DOWNLOAD PDF CURRENT ISSUES IN LYMPHOMA (DIAGNOSTIC ONCOLOGY ; VOL 4, NO 1)

Chapter 1 : Archives - Cardiovascular Diagnosis and Therapy

This bar-code number lets you verify that you're getting exactly the right version or edition of a book. The digit and digit formats both work.

Since the publication of the World Health Organization classifications of lymphoma, additional immunohistochemical tests and other ancillary methods such as flow cytometry, cytogenetic and other molecular biology techniques, have been applied in routine clinical work. Due to the utilization of these methodologies, there has been great progress in the pathological diagnosis and classification of lymphomas in the mainland of China. Nonetheless, lymphoma pathology still remains very challenging in the field of diagnostic pathology. Here, we summarize the common misdiagnoses and pitfalls when dealing with lymphoma cases, the cause of the errors and strategies to avoid inaccurate diagnoses. Lymphoma; pitfalls; diagnosis Submitted Mar 27, Accepted for publication Sep 28, For typical ultrasound or computed tomography CT -guided biopsies, we recommend using an 18 gauge G cutting needle to ensure enough tissue is acquired for hematoxylin and eosin HE staining, immunohistochemistry and molecular testing. Another problem that can arise is when the tissue sampling is not representative of the lesion, which may lead to misdiagnosis. To avoid this problem, pathologists should be in regular communication with clinicians and convey to them the requirement for the specimen. Whenever possible, an excisional biopsy is preferred. Training of junior pathologists in tissue sampling is also important. Inadequate processing of tissue Tissue processing involves the fixation, dehydration, embedding, sectioning, staining and mounting of the tissue. Each step is important in yielding adequately stained sections to allow for an accurate diagnosis. Any detail of this process that is neglected may cause potential diagnostic pitfalls. For example, lymph nodes must be fixed promptly and be sliced before fixation, because the fibrous capsule of the lymph node resists the penetration of the fixative. Tissue that is not fixed properly can lead to alterations in morphology and immunohistochemical results. Microscopically, fixed lymph nodes that have not yet been cut often have a peripheral rim of well-preserved structure. The centers of the lymph nodes, however, do not get fixed completely. The center then appears to consist of shrunken lymphocytes, some of which have acentric nuclei and look like plasma cells. Figure 1 Poorly fixed diffuse large B cell lymphoma of the testis. This occurs when the technician dries the slide with a hairdryer without putting it into xylene to make the slide clear. The nuclei of the lymphocytes shrink to darkly stained dots that lack any detail, again making an accurate diagnosis difficult Figure 2. We encountered this problem for several years until Liu et al. Figure 2 A A tissue section of a splenic marginal zone lymphoma that was dried with a hairdryer. Inadequate clinical information Since surgical pathology is part of clinical medicine, one cannot make an accurate lymphoma diagnosis without adequate clinical information. The World Health Organization WHO emphasizes that diagnosis of such pathologies should integrate clinical, morphological, immunophenotypical, and molecular genetic data. Therefore, regular multidisciplinary discussion plays an important role in the diagnosis of many diseases, especially challenging cases such as lymphomas. Errors due to personal subjectivity Although current diagnoses are based on combining results from ancillary techniques, the final diagnosis is still the subjective conclusion of a pathologist. Due to variations in training background and practical experience, pathologists sometimes draw different conclusions from the same objective specimen. These discrepancies can delay the proper treatment for patients, and in extreme circumstances can cause legal problems. Errors relating to immunohistochemistry As summarized by Bridget S. Wilkins 3 , immunohistochemistry-related errors are shown in Table 1. Table 1 Errors relating to immunohistochemistry Full table In our experience, the most common error is insufficient range of antibody tests. With an insufficient range of tests, there may be inadequate diagnostic precision. For example, a splenic mantle cell lymphoma was categorized as marginal zone lymphoma and later diagnosed as DLBCL when the patient developed cervical lymph node enlargement. This misdiagnosis likely occurred because CD5 and Cyclin D1 expression were not initially examined Figure 3. HE, hematoxylin and eosin. The

