an important consideration. Frozen sections of seminoma can be difficult to differentiate from non-Hodgkin malignant lymphoma or embryonal carcinoma. In this setting, cytological smears showing a TB are extremely helpful.

The where of the “tigroid” background

By far, the most common tumour showing this background is seminoma (Figs. 1, 2, 3A), and since they are the same entity, ovarian dysgerminoma and pineal germinoma⁶⁻⁸. Indeed, for most pathologists the association is so evident that it is almost considered pathognomonic, and as it often occurs in medicine, it is not the case. It is important to mention that spermatocytic tumour, once called spermatocytic seminoma does not show this characteristic background^{9,10}. The most probable reason for its absence is that

spermatocytic tumour lacks glycogen. Table I shows the neoplasms in which a TB has been described or mentioned. Almost all have in common a high glycogen content. In addition to seminoma, carcinomas, sarcomas (mostly round cell) and very rarely lymphomas may show it. A very important observation is that except for parathyroid adenomas and adenomatoid tumour all these neoplasms are malignant.

Regarding carcinomas, a small subset of squamous cell carcinomas may have a high glycogen cytoplasmic content and may show a prominent TB^{2,11}, not necessary accompanied by a clear cytoplasm as illustrated by the case reported by Xie et al.². Similarly, it has been reported in clear cell adenocarcinoma of the female genital tract that is another tumour in which glycogen cytoplasmic content is high^{5,12}. This background together with basement membrane material (“raspberry bodies”) is a useful diagnostic feature that permits a precise cytological recognition. Another

Table I. Neoplasms in which a “tigroid” background can be present.

Germ cell tumours	Seminoma/Dysgerminoma/Germinoma
Carcinomas	Squamous cell carcinoma (clear cell or glycogen rich variants)
	Clear cell adenocarcinoma of the female genital tract
	Fetal adenocarcinoma of the lung
	Hyalinizing clear cell carcinoma of the salivary gland
	Glycogen-rich carcinoma of breast
Sarcomas	Ewing's sarcoma
	Rhabdomyosarcoma
	Clear cell sarcoma
Other	Anaplastic lymphoma kinase positive large B-cell lymphoma
	Paratesticular adenomatoid tumour
	Papillary tumour of the pineal region
	Parathyroid adenoma

