MODERN AND MOLECULAR PATHOLOGY IN DIFFICULT DIAGNOSTIC CASES

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Since the beginning of 20th century when there have been used different histochemical techniques, the development of modern pathology included such methods as electron microscopy (with first studies in 40-ties golden era in 70-ties last century), immunohistochemistry (introduced in 60-ties and now widely used) and molecular biology (with the most dynamic development, now) based on genetic studies. The new techniques allow for better, in meaning of more precise, diagnosis. Here we would like present 3 extraordinary cases from daily diagnostic practice. Without multiple studies our final diagnosis and cases solution wouldn't be possible.

Case A. 23 years old female patient with a some clinical symptoms was directed for further morphological diagnosis. In Febuary 2006 mediastinal tumor biopsy was done, and at that time diagnosis of Hodgkin disease was made. One month later, in another hospital using the primary biopsy material immunohistochemical (IHC) studies were done with the following expression: CD30 ±, LCA neg., CD3 neg., CD20 neg., CD43 neg., Alk 1 neg., CAM 5.2 neg., Ki 67+ (close to 40%). The opinion in next center on cases in April 2006 was: possible anaplastic lymphoma form large T cells (ALCL) with atypical phenotype. However, parallel consultation in another city was as follows: according to performed studies lymphoma and thymoma could excluded, the differential diagnosis should include embryonal tumor. In spite of that patient was given typical for ALCL chemotherapy, but no tumor response was noted. In November 2006, the patient developed subcutaneous breast tumor and BAC examination revealed neoplastic cells. The IHC performed on this tumor sample showed cells with hPL (human placental lactogen) + and CD 30± , and negative expression of the following: PLAP, beta hCG, LCA, CD 3, CD 43, Alk 1, AE1/AE3, e-cadherin, HER 2. According to morphology and IHC results there was suggested diagnosis of trophoblastic tumor. One moth later patient received typical for embryonal tumors chemotherapy with partial tumor response in meaning of decreased tumor size. In July 2007 mediastinal tumor resection was done. The morphology of this tumor corresponded to malignant epithelial tumor with IHC results as: VIM+, CD 30±, S100±, chromogranin ±, and negative for: AE1/AE3, CAM 5.2, LCA, EMA, CD15, CD20, CD3, UCHL 1, Alk 1, AFP, PLAP, CD117, SYN, SER, NCAM, CD68, CD 1a, desmin, CEA, TTF 1,

CALC, CK 7, HMB45, bcl2, NSE, and CD 99. Later additionally hPL was done with positive expression. Patient died in 2008.

Case B. 56 year old female patient was admitted to gynecology clinic for uterine resection due to vaginal bleeding. The last menstruation bleeding before those szmptoms was 6 years ago. The clinical history was negative, and the only laboratory abnormality was increased level of hCG. Hysterectomy was done and uterus of diam. 12cm with mass that involved also intestines, urinary bladder, omentum and Douglas sinus was removed. The rapid intraoperative diagnosis was: malignant tumor with excessive necrosis, and latter from paraffin blocks: malignant tumor probably leiomyosarcoma. The IHC done on tumor samples revealed the following results: hCG+, CK AE1/AE3+, CK7+, CK 5/6/18 neg., CK20 neg., vimentin+, Ki-67+(80-90%), p63 neg., SMA, neg. desmin neg., ER neg., PR neg. PLAP neg. According to those studies epithelioid trophoblastic tumor diagnosis was made.

Trophoblastic diseases include e.g.: exaggerated placental site, partial hydatidiform mole, complete hydatidiform mole, invasive mole, choriocarcinoma, placental site trophoblastic tumor, epithelioid trophoblastic tumor (ETT), and according to hCG expression this group of lesions should be differentiated from a subtype of endometrial carcinoma (EC). There is broad diversity of IHC studies results in trophoblastic diseases, and according to previous publications transmission electron microscopy (EM) studies could be done. In ETT, EM studies one should expect: presence of undifferentiated cells with fewer cytoplasmal organelles, mononuclear or binuclear cells with abundant cytoplasm, bundles of well-developed intermediate-type filaments. In such a cases sometimes diagnostic is presence of desmosomal junction. There were also published cases with features similar to adenocarcinoma. On the other hand EC studied by EM usually reveals: no stroma between cells and presence of foam (fat positive) cells which are not histocytes. There were reports that EC may have trophoblastic differentiation (with hCG+ cells). After all aforementioned studies done and discussion the final diagoses were as follows, case A: epithelioid trophoblastic tumor, and case B: в-hCG secreting endometrial carcinoma.

Case C. 27 year old female with chronic kidney 12 years of systemic lupus underwent cadaveric donor’s kidney transplantation. Few days after transplantation systemic malignancy in a donor was established. The transplant host after months of rigorous follow-up revealed in PET studies suspicious mass nearby transplanted kidney. In September 2007 transplanted kidney biopsy revealed infiltrating adenocarcinoma and immediate transplantectomy was performed. Then patient underwent several abdominal surgeries and finally died in December. The tumor removed from transplant recipient in the following IHC were done: CK 7, CK 20, CK HMW, p501s, p504s, TTF 1, synaptophisin and mucin. At the end we performed FISH analysis of sex chromosomes and proved that the tumor cells were from male donor.

Literature

For case A and B:

1. Allison KH, Love JE, Garcia RL: Epithelioid trophoblastic tumor: review of a rare neoplasm of the chorionic-type intermediate trophoblast. Arch Pathol Lab Med 2006, 130: 1875-1877.
2. Chatzaki E, Gallagher CJ, Iles RK et al.: Characterisation of the differential expression of marker antigens by normal and malignant endometrial epithelium. Br J Cancer 1994, 69:1010-1014.
3. Grenache DG, Moller KA, Groben PM: Endometrial adenocarcinoma associated with elevated serum concentration of free beta subunit of human chorionic gonadotropin. Am J Clin Pathol. 2004, 121:748-753
4. Hamazaki S, Nakamoto S, Okino T, et al.: Epithelioid trophoblastic tumor: morphological and immunohistochemical study of three lung lesions. Hum Pathol 1999, 30:1321-1327.
5. Kajo K, Zubor P, Spacek J, Ryska A: Carcinosarcoma of the uterus with melanocytic differentiation. Pathol Res Pract 2007, 203:753-758.
6. Zimmermann G, Ackermann W, Alexander H: Epithelial human chorionic gonadotropin is expressed and produced in human secretory endometrium during the normal menstrual cycle. Biol Reprod 2009, 80:1053-1065.

For case C:

7. Morath C, Mueller M, Goldschmidt H, et al.: Malignancy in renal transplantation. J Am Soc Nephrol 2004, 15: 1582-1588.
8. Harvey L, Fox M: Transferral of malignancy as a complication of organ transplantation: an insuperable problem? J Clin Pathol 1981, 34: 116-122.

КЛИНИКО-МОРФОЛОГИЧЕСКИЕ КЛАССИФИКАЦИОННЫЕ ПОДХОДЫ ПРИ ДИАГНОСТИКЕ ГИПЕРПЛАСТИЧЕСКИХ ПРОЦЕССОВ ЭНДОМЕТРИЯ

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За последние десятилетия отмечен рост частоты в популяции и омоложение гиперпластических процессов эндометрия с тенденцией к их рецидивированию и неблагоприятным прогнозом в плане озлокачествления, а также тяжелыми последствиями для общего состояния здоровья женщины, ее репродуктивной функции (на основании ретроспективного анализа базы данных Белорусского канцер-регистра, базы данных регистра «Биопсия»). По данным разных исследований,