use of an insufficient panel of immunostains can also cause the misdiagnosis of an ALK positive lymphoma as Hodgkin lymphoma or reactive lymphoid proliferation. Several outside medical centers were consulted for their opinion on a case and did not include ALK in their initial panel of antibodies Figure 4. Knowledge of immunohistochemical staining in normal tissue compared to the various types of lymphomas Familiarity with the immunohistochemical staining pattern of the normal lymph node and the variation observed in lymphoma is critical to the accurate diagnosis of lymphoma. Recognizing the different distribution pattern of CD20 and CD3 positive lymphocytes between normal and lymphoma conditions is essential for the correct diagnosis. In addition, B cell lymphoma-2 Bcl-2 positivity in the follicular center must be evaluated by the number and distribution pattern of germinal center T cells. This is critical in differentiating follicular lymphoma from reactive proliferation. Furthermore, Bcl-2 positivity cannot be used to distinguish between follicular lymphoma and other small B cell lymphomas, because all of these conditions may express Bcl Specificity of antibodies It is beneficial for pathologists to understand the specificity of antibodies. For example, it is important to know that a monoclonal antibody has specificity for one epitope on one antigen and not for the entire cell expressing that antigen. Cross-lineage expression of antigens can occasionally occur, such as aberrant expression of CD20 in T and NK cell lymphomas or CD3 expression in non-T cell lymphomas. Most monoclonal antibodies that are commonly used have been developed with high sensitivity for use with formalin fixed, paraffin-embedded tissues. However, some antibodies stain with less sensitivity than would be expected, and can vary with fixation, so that true positive cells may be missed. Non-hematolymphoid tumors may express some CD markers, such as CD45, however, this is rarely expressed in carcinomas and sarcomas 4 , 5. Malignant melanoma can be CD56 and CD positive and have an atypical plasmacytoid morphology, which can lead to the misdiagnosis of plasmacytoma. Moreover, immunohistochemistry is oftentimes laboratory specific, which can explain the variation in immunohistochemical staining between different groups. Therefore, it is essential that a pathologist be familiar with the staining results of a particular laboratory. In addition to immunohistochemistry, flow cytometry is another important tool in diagnostic hematopathology. Flow cytometric immunophenotyping offers the sensitive detection of antigens when antibodies may not be available for formalin fixed paraffin-embedded immunohistochemical immunophenotyping. However, formalin fixed, paraffin-embedded immunohistochemical immunophenotyping is advantageous because it preserves the architecture of the tissue. Additionally, some antibodies are available for immunohistochemistry and not flow cytometry, allowing for the immunohistochemical evaluation of the expression of the proteins in which these antibodies target. Taken together, these techniques should be used as complimentary tools in diagnostic hematopathology. Errors relating to molecular genetic tests As more molecular and cytogenetic techniques are undertaken in the department of pathology, they become important supplementary methods to immunohistochemistry. Compared with immunohistochemistry, these techniques are more complex and interpretation of the results requires specialized training. Analyzing these results involves understanding the sensitivity, specificity and limitations of each test. The presence of monoclonality does not necessarily correlate with malignancy, and the results must be interpreted in the context of clinical, morphological, immunohistochemical and other findings. Particularly with small biopsies, there can be pseudo-monoclonality which just reflects the physiological immunoreactions to the highly aggregated super antigen 6 rather than the malignancy. Fortunately, with the development of immunohistochemistry, many molecular changes can now be detected at the level of protein expression, with examples being ALK, MYC and mutation of the epidermal growth factor receptor EGFR at exons 19 and Errors due to complexities in the classification and diagnosis of lymphomas Errors in the classification of lymphomas are prevalent due to the complexities of the WHO classification system. The variability in an accurate diagnosis differs by each histological subtype of lymphoma. They also indicated that, on average, even among hematopathologists, the frequency of misdiagnosis of lymphoma is approximately 9. Among all of the misdiagnoses of lymphomas, the most imperative to distinguish between is reactive lymphoid disorders from truly neoplastic lesions, because misclassifications can have serious consequences in terms of treatment. Other types of lymphomas that are

often misdiagnosed and the key points to properly diagnosing them are described in the following references 8 - An example of an uncommon case with full morphological examination, immunophenotyping and molecular genetics is presented here to demonstrate the complexities encountered by experienced pathologists Figure 6. In addition to the immunohistochemical results shown in Figure 6 , the Epstein-Barr encoding region EBER in situ hybridization indicated that large B cells were present. The diagnoses by different pathologists included: The patient died 6 months after the initial diagnosis. Conclusions Adequate tissue specimens that are properly prepared and access to detailed background clinical information are essential to final pathological diagnoses. Acknowledgements The author would like to thank all the colleagues in the department for their providing the difficult cases and preparation of the slides. The author declares no conflict of interest. Standardization of pathologic diagnosis of lymphomas. Slide drying after staining is the culprit of poor hematoxylin-eosin staining. Pitfalls in lymphoma pathology: J Clin Pathol ; Aberrant leukocyte common antigen expression in metastatic small cell lung carcinoma: Appl Immunohistochem Mol Morphol ; Common leukocyte antigen staining of a primitive sarcoma. Application of clonal antigen receptor rearrangement in lymphoma diagnosis. Pitfalls in classifying lymphomas. J Med Assoc Thai ; Pitfalls in diagnostic hematopathology: Int J Clin Exp Pathol ;2: Pitfalls in diagnostic hematopathology -- Part II. Int J Clin Exp Pathol ;3: Common misdiagnoses in lymphomas and avoidance strategies. Pitfalls in the pathological diagnosis of lymphoma. Chin Clin Oncol

