Tzanck Smear in Dermatologic Practice

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BACKGROUND

The Tzanck smear, also known as the Tzanck test, was introduced in 1947 by the Frenchman Arnold Tzanck (Grossman & Silvers, 1992). It is a quick, inexpensive, and noninvasive method for the diagnosis of cutaneous diseases. In 1951, the effectiveness of the Tzanck smear was confirmed for the diagnosis of varicella zoster virus and herpes simplex virus (HSV; Blank et al., 1951). Its use subsequently expanded to the diagnosis of other cutaneous diseases such as pemphigus vulgaris. Since then, the Tzanck smear has been used as a rapid technique for evaluating various erosive vesiculobullous, tumoral, and granulomatous diseases. It can aid in the diagnosis of infectious diseases such as bullous impetigo and bullous diseases including pemphigoid and congenital epidermolysis bullosa. It has been used to evaluate malignancies like basal cell carcinoma (BCC) and benign growths such as seborrheic keratosis. Cutaneous leishmaniasis is a granulomatous disease that is frequently diagnosed by Tzanck smear (Eryilmaz et al., 2014). It is particularly useful in areas that are challenging to biopsy such as the oral mucosa and periocular region. Furthermore, this diagnostic test has great utility in situations where a diagnosis cannot be determined through methods such as polymerase chain reaction (PCR) and histopathology (Oranje & Folkers, 1988).

INDICATIONS

The Tzanck smear is a useful diagnostic procedure. Tzanck smears may be used to diagnose other cutaneous infections and blistering diseases and to detect herpesvirus as well as other skin conditions (Gupta & Singhi, 2005). It may be implemented in the acute setting to rapidly diagnose cutaneous herpetic infections. The Tzanck smear has been used for the diagnosis of pemphigus vulgaris, specifically in the early stages of the disease (Eryilmazet al., 2014). Importantly, this smear can help distinguish between Stevens–Johnson syndrome (SJS)/toxic epidermal necrolysis and staphylococcal scalded skin syndrome (SSSS) by the presence or absence of inflammatory cells, respectively (Table 1). The distinction between SJS/toxic epidermal necrolysis and SSSS must be made rapidly to initiate correct therapy in these disorders with high morbidity and mortality.

COLLECTION INSTRUCTIONS

1. After obtaining consent from the patient, select an intact blister that is preferably less than 3 days old to ensure cytomorphology is present.
2. Using a scalpel blade, gently deroof the lesion.
3. Scrape the base of the lesion from its advancing border in case of an erosion.
4. Smear the tissue onto a clean microscope slide.
5. Allow it to dry in the air.
6. Fix the specimen with preservative such as methanol.
7. Stain the sample with a Giemsa stain or other appropriate stain to prepare the slide for visualization under the microscope.

DIAGNOSIS

TABLE 1. Dermatologic Diagnoses Using Tzanck Smear

Disease	Clinical Presentation	Cytologic Appearance
HSV	Ulcerative vesicles with oral involvement or genital involvement for HSV-1 and HSV-2, respectively (Rechenchoski et al., 2017)	Multinucleated giant cells (Ljubojević Hadžavdić et al., 2018), like those seen in Figure 1
Eosinophilic pustular folliculitis	Multiple pustules with erythema and erosion (Yoshida et al., 2021)	Multinucleated giant cells with eosinophils (Yoshida et al., 2021)
Bullous impetigo	Local superficial blisters (Mannschreck et al., 2020)	Acantholytic cells and neutrophils (Yaeen et al., 2015)
Irritant contact dermatitis	Dry, red, scaly rash, and well-demarcated lichenified lesions (Bains et al., 2019)	Numerous polymorphonuclear leukocytes (Yaeen et al., 2015)
Basal cell carcinoma	Asymptomatic papules, plaques, or nodules that may bleed or form ulcers that do not heal (Ferrante di Ruffano et al., 2018)	"Palisade" arrangements of basal cells positioned around the margins of dense masses of larger cells (Ferrante di Ruffano et al., 2018)
Cutaneous leishmaniasis	Ulcerated nodules or plaques on exposed areas (Micheletti et al., 2017)	Leishman–Donovan bodies (V. Ruocco & Ruocco, 1999)
Staphylococcal scalded skin syndrome	Blisters distant from the site of infection (Mannschreck et al., 2020)	Many acantholytic keratinocytes without inflammatory cells (Woods & Walker, 1996)
Stevens–Johnson syndrome/toxic epidermal necrolysis	Mucous membrane erosions involving at least two sites (Bains et al., 2019; Roujeau, 1997)	Few necrotic keratinocytes along with fibroblasts and inflammatory cells (Woods & Walker, 1996)

CLINICAL STUDIES

In a study comparing the diagnostic reliability of Tzanck smear, the results showed substantial reliability for erosive vesiculobullous and granulomatous lesions (0.79 and 0.68, respectively) and moderate reliability for tumoral lesions. Thus, Tzanck smears for erosive vesiculobullous or granulomatous lesions are reliable, but tumoral lesions may require additional testing (Eryilmaz et al., 2014). A hospital-based cross-sectional study was conducted over a period of 20 months to assess the utility of Tzanck smears in supporting or excluding a diagnosis of immunobullous lesions or herpetic infections (Panwar et al., 2017). This study recommends the use of Tzanck smears as a first line diagnostic tool for vesiculobullous, erosive, and pustular lesions. The diagnostic accuracy of exfoliative cytology, a noninvasive test that uses Tzanck smears, in detecting BCC in adults was reviewed (Ferrante di Ruffano et al., 2018). Compiled data from seven studies estimated high sensitivity and high specificity of exfoliative cytology to be 97.5%and 90.1%, respectively. This suggests that exfoliative cytology can help corroborate BCC in patients with skin lesions suspecting BCC. In a study comparing diagnoses of 200 pigmented skin lesions by various dermatologists, the diagnostic reliability of Tzanck cytology and dermatoscopy were determined to be equal (Wang, 2012). With a diagnostic accuracy of 90.5%, equal to dermatoscopy, Tzanck smears could be a helpful tool for differentiating between nonmelanocytic and melanocytic lesions at the bedside (Wang, 2012).