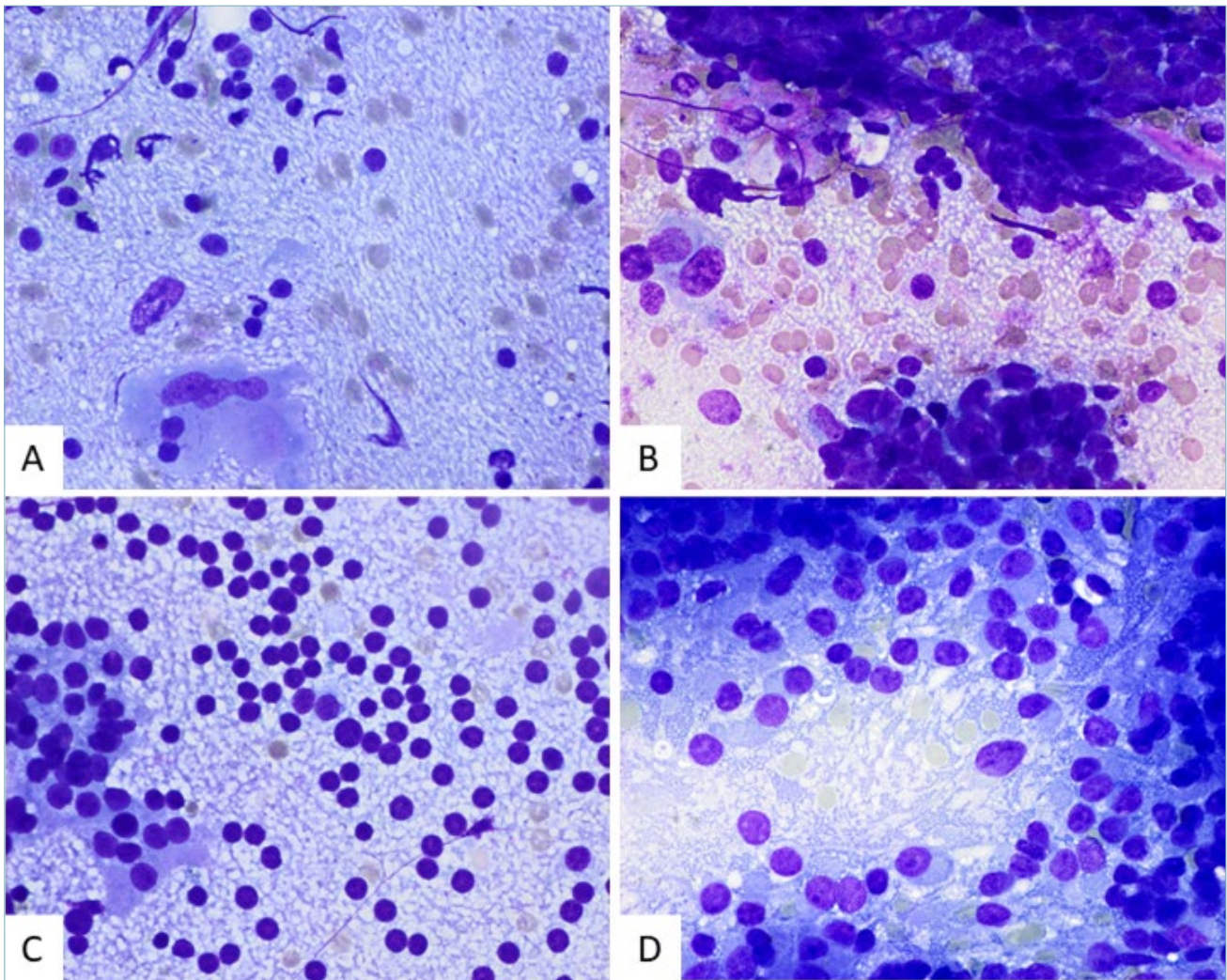


Figure 3. (A) A peculiar case of seminoma almost devoid of neoplastic cells. Only a single naked tumoural nucleus accompanied by numerous lymphocytes and occasional macrophages is visible. In this setting, the characteristic background results very helpful for diagnosis (Diff-Quik, x600). (B) Foetal adenocarcinoma showing a similar background (Diff-Quik, x600). (C) The “tigroid” background is also present in a case of parathyroid adenoma composed of chief cells (Diff-Quik, x600). (D) A case of papillary tumour the pineal region showing the characteristic background. Note that in all four cases numerous naked nuclei are present.

carcinoma in which this precise background is present is fetal adenocarcinoma of the lung. This rare tumour resembles normal foetal lung and neoplastic cells contain vacuoles with high glycogen content. In the report of 4 cases by Geisinger et al.¹³ it is described as a relevant finding. We have personal experience with one case in which it was evident (Fig. 3B). Hyalinising clear cell carcinoma is an uncommon carcinoma most commonly arising from intraoral minor salivary glands. Its clear aspect is due to cytoplasmic accumulation of glycogen. Due to its rarity and location, the cytological experience is limited. The case

reported by Yaun and Hsieh¹⁴ revealed a prominent TB that in this precise setting can allow the pathologist to consider this tumour since this background is not seen in other salivary gland neoplasms. As expected, glycogen-rich carcinoma of the breast also shows a TB^{15,16}. In our experience, parathyroid adenoma can occasionally show this background (Fig. 3C). Such a finding in parathyroid adenoma has been mentioned and illustrated in twitter by Ali¹⁷ and Özbek¹⁸. It is not surprising since parathyroid chief cells have a clear and well glycogenated cytoplasm. This finding can be useful during intraoperative procedures when sur-

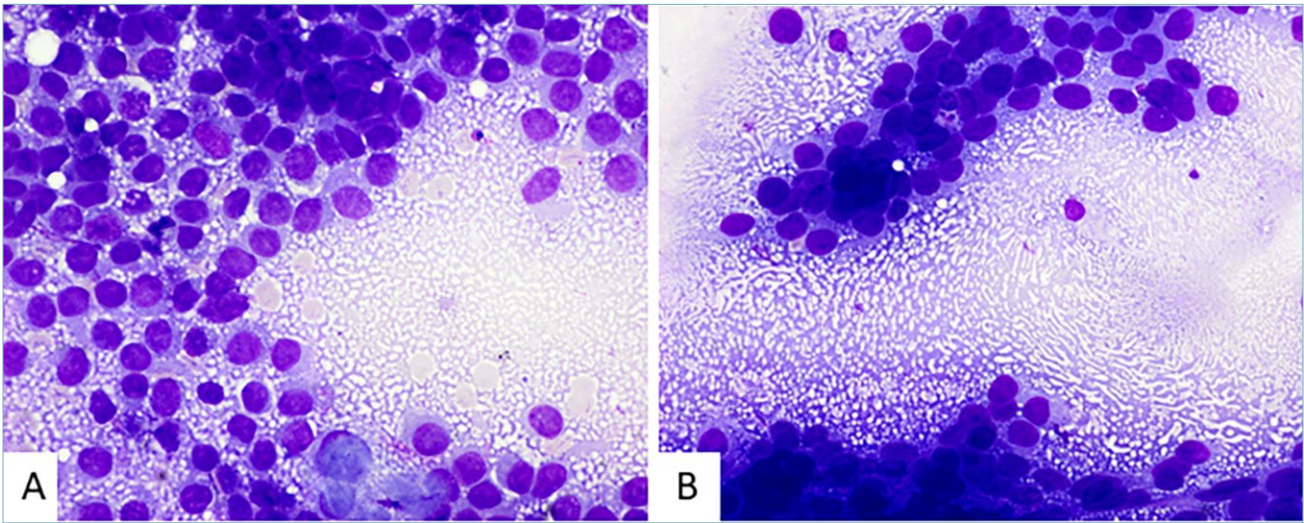


Figure 4. (A) Smears from Ewing's sarcoma shown "tigroid" material (Diff-Quik, x600). (B) Rhabdomyosarcoma is another small round cell sarcoma that can show this peculiar background (Diff-Quik, x600).

geons ask pathologists to differentiate parathyroid from thyroid or lymph node tissue. Another benign epithelial tumour in which a "tigroid-like" background has been mentioned is adenomatoid tumour. In the paratesticular case reported by Monappa et al.⁴ the TB coupled with cellular dissociation and large vacuolated cytoplasm induced confusion with seminoma. It is interesting to remark that this is the only case to report a "tigroid-like" background in alcohol-fixed, Papanicolaou stained smears.

