THE SIGNIFICANCE OF ROUTINE BLOOD TESTS IN PATIENTS WITH HEAD AND NECK CANCERS

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Summary

More research suggest that parts of complete blood count might indicate disease-free and overall survival in patients with various cancers and therefore also in patients with head and neck cancer. Therefore, the aim of this paper was to review current knowledge upon significance of complete blood count in head and neck cancers. PubMed was searched in the last 10 years in order to find out references upon this topic and 19 articles were included. Leukocytosis and thrombocytosis negatively correlate with treatment outcome in patients with head and neck cancers, however not in all studies. High preoperative values of neutrophil and lymphocyte ratio suggest poorer disease outcome, i.e. shorter disease free period and overall survival in patients with head and neck cancer. It seems that published data provide an additional practical guidelines for evaluation of disease course in patients with head and neck cancer.

KEY WORDS: *head and neck cancer, complete blood count*

ZNAČAJ RUTINSKIH KRVNIH PRETRAGA
U BOLESNIKA S KARCINOMIMA GLAVE I VRATA

Sažetak

Sve vise je istraživanja koja pokazuju kako elementi kompletne krvne slike mogu ukazati na period bez bolesti i ukupno preživljenje u bolesnika s raznim karcinomima. PubMed pregledom nađeno je 19 radova objavljenih zadnjih 10 godina o rutinskim laboratorijskim pretragama i karcinomima glave i vrata. Leukocitoza i trombocitoza su negativno povezane s ishodom liječenja u većini slučajeva bolesnika s orofaringealnim karcinomom, iako ne u svim istraživanjima. Visoke prijeoperacijske vrijednosti odnosa neutrofila i limfocita ukazuju na lošiji ishod bolesti odnosno na kraći period bez bolesti i na lošije ukupno preživljenje u bolesnika s karcinomima glave i vrata. Čini se kako rezultati istraživanja omogućuju dodatne praktične vodiče u prognostici tijeka bolesti u bolesnika koji boluju od karcinoma glave i vrata.

KLJUČNE RIJEČI: *karcinomi glave i vrata, komplenta krvna slika*

INTRODUCTION

Current prognostic criteria in predicting outcomes in patients with head and neck cancer are inadequate and easily so far available biomarkers are re-evaluated. Recent studies have shown that the presence of systemic inflammation correlates with poorer disease-free and overall survival in patients with cancer (1,2,3). Anemia, hemoglobinemia, thrombocytosis and leukocytosis are thought to be an adverse prognostic factors in various malignancies (1,2,3). Recently, it has been shown that the preoperative neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) as well as lymphocyte to monocyte ratio (LMR) might indicate patients which will respond poorly to the treatments and who have worse disease-free survival (DFS) together with overall disease survival (OS) in many cancers such as small cell lung carcinoma, esophageal carcinoma, pancreatic adenocarcinoma and head and neck cancers (1,2,3,4).

MATERIALS, METHODS AND RESULTS

PubMed was searched in the last 10 years in order to find out references upon this topic. 19 articles were included. Key words were: oral cancer, head and neck cancer, complete blood count, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, lymphocyte/monocyte ratio, anemia, hemoglobinemia, thrombocytosis, leukocytosis.

DISCUSSION

Chen et al. (4) analyzed 618 patients with oral cancer and found out that the incidence of leukocytosis was 7.2%. Median survival of patients was low if the patient had leukocytosis, moreover the incidence of leukocytosis was high during the course of the disease, and had an adverse impact on overall survival. Therefore, the same authors concluded that periodic evaluation of serum white cell count should be performed postoperatively. Additionally, Peter et al. (5) followed 261 patients with primary squamous cell carcinoma of the oral cavity, pharynx, or larynx. One of the most frequent laboratory pathologies was leukocytosis (20 %). Contrary to these results, Kruse et al. (6) who analyzed 278 patients with oral cancer and

who could not report significant correlation between WBC count and the development of recurrence or metastases. It seems that the elevated WBC count does not seem to be a predictor for recurrence or for further metastases. Tsai et al. (7) reported that white blood cell (WBC) count, monocyte, and neutrophil counts and neutrophil lymphocyte ratio increased with the advancement of clinical stage (i.e. T4) and poorer tumor differentiation in patients with oral cancer, however, the lymphocyte count decreased. Furthermore, Tsai et al. reported that the higher pretreatment circulating monocyte count was an independent prognostic factor for cancer-specific survival in 202 patients with oral cavity cancer and that monocyte count was increased in patients with lymph node metastasis.

