Chapter 27

CANCER OF UNKNOWN PRIMARY SITE

Tülay EREN¹

INTRODUCTION

While primary tumor can be detected in approximately 98% of patients with metastatic cancer, primary site can not be found in the remaining 2%. This group of diseases is termed as cancer of unknown primary site (CUP). In postmortem examination of patients whose primary site can not be detected with clinical investigations, primary tumor can be detected in 75% of patients. The size is under 10 mm in most of the primary tumors detected [1, 2].

For making the diagnosis of CUP; following thorough history and physical examination, whole blood count, biochemical analyses, urinalysis, thoracoabdominal computerized tomography (CT), for women breast ultrsaonographic examination and mammography and for men prostate-specific antigen (PSA) investigations can be carried out. In pathological examinations in addition to histological evaluation, immunohistochemical (IHC) staining is performed. If imaging techniques used remain inadequate, Positron Emission Tomography (PET) investigation can also be conducted [3].

New developments in imaging techniques and immunohistochemical methods made a novel classification of CUP's possible. Together with tissue-of-origin molecular profiling and next-generation sequencing (NGS), which have been used commonly, individualized treatment approaches have started to become popular.

CLINICAL EVALUATION

Imaging

Unless there is counter indication, all CUP patiens should undergo intravenous (IV) contrast thorax, abdominal and pelvic computerized tomography (CT) investigation. In the selection of other imaging techniques, clinical picture of the patients should be guiding [4]. In women whose isolated axillarly lymphadenopathy (LAP) pathology results turn out to be adenocarcinoma and who do not have

¹ Uzm. Dr, S.B.Ü Dışkapı Yıldırım Beyazıt Eğitim ve Araştırma Hastanesi, tulayeren78 @gmail.com

REFERENCES

- Hainsworth, J.D. and F.A. Greco, Cancer of Unknown Primary Site: New Treatment Paradigms in the Era of Precision Medicine. Am Soc Clin Oncol Educ Book, 2018(38): p. 20-25.
- Pentheroudakis, G., V. Golfinopoulos, and N. Pavlidis, Switching benchmarks in cancer of unknown primary: from autopsy to microarray. Eur J Cancer, 2007. 43(14): p. 2026-36.
- 3. Tomuleasa, C., et al., How to Diagnose and Treat a Cancer of Unknown Primary Site. J Gastrointestin Liver Dis, 2017. 26(1): p. 69-79.
- 4. Varadhachary, G.R. and M.N. Raber, Cancer of unknown primary site. N Engl J Med, 2014. 371(8): p. 757-65.
- 5. Zhang, J.J., et al., [MRI findings and pathological features of occult breast cancer]. Zhonghua Zhong Liu Za Zhi, 2018. 40(1): p. 40-45.
- Koivunen, P., et al., Unknown primary: diagnostic issues in the biological endoscopy and positron emission tomography scan era. Curr Opin Otolaryngol Head Neck Surg, 2015. 23(2): p. 121-6.
- 7. Saliminejad, M., et al., The yield and cost of colonoscopy in patients with metastatic cancer of unknown primary. Aliment Pharmacol Ther, 2013. 38(6): p. 628-33.
- Losa, F., et al., SEOM clinical guideline on unknown primary cancer (2017). Clin Transl Oncol, 2018. 20(1): p. 89-96.
- 9. Noij, D.P., et al., Diagnostic value of diffusion-weighted imaging and (18)F-FDG-PET/CT for the detection of unknown primary head and neck cancer in patients presenting with cervical metastasis. Eur J Radiol, 2018. 107: p. 20-25.
- Cengiz, A., S. Goksel, and Y. Yurekli, Diagnostic Value of (18)F-FDG PET/CT in Patients with Carcinoma of Unknown Primary. Mol Imaging Radionucl Ther, 2018. 27(3): p. 126-132.
- 11. Kwee, T.C. and R.M. Kwee, Combined FDG-PET/CT for the detection of unknown primary tumors: systematic review and meta-analysis. Eur Radiol, 2009. 19(3): p. 731-44.
- 12. Bochtler, T., H. Loffler, and A. Kramer, Diagnosis and management of metastatic neoplasms with unknown primary. Semin Diagn Pathol, 2018. 35(3): p. 199-206.
- Lin, F. and H. Liu, Immunohistochemistry in undifferentiated neoplasm/tumor of uncertain origin. Arch Pathol Lab Med, 2014. 138(12): p. 1583-610.
- 14. Conner, J.R. and J.L. Hornick, Metastatic carcinoma of unknown primary: diagnostic approach using immunohistochemistry. Adv Anat Pathol, 2015. 22(3): p. 149-67.
- 15. Selves, J., et al., Immunohistochemistry for Diagnosis of Metastatic Carcinomas of Unknown Primary Site. Cancers (Basel), 2018. 10(4).
- Chu, P.G. and L.M. Weiss, Keratin expression in human tissues and neoplasms. Histopathology, 2002. 40(5): p. 403-39.
- 17. Bahrami, A., L.D. Truong, and J.Y. Ro, Undifferentiated tumor: true identity by immunohistochemistry. Arch Pathol Lab Med, 2008. 132(3): p. 326-48.
- Erlander, M.G., et al., Performance and clinical evaluation of the 92-gene real-time PCR assay for tumor classification. J Mol Diagn, 2011. 13(5): p. 493-503.
- Weiss, L.M., et al., Blinded comparator study of immunohistochemical analysis versus a 92-gene cancer classifier in the diagnosis of the primary site in metastatic tumors. J Mol Diagn, 2013. 15(2): p. 263-9.
- Greco, F.A., et al., Poorly differentiated neoplasms of unknown primary site: diagnostic usefulness of a molecular cancer classifier assay. Mol Diagn Ther, 2015. 19(2): p. 91-7.