Chapter 2 : Current Treatment and Controversy of Primary Gastric Lymphoma

Fifty-one patients with lymphoblastic lymphoma (LBL) treated with one of five successive intensive chemotherapy protocols for acute lymphoblastic leukemia (ALL) since were reviewed. The patients were divided into leukemic and nonleukemic groups, and their clinical and laboratory parameters.

Patel 1 and Moises I. Patel and Moises I. This is an open access article distributed under the Creative Commons Attribution License , which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited. It is a condition with a low incidence of 3. This case involves a year-old male with history of LT for chronic HCV induced cirrhosis who presented with abdominal distension related to worsening ascites. Diagnosis of monomorphic PTLD with primary effusion lymphoma-like morphology and immunophenotype was established. This case highlights the complexity in diagnosis, different diagnostic modalities, and rare clinical presentations of PTLD. It is a well-recognized condition with a relatively low incidence of 3. Diagnosis is made using tissue biopsy and in rare instances using body-fluid analysis. Case A year-old Caucasian male with history of a LT for chronic hepatitis C HCV induced cirrhosis in presented with worsening abdominal distension. Patient developed HCV graft infection with resulting cirrhosis. In , he was treated with Sofosbuvir and Simeprevir achieving sustained virologic response. His graft cirrhosis was complicated by mild ascites controlled with diuretics. On presentation, the patient was hemodynamically stable with a nontender and distended abdomen with fluid wave on exam. Laboratory testing on admission showed an elevated creatinine of 1. Flow cytometry and immunohistochemical stain results demonstrated a T-cell predominant sample without aberrant markers for either T-cells or B-cells. Clonal IgH gene rearrangement was negative. Given concern for a nonhematopoietic tumor and metastatic disease, a CT abdomen-pelvis and whole-body PET CT scan were obtained and a localized malignant focal point or lymphadenopathy was excluded Figure 2. HIV serology was negative. Ascitic fluid immunohistochemical staining results. Ascitic fluid cytology with Diff-Quick stain demonstrating large atypical lymphocytes with round to anaplastic nuclei, dispersed chromatin, and basophilic cytoplasm marked by the arrows. With a growing concern for primary effusion lymphoma PEL in the setting of worsening ascites, cytogenetic analysis of the ascitic fluid was performed in this case given nondiagnostic cytology, immunostaining, and flow cytometry. An abnormal male karyotype with two clones with a t 8;14 translocation, along with multiple structural and numerical abnormalities, was noted. Epstein-Barr encoded region in situ hybridization on the ascitic fluid was positive within tumor cells. After secondary review at an outside institution, the patient was diagnosed with monomorphic PTLD with primary effusion lymphoma-like morphology and immunophenotype. His immunosuppressive therapy was discontinued during a posthospitalization clinic visit and he was referred to oncology. Patient had a repeat staging PET scan with no FDG avid lymphadenopathy or visceral disease two months after the initial scan. His performance status continued to deteriorate and he required frequent therapeutic paracentesis despite chemotherapy. Patient was subsequently lost to follow-up one month after the last chemotherapy infusion. Cellular proliferation observed in PTLD has been linked to the degree of chronic immunosuppression and decreased cell-mediated immunity. Other associated risk factors include specific immunosuppressants i. Based on a single-center cohort study, the estimated incidence in LT patients was 4. Another similar study found a disease prevalence of 3. Generally nodal or extranodal tissue biopsy following radiographic evaluation is the primary diagnostic methodology for PTLD. There have been rare instances where diagnosis via body-fluid analysis have been described in literature. Another cohort study found 17 cases of post-LT PTLD with extranodal presentations involving the skin, gastrointestinal tract, urinary tract, and so forth. A malignant focal point was absent in 4 of these cases, with diagnostic fluid flow cytometry used in 2 subjects with ascites as their primary clinical manifestation [2]. There have also been a few case reports of PTLD occurring in pleural fluid [9]. Given the cytological findings and absence of a malignant focal point in this case, consideration was given to primary effusion