Concerning sarcomas, Ewing sarcoma/primitive neuroectodermal tumour, despite its small cytoplasm, has PAS positive small vacuoles that contain glycogen and can be responsible of a TB¹⁹. They are less frequently present in rhabdomyosarcoma. The study by de Almeida et al.²⁰ reported its presence in 4 of 20 rhabdomyosarcomas and related it to the high glycogen content and small vacuoles present in tumoral cells. We have personal experience with both tumours (Fig 4A, B) and from a practical perspective, the presence of the TB in these round cell sarcomas is a helpful clue for differentiation from malignant lymphoma. Except for one reported case of anaplastic large cell lymphoma²¹, malignant lymphomas show no TB. Other sarcoma in which this background is reported is clear cell sarcoma or malignant melanoma of soft parts^{3,22,23}. As expected, the later shows a clear to pale eosinophilic cytoplasm that contains glycogen. The possibility of a TB has been mentioned in synovial sarcoma, clear cell renal cell carcinoma and melanoma¹⁴. Our personal experience and review of cytological reports concerning these entities do not

mention such association so it must be very rare. Regarding central nervous system tumours, germinoma, a seminoma equivalent that usually arises in the pineal region typically shows the TB⁸. Most neuropathologists prefer wet-fixed cytological samples with either alcohol or formaldehyde to air-dried smears so that TB is rarely mentioned in brain tumours. We reported its presence in a papillary tumour of the pineal region a rare and peculiar neoplasm that has a high glycogen content (Fig. 3D)²⁴. Both germinoma and papillary tumour share a common pineal location and a TB. However, other cytological features differ considerably allowing a precise recognition during intraoperative consultations.

Due to its technical simplicity and quality of staining, air-dried, Romanowsky-based stains (May-Grunwald-Giemsa, Diff-Quik) are becoming more popular among cytologists and pathologists who use cytology as an aid during intraoperative consultations. We therefore expect that the list of tumours showing a TB will increase as more glycogen-rich neoplasms are sampled. However, it will continue to be a list with a small number of entities, so this finding will usually be of diagnostic utility, as in the cases we have discussed.

The why of the "tigroid" background

This is probably the most interesting and difficult issue to answer. It seems that almost all tumours showing this background have in common a high glycogen

content and very often a clear cytoplasm. The latter can also be due to lipid or mucin accumulation. However, tumours in which clear cells are so because of mucin or lipid-rich cytoplasm show no TB. The latter is probably due to cytoplasmic fragmentation during smearing and non-homogenous mixing of glycogen and disrupted cytoplasmic material. Cells cannot store glucose as single molecules because it will result in an osmotic imbalance. Therefore, they store it as a large polymer that is osmotically inactive. Glycogen is a large, branched polymer of glucose residues that is stored free in the cytoplasm in the form of glycogen granules. Such granules contain glycogen and proteins and exist in three forms (a,b,d). a-Granules in the liver are formed by several b-granules and can measure up to 300 nm. These large granules are visible as electron dense aggregates using electron microscopy. Glycogen, as opposed to lipids is a hydrophilic molecule and it will interact with the water content of the cytoplasm. Electron microscopy studies have shown that most of the neoplasms showing a TB contain large amounts of glycogen. As mentioned before, adequate air-drying of the smears is a prerequisite for the visualization of the TB. If by any means, the slides are wet or the aspirated lesion contains a cystic component the background will dissolve and disappear. Air-drying should be followed by staining with Romanowsky based stains that use methanol as a fixative. It seems that once air-dried methanol does not dissolve the non-homogeneous mixture of glycogen and cytoplasmic contents.

Conclusion

In addition to cytologic smears from seminoma and related tumours (germinoma and dysgerminoma) other neoplasms can show a TB. All share a high cytoplasmic glycogen content, clear cell morphology and cytoplasmic fragility. This peculiar background is seen in air-dried and Romanowsky stained FNA and intraoperative cytologic samples. It is not present in effusions, liquid-based cytology and very rarely in Papanicolaou stained smears. TB is not a constant finding in the aforementioned tumors; therefore, although its presence is of diagnostic utility, its absence does not exclude the diagnosis.

CONFLICT OF INTEREST

The Authors declare no conflict of interest.

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ETHICAL CONSIDERATION

Not applicable.

AUTHORS' CONTRIBUTION

All authors have contributed to the conception and design of the study and analysis of data. JAJ-H wrote the manuscript. All authors have read and agreed to the published version of the manuscript.

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