Kargus et al. (8) reported that in 51 patients (out of 288 with head and neck cancer) who had recurrence, three were in the thrombocytosis group, and 45 patients with recurrence were in the normal thrombocyte range. Furthermore, Perisanidis et al. (9) evaluated postoperative platelet count changes in 102 patients with oral and oropharyngeal squamous cell carcinoma and have shown that the failure of platelets to recover to normal range by the seventh postoperative day is an independent adverse prognostic factor in patients with oral and oropharyngeal cancer undergoing neoadjuvant treatment and surgery. Shoultz-Henley et al. (10) pretreatment platelet elevation is a promising predictor of prognosis in 433 patients with oropharyngeal cancer patients treated with chemo-radiation.

Grimm et al. (11) reported that NLR correlated significantly with PLR. LMR inversely correlated with NLR and PLR after analysis was performed on 146 patients with OSCC. Perisanidis et al. (12) analyzed 97 patients with oral cancer undergoing preoperative chemo-radiotherapy regarding DFS. The same authors (12) reported that a high pretreatment NLR is a significant independent predictor of shorter DFS in patients with oral cancer receiving preoperative chemo-radiotherapy. Fang et al. (13) analyzed data from 226 patients with oral cancer and reported that elevated NLR was significantly associated with pathological tumor status, pathologic nodal metastasis, tumor depth, disease-free survival and overall survival. The influence NLR on disease-free survival and overall survival still existed after adjusting for tu-

mor status, lymph node metastasis, and tumor cell differentiation. Song et al. (14) showed that high preoperative NLR is associated with increased wound complications and poor survival in patients with hypopharyngeal squamous cell carcinoma after radical resections.

Rassouli et al. (15) concluded that PLR is an independent predictor of mortality, NLR is an independent predictor of recurrence in 273 head and neck cancer patients. Huang et al. (16) reported that high circulating neutrophil count and monocyte count predict worse overall and recurrence-free survival, while high circulating lymphocyte count predicts better recurrence-free survival and marginally better overall survival in these patients who are HPV positive. However, this association was not apparent in HPV-negative patients. He et al. (17) concluded that pretreatment NLR and percentages of neutrophil and lymphocytes were independent prognostic variables of survival in 1410 patients with nasopharyngeal carcinoma. Jin et al. (18) found out that pretreatment NLR was a significant prognostic variable of poor prognosis in 229 patients with metastatic nasopharyngeal carcinoma. Jiang et al. (19) identified that pretreatment LMR was an independent prognostic factor for 672 patients with metastatic nasopharyngeal carcinoma.

Grimm et al. (20) analyzed 187 patients with OSCC. CRP levels, Hb levels, and WBC count and showed significant differences between non-recurrent and recurrent group of OSCC. On univariate analysis, patients with high pre-treatment LPI (LPI ≥ 2) had a significant poorer prognosis. Multivariate analysis showed that the most important independent prognostic factor was high pre-treatment LPI (LPI ≥ 2). Moreover, pre-treatment LPI ≥ 2 showed high probability that loco-regional recurrence will be present later. The same study (20) highlights the combination of inflammatory CRP levels, Hb levels, and WBC count as the most important independent prognostic factor in predicting disease recurrence of patients with OSCC. LPI can be used as a pre-treatment inflammatory biomarker that may identify OSCC with a more aggressive biological phenotype of the disease and might be helpful for guiding further post-operative treatment in OSCC.

Rachidi et al. (21) reported that NLR is a robust predictor of overall survival in oral, pharyngeal, and laryngeal squamous cell carcinomas

Fang et al. (22) analyzed data from 226 patients with oral cancer and reported that elevated NLR was significantly associated with tumor status, nodal metastasis, tumor depth, disease-free survival and overall survival. The level of NLR on DFS and OS has been shown to exist still after adjusting data for tumor status, lymph node metastasis, and tumor cell differentiation.

CONCLUSION

It seems that this data provides an additional practical guideline of further postoperative management patients with head and neck cancer.

REFERENCES

1. Toiyama Y, Inoue Y, Kawamura M, Kawamoto A, Okugawa Y, Hiro J,et al. Elevated platelet count as predictor of recurrence in rectal cancer patients undergoing preoperative chemo-radiotherapy followed by surgery. Int Surg. 2015;100:199-207.

2. Peng B, Wang YH, Liu YM, Ma LX. Prognostic significance of the neutrophil to lymphocyte ratio in patients with non-small cell lung cancer: a systemic review and meta-analysis. Int J Clin Exp Med. 2015;8:3098-106.

3. Sugiura T, Uesaka K, Kanemoto H, Mizuno T, Okamura Y. Elevated preoperative neutrophil-to-lymphocyte ratio as a predictor of survival after gastroenterostomy inpatients with advanced pancreatic adenocarcinoma. Ann Surg Oncol. 2013;20:4330-7.

4. Chen YW, Chen IL, Lin IC, Kao SY. Prognostic value of hypercalcaemia and leucocytosis in resected oral squamous cell carcinoma. Br J Oral Maxillofac Surg. 2014;52:425-31.