- Pentheroudakis, G., A. Stoyianni, and N. Pavlidis, Cancer of unknown primary patients with midline nodal distribution: midway between poor and favourable prognosis? Cancer Treat Rev, 2011. 37(2): p. 120-6.
- 22. Bugat, R., et al., Summary of the Standards, Options and Recommendations for the management of patients with carcinoma of unknown primary site (2002). Br J Cancer, 2003. 89 Suppl 1: p. S59-66.
- 23. Dowell, J.E., et al., A randomized Phase II trial in patients with carcinoma of an unknown primary site. Cancer, 2001. 91(3): p. 592-7.
- 24. Hainsworth, J.D., et al., Paclitaxel/carboplatin/etoposide versus gemcitabine/irinotecan in the first-line treatment of patients with carcinoma of unknown primary site: a randomized, phase III Sarah Cannon Oncology Research Consortium Trial. Cancer J, 2010. 16(1): p. 70-5.
- 25. Hainsworth, J.D., et al., Molecular gene expression profiling to predict the tissue of origin and direct site-specific therapy in patients with carcinoma of unknown primary site: a prospective trial of the Sarah Cannon research institute. J Clin Oncol, 2013. 31(2): p. 217-23.
- 26. Moran, S., et al., Epigenetic profiling to classify cancer of unknown primary: a multicentre, retrospective analysis. Lancet Oncol, 2016. 17(10): p. 1386-1395.
- 27. Handorf, C.R., et al., A multicenter study directly comparing the diagnostic accuracy of gene expression profiling and immunohistochemistry for primary site identification in metastatic tumors. Am J Surg Pathol, 2013. 37(7): p. 1067-75.
- Hainsworth, J.D., et al., A retrospective study of treatment outcomes in patients with carcinoma of unknown primary site and a colorectal cancer molecular profile. Clin Colorectal Cancer, 2012. 11(2): p. 112-8.
- 29. Greco, F.A. and J.D. Hainsworth, Renal Cell Carcinoma Presenting as Carcinoma of Unknown Primary Site: Recognition of a Treatable Patient Subset. Clin Genitourin Cancer, 2018. 16(4): p. e893-e898.
- Kumarakulasinghe, N.B., N. van Zanwijk, and R.A. Soo, Molecular targeted therapy in the treatment of advanced stage non-small cell lung cancer (NSCLC). Respirology, 2015. 20(3): p. 370-8.