IMPORTANT IMPLICATIONS

The Tzanck smear is comparable with punch biopsy in the rapid bedside diagnosis of cutaneous leishmaniasis with a sensitivity of 64%–77% versus 44% for a punch biopsy (Micheletti et al., 2017). Tzanck smears are also useful when HSV is suspected. Simply by altering the stain used, from Giemsa to methylene blue, the sensitivity increases from 76.9% to 86.3%, whereas the specificity increases from 91.3% to 100% (Micheletti et al., 2017). These stains have different properties and characteristics that contribute to the versatility and utility of the Tzanck smear. This technique has been found to be 97% sensitive and 86% specific for detecting BCC, although biopsies must still be taken (Micheletti et al., 2017). In terms of fungal infections, Tzanck smear can be used in place of potassium hydroxide preparations to aid in determining fungal hyphae, pseudohyphae, and spores. Specific stains such as Giemsa can differentiate between Candida and dermatophytes (Kelly & Shimoni, 2009). This smear can assist in differentiating a benign process such as erythema toxicum neonatorum from a life-threatening disseminated Candida infection sparing patients from more invasive testing and inappropriate treatment (Micheletti et al., 2017). Although other techniques like PCR have better sensitivity and specificity for diagnosis, Tzanck smear is relatively less expensive and time consuming while still reliable in diagnosing herpetic infections (Ozcan et al., 2007; Panwar et al., 2017). The smear also eliminates the need for biopsy in diagnosing certain cutaneous infections such as candidiasis and leishmaniasis (Panwar et al., 2017).

LIMITATIONS OF TZANCK SMEAR

- Administrative burden of laboratory certification
- Difficulty distinguishing diseases without specific cytologic findings
- May necessitate follow up with other techniques for clinical diagnosis; Limited utility in outpatient settings
- High false-positive and false-negative rates in diagnosing herpetic infections

DISCLOSURES & CONFLICTS OF INTEREST

Authors have no financial disclosures or conflicts of interest to report

REFERENCES

Blank, H., Burgoon, C. F., Baldridge, G. D., McCarthy, P. L., Urbach, F. (1951). Cytologic smears in diagnosis of herpes simplex, herpes zoster, and varicella. Journal of the American Medical Association, 146(15), 1410–1412. 10.1001/jama.1951.63670150005012b

Eryilmaz, A., Durdu, M., Baba, M., Yildirim, F. E. (2014). Diagnostic reliability of the Tzanck smear in dermatologic diseases. International Journal of Dermatology, 53(2), 178–186. 10.1111/j.1365-4632.2012.05662.x

Ferrante di Ruffano, L., Dinnes, J., Chuchu, N., Bayliss, S. E., Takwoingi, Y., Davenport, C.,Matin, R.N., O'Sullivan, C., Roskell, D., Deeks, J. J.,Williams, H. C. (2018). Exfoliative cytology for diagnosing basal cell carcinoma and other skin cancers in adults. In González, U. (Ed.), Cochrane Database of Systematic Reviews, 2018(12), CD013187. 10.1002/14651858.CD013187

Grossman, M. C., Silvers, D. N. (1992). The Tzanck smear: Can dermatologists accurately interpret it? Journal of the American Academy of Dermatology, 27(3), 403–405. 10.1016/0190-9622(92)70207-V

Gupta, L. K., Singhi, M. K. (2005). Tzanck smear: A useful diagnostic tool. Indian Journal of Dermatology, Venereology and Leprology, 71(4), 295–299). 10.4103/0378-6323.16632

Kelly, B., Shimoni, T. (2009). Reintroducing the Tzanck smear. American Journal of Clinical Dermatology, 10(3), 141–152. 10.2165/00128071-200910030-00001

Micheletti, R.G., Dominguez, A. R.,Wanat, K. A. (2017). Bedside diagnostics in dermatology: Parasitic and noninfectious diseases. Journal of theAmerican Academy of Dermatology, 77(2), 221–230. https://doi.org/10.1016/j.jaad.2016.06.035

Oranje, A. P., Folkers, E. (1988). The Tzanck smear: Old, but still of inestimable value. Pediatric Dermatology, 5(2), 127–129. 10.1111/j.1525-1470.1988.tb01154.x

Ozcan, A., Senol,M., Saglam,H., Seyhan,M., Durmaz, R., Aktas, E.,Ozerol, I. H. (2007). Comparison of the Tzanck test and polymerase chain reaction in the diagnosis of cutaneous herpes simplex and varicella zoster virus infections. International Journal of Dermatology, 46(11), 1177–1179. 10. 1111/J.1365-4632.2007.03337.X

Panwar, H., Joshi, D., Goel, G., Asati, D., Majumdar, K., Kapoor, N. (2017). Diagnostic utility and pitfalls of Tzanck smear cytology in diagnosis of various cutaneous lesions. Journal of Cytology, 34(4), 179–182. 10.4103/JOC.JOC_88_16

Wang, L. T. (2012). Clarification on dermatoscopy versus Tzanck smear test: A comparison of the value of two tests in the diagnosis of pigmented skin lesions. Journal of the American Academy of Dermatology, 66(5), 852–853.10.1016/j.jaad.2011.11.966