lymphoma as the etiology of the worsening abdominal distension and ascites. In a gene analysis profile study, the impact of HHV8 and EBV on cellular gene expression and pathogenesis of lymphomatous effusions was evaluated. The latter group were found to induce translocation involving the c-myc locus [13]. This patient was diagnosed with monomorphic PTLD with primary effusion lymphoma-like morphology and immunophenotype. Lymphoproliferative disorders in posttransplant patients are a well-recognized phenomenon. Therapy initially involves deescalation of immunosuppression, followed by the initiation of immunotherapy i.

Chapter 3 : Lymphoma: looking from the present to the future - Cheson - Chinese Clinical Oncology

Abstract: Since the publication of the World Health Organization classifications of lymphoma, additional immunohistochemical tests and other ancillary methods such as flow cytometry, cytogenetic and other molecular biology techniques, have been applied in routine clinical work.

 In this paper, the authors report an extremely rare case of a year-old woman who exhibited an abnormal uterine bleeding, pelvic pain, and dysmenorrhea history. The transvaginal ultrasound showed an anteverted uterus measuring cm3 in volume, with intramural leiomyomas. She underwent a total laparoscopic hysterectomy with bilateral salpingectomy. The histologic evaluation of the specimen showed a follicular lymphoma with diffuse pattern in the endometrium. This report illustrates the difficulty in the diagnosis of primary lymphomas of the female genital tract. Most of the sites related to this disease are in the gastrointestinal tract and the central nervous system. However, less commonly this pathology may also arise from adrenal glands, thyroid, breasts, bone, prostate, and female genital tract [5 â€” 7]. Immunohistochemistry studies are important to achieve a correct diagnosis [12 â€” 14]. The ovaries are the most common site of PLFGT, followed by the uterine cervix and the uterine body, which is very rare [9 , 15]. Usually, in these women the endometrial involvement is secondary to a systemic lymphoma affecting the cervix [15]. Case Report A year-old woman, G4 P2 C2, came to our service complaining about abnormal uterine bleeding, pelvic pain, and dysmenorrhea for the last 6 months. She had a past surgical history of cholecystectomy, cesarean section, abdominoplasty, and bilateral tubal ligation. The gynecological examination was unremarkable. On bimanual examination, the uterus was mobile and had a normal size. There was no increase in the volume of the ovaries. Transvaginal ultrasound showed an anteverted uterus, measuring cm3, with a heterogeneous pattern, with intramural leiomyomas at the posterior uterine wall. Pap smear was negative for neoplasia. She underwent a laparoscopic hysterectomy with bilateral salpingectomy for a presumed abnormal uterine bleeding and leiomyomas not responding to clinical treatment. The laparoscopic hysterectomy was performed according to the previously reported surgical technique [16]. The surgical procedure was uneventful and lasted 90 minutes. Estimated intraoperative blood loss was 20 cc. The patient was discharged from the hospital, 24 hours after the surgery. The histological evaluation of the specimen identified a dense lymphoid infiltrated in the endometrium, with a diffuse follicular pattern. After clinical staging, the disease was diagnosed as follicular lymphoma of the endometrium stage IV, due to the involvement of the bone marrow. Discussion Lymphomas are malignant tumors that affect the immune system, most commonly, the lymph nodes. Primary lymphoma involving the female genital tract is an uncommon condition, in which the ovaries and cervix are the most frequently affected sites [8 â€” 10 , 15]. The involvement of extra nodal sites means the worst prognosis [22]. Ann Arbor staging system. It usually occurs in women during the fifth decade of life. Nevertheless, it depends on the histological subtype; as an example, diffuse large B-cell lymphoma is more common between 35 and 45 years old, whereas follicular lymphoma is more frequent in people aged over 50, and Burkitt lymphoma affects children from five to ten years old [23]. The diagnosis is very difficult because of the rarity of this entity. In addition, there is no typical presentation of the symptoms; usually, it depends on the site where the cancer is confined [23]. Some of the symptoms of PLFGT are abnormal uterine bleeding, pelvic pain, abdominal distension, and bloating [17 â€” 19]. In the follicular lymphoma subtype, the clinical presentation usually has an indolent course. Survival rate is very high even without treatment, but it can exhibit a variable clinical presentation, with some patients suffering from aggressive disease [23]. Since clinical evaluation and imaging studies cannot give a definitive diagnosis, most PLFGT is initially treated as being any other common gynecologic malignancy. The definitive diagnosis is obtained after surgery during the pathological examination of the surgical specimen [8]. Immunohistochemistry plays a fundamental role in the