5. Peter F, Wittekindt C, Finkensieper M, Kiehntopf M, Guntinas-Lichius O. Prognostic impact of pretherapeutic laboratory values in head and neck cancer patients. J Cancer Res Clin Oncol. 2013;139:171-8.

6. Kruse AL, Luebbers HT, Grätz KW. Evaluation of white blood cell count as a possible prognostic marker for oral cancer. Head Neck Oncol. 2011;3:13.

7. Tsai YD, Wang CP, Chen CY, Lin LW, Hwang TZ, Lu LF,et al. Pretreatment circulating monocyte count associated with poor prognosis in patients with oral cavity cancer. Head Neck. 2014;36:947-53.

8. Kargus S, Weber FE, Luebbers HT, Zemann W, Graetz KW, Kruse AL. Pretreatment thrombocytosis: a prognostic marker for oral squamous cell carcinoma? Oral Maxillofac Surg. 2012;16:197-200.

9. Perisanidis C, Kornek G, Pöschl PW, Holzinger D, Pirklbauer K, Schopper C, et al. High neutrophil-to-lymphocyte ratio is an independent marker of poor disease-specific survival in patients with oral cancer. Med Oncol. 2013;30:334.

10. Shoultz-Henley S, Garden AS, Mohamed AS, Sheu T, Kroll MH, Rosenthal DI, et al. Prognostic value of pre-therapy platelet elevation in oropharyngeal cancer patients treated with chemoradiation. Int J Cancer. 2016; 138:1290-7.

11. Grimm M, Rieth J, Hoefert S, Krimmel M, Rieth S, Teriete P, et al. Standardized pretreatment inflammatory laboratory markers and calculated ratios in patients with oral squamous cell carcinoma. Eur Arch Otorhinolaryngol. 2016;273:3371-84.]

12. Perisanidis C, Mittlböck M, Schoppmann A, Kornek G, Starlinger P, Stift A, et al. Postoperative failure of platelet recovery is an independent risk factor for poor survival in patients with oral and oropharyngeal cancer. Clin Oral Investig. 2013;17:913-9.

13. Fang JF, Huang Y, Chen QX. Preoperative platelet lymphocyte ratio (PLR) is superior to neutrophil lymphocyte ratio (NLR) as a predictive factor in patients with esophageal squamous cell carcinoma. World J Surg Oncol. 2014;12:58.

14. Song Y, Liu H, Gao L, Liu X, Ma L, Lu M, at al. Preoperative neutrophil-to-lymphocyte ratio as prognostic predictor for hypopharyngeal squamous cell carcinoma after radical resections. J Craniofac Surg. 2015; 26: e137-40.

15. Rassouli A, Saliba J, Castano R, Hier M, Zeitouni AG. Systemic inflammatory markers as an independent prognosticators of head and neck squamous cell carcinoma. Head Neck. 2015; 37:103-10.

16. Huang SH, Waldron JN, Milosevic M, Shen X, Ringash J, Su J, et al. Prognostic value of pretreatment circulating neutrophils, monocytes and lymphocytes in oropharyngeal cancer stratified by human papillomavirus status. Cancer. 2015;121:545-55.

17. He JR, Shen GP, Ren ZF, Qin H, Cui C, Zhang Y, et al. Pretreatment levels of peripheral neutrophils and lymphocytes as an independent prognostic factors in patients with nasopharyngeal carcinoma. Head Neck. 2012;34:1769-76.

18. Jin Y, Ye X, He C, Zhang B, Zhang Y. Pretreatment neutrophil-to-lymphocyte ratio as predictor of survival for patients with metastatic nasopharyngeal carcinoma. Head Neck. 2015; 37 (1): 69-75.

19. Jiang R, Cai XY, Yang ZH, Yan Y, Zou X, Guo L, et al. Elevated peripheral blood lymphocyte-to-monocyte ratio predicts a favorable prognosis in the patients with metastatic nasopharyngeal carcinoma. Chin J Cancer. 2015;34:237-46.

20. Grimm M, Lazariotou M. Clinical relevance of a new pre-treatment laboratory prognostic index in patients with oral squamous cell carcinoma. Med Oncol. 2012;29:1435-47.

21. Rachidi S, Wallace K, Wrangle JM, Day TA, Alberg AJ, Li Z. Neutrophil-to-lymphocyte ratio and overall survival in all sites of head and neck squamous cell carcinoma. Head Neck. 2016;38(Suppl 1) E1068-E1074.

22. Fang HY, Huang XY, Chien HT, Chang JT, Liao CT, Huang JJ, et al. Refining the role of preoperative C-reactive protein by neutrophil/lymphocyte ratio in oral cavity squamous cell carcinoma. Laryngoscope. 2013; 123(11):2690-9.

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