characterization of the antibodies and in the classification of the subtypes of lymphomas [27 , 28]. The second most common is the follicular lymphoma, followed by Burkitt lymphoma [9]. Immunohistochemical studies are useful to achieve a correct diagnosis, as some low-grade lymphomas particularly follicular lymphomas and MALT-type lymphomas are difficult to be distinguished from benign reactive diseases such as severe chronic cervicitis or follicular cervicitis [12 â€” 14]. In this case, the patient presented no specific symptoms. She underwent a total laparoscopic hysterectomy for a presumed benign disease leiomyoma and increased uterine bleeding. The diagnosis of follicular lymphoma with diffuse pattern coming from the endometrium was confirmed after anatomopathological and immunohistochemical evaluations. The treatment of PLFGT consists of a multimodal approach, including the gynecologist, the clinical oncologist, and the radiation oncologist, trying to individualize each treatment. Chemotherapy induces irreversible damage to the ovarian tissue, which leads to premature ovarian failure. This is an important issue that must be discussed with the patient, and the possibility of oocyte or embryo cryopreservation must be remembered in those patients who desire future childbearing [9]. Temporary ovary suppression with GnRH agonists is another alternative, to attempt to reduce the occurrence of premature ovarian failure. However, this procedure is still controversial [29]. Patients who have indication for radiotherapy treatment may be benefited from the ovarian transposition. In this procedure, the ovaries are sutured into the paracolic gutter, in order to attempt to maintain them outside the radiation field, postoperatively [30]. R-CHOP regimen is the standard treatment for follicular lymphoma and includes rituximab plus cyclophosphamide, hydroxydaunorubicin, oncovin vincristine , and prednisone or prednisolone. The cyclophosphamide is considered a high-risk gonadotoxic drug, oncovin a medium risk [29]. In the posttreatment follow-up, tumor remission is usually evaluated by PET-CT positron emission tomography-computed tomography [23]. Different clinical presentations may lead to a difficult diagnosis, frequently misunderstood during the preoperative setting. Although rare, PLFGT should be considered in the differential diagnosis of organic diseases, leading to increased uterine bleeding and pelvic pain. Conflicts of Interest The authors declare that they have no conflicts of interest. View at Google Scholar J. Van den Broecke, C. View at Google Scholar A. View at Google Scholar F. View at Google Scholar W. View at Google Scholar V. View at Google Scholar S.

Chapter 4 : Issue Archive | Value-Based Cancer Care

Critical Reviews in Oncology/Hematology, Vol. 1, No. 1 Differential diagnostic problems in the radiologic evaluation of histiocytic lymphoma Cancer, Vol. 48, No.

Chapter 5 : January 1, Issue of JAMA Oncology | JAMA Network

International Journal of Hematologic Oncology welcomes unsolicited article proposals. CURRENT ISSUE. December VOL. 6 NO. 4. Volume 7, Issue 1 / March

Chapter 6 : Cancer Control Journal Issue Archive | Moffitt

DOI: /JCO Journal of Clinical Oncology - published online before print September 22, PMID: Treatment of lymphoblastic lymphoma in adults.

Chapter 7 : Nucleic Acid Aptamers as Potential Therapeutic and Diagnostic Agents for Lymphoma

An international working group has revised guidelines for assessing response criteria in patients with malignant lymphoma to reduce variability in reporting and to take account of the increased use of new diagnostic techniques such as fluorodeoxyglucose ([18 F]FDG)-PET.

DOWNLOAD PDF CURRENT ISSUES IN LYMPHOMA (DIAGNOSTIC ONCOLOGY ; VOL 4, NO 1)

Chapter 8 : Archives - Translational Cancer Research

Lymphoma: looking from the present to the future. The world of lymphoma is rapidly changing. Therefore, it is with great pleasure that we are publishing this special edition of Chinese Clinical Oncology (CCO) to highlight the recent progress.

Chapter 9 : Pitfalls in the pathological diagnosis of lymphoma - Li - Chinese Clinical Oncology

The Leukemia & Lymphoma Society (LLS) will be hosting its 8th Annual Rocky Mountain Blood Cancer Conference on Saturday, April 7, , at the Hyatt Regency Aurora-Denver Conference Center. LLS Blood Cancer Conferences are free education events for blood cancer patients, survivors, caregivers, family members and healthcare professionals.