

Hematology & Oncology Abstracts

Presepsin (sCD14) as a marker of serious Bacterial infections in chemotherapy induced severe neutropenia

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Background: Timely detection of serious bacterial infections or prediction of sepsis and death is one of paramount importance in neutropenic patients especially in pediatric oncology settings.

Methods: This study was carried out to evaluate serum soluble CD14 in pediatric neutropenia in cancer patients. We measured sCD14 in 39 severe neutropenic episodes in Mahak pediatric oncology center from September 2012 to January 2013. Blood cultures were taken for all cases. Fifteen episodes had positive bacterial cultures and eighteen had fever. The mean sCD14 values were compared in the presence or absence of fever, positive blood culture and other clinical conditions. Also, mean levels compared in different white cell counts and different four combination settings of fever and blood culture.

Findings: Presepsin level was statistically higher in febrile patients, in the presence of oral mucositis, indwelling catheter infection, otitis media, post toxic epidermal necrolysis sepsis, and in instances of death within 15 days. White cell count did not affect sCD14 level. In combinations of fever and blood culture positivity (non-mixed), mean sCD14 values were ranked as follow: febrile culture negatives, febrile culture positives, afebrile culture positives and afebrile culture negatives.

Conclusion: Although sCD14 was not sensitive in detection of bacteremia, in the absence of clinically detectable source of infection it was significantly higher in culture positives cases.

Keywords: soluble CD14, cancer, neutropenia, infection

The role of Positron Emission Tomography with Computed Tomography (PET/CT) in childhood cancers

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The use of Positron Emission Tomography (PET) with Computed Tomography (PET/CT) is rapidly expanding in childhood cancers including brain tumors, lymphomas, soft tissue tumors, and bone tumors such as osteosarcoma and Ewing sarcoma, thyroid cancers and rare tumors. Clinical applications of PET/CT in children with brain tumors include: to evaluate for recurrent tumor, to differentiate between recurrent tumor and post-treatment necrosis, to localize the areas of high grade disease in order to guide biopsy and treatment planning. Clinical applications of PET/CT in children with lymphomas include: initial staging of patients to determine the extent of disease, to determine response to chemotherapy or radiation therapy, post-chemotherapy assessment for patients with advanced

stage of aggressive non-Hodgkin's lymphoma, and Hodgkin's lymphoma with residual CT abnormalities or initial bulky disease, to plan the duration of chemotherapy for patients with Hodgkin's and non-Hodgkin's lymphoma, and to plan the duration and the type of treatment for limited stage of aggressive lymphoma. FDG uptake is generally greater in higher grade than lower grade lymphomas. FDG-PET reveals disease sites that are not detected by conventional staging methods, resulting in upstaging of disease with potential therapeutic review. FDG-PET is useful for assessing the need for bone marrow biopsy, and residual or recurrent soft tissue masses seen on CT after therapy. Clinical applications of PET/CT in children with sarcomas include: to evaluate the primary soft tissue mass prior to biopsy to identify high grade areas and to guide biopsy, for staging of locally advanced high grade soft tissue sarcomas, for detecting of suspected local recurrence of soft tissue sarcoma after definitive treatment, for staging of Ewing's sarcoma, and for initial staging and evaluation of potential recurrence in osteosarcoma. Clinical applications of PET/CT in children with neuroblastoma include: evaluation of the extent of viable tumor tissue in primary tumor, staging and disease evaluation of MIBG-negative tumors, evaluation of residual mass or primary site for recurrent or residual tumor at post-treatment stage particularly if conventional studies are not helpful or equivocal, as well as evaluation for local recurrence or distant metastases at post-treatment stage or marrow transplantation. [11C]-Hydroxyephedrine ([11C]-HED), an analogue of norepinephrine, and [11C]-epinephrine PET have also been used in evaluating neuroblastoma. Uptake of these tracers is demonstrated within minutes after tracer administration, an advantage over MIBG imaging. In osteosarcoma and Ewing's sarcoma, FDG-PET may play an important role in monitoring response to therapy. Another diagnostic role may be in assessing patients with suspected metastatic disease. Clinical applications of PET/CT in children with thyroid cancers include: detection and localization of suspected recurrence after definitive therapy in patients with elevated thyroglobulin levels and negative radiiodine scan (papillary and follicular carcinomas). Thyroid "incidentalomas" found on 18 FDG scanning appear to have a high rate of malignancy and should be assessed by fine-needle aspiration. Clinical applications of PET/CT in children with rare tumors include: monitoring hepatoblastomas during and after therapy by FDG-PET.

Initial lymphocyte count in patients with acute immune thrombocytopenic purpura: can it predict persistence of the disease?

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Background: It has been suggested that initial total leukocyte count (TLC) and initial absolute lymphocyte count (ALC) can predict development of chronic/persistent disease in children with acute immune thrombocytopenia purpura (ITP). However, this association has not confirmed by other studies. This study aimed to investigate probable association between initial TLC and ALC with development of chronic/persistent ITP.

Methods: The present study was carried out at Aliasghar children hospital and all children with diagnosis of acute ITP were identified from 2001 to 2008. Data gathered retrospectively by reviewing patients' records. Initial TLC and ALC were compared between recovered patients and those with chronic/persistent ITP.

Findings: 116 children with diagnosis of acute ITP were included in the study. Respectively, 59(50.8%) and 57(49.2%) cases were categorized in recovered(group 1) and chronic/persistent(group 2) ITP. Mean TLC was 8470±3691 Cell/L in study patients, 8644±4194 Cell/L in group 1 and 4194±8290 Cell/L in group 2 which was not statistically significant. Mean ALC was 4176±2037 Cell/L. Mean lymphocyte count in group 1 was significantly higher(4542±2100 Cell/L) compared to group 2(3797±1916 Cell/L)(p<0.04). Logistic regression analysis showed that ALC < 5000 Cell/L is a predictor of chronic/persistent ITP (Odds ratio: 2.757, 95% CI 1.215 - 6.260, p<0.015). Sensitivity, positive and negative predictive values for ALC <5000 Cell/L were calculated as 80%, 57%, and 68% respectively.

Conclusion: Our findings indicated that initial ALC but not TLC is a predictor of chronic/persistent ITP in children with acute ITP. Further studies are recommended to explore underlying mechanisms causing a lower initial ALC contributes to development of chronic/persistent ITP.

Keywords: immune thrombocytopenia purpura, total leukocyte count, absolute lymphocyte count, chronic/persistent ITP

Epandymoma as a secondary malignancy after treatment of non- Hodgkin lymphoma

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Background: Therapeutic advances in the treatment of pediatric neoplasms have improved the prognosis but have also increased the risk of developing rare second malignant neoplasms(SMN) in late period after chemotherapy or radiation course.

Case Presentation: We report a 14 year-old boy therapy-related solid tumors(brain ependymoma after non Hodgkin lymphoma). Short latency period after primary tumor with that is a rare case among secondary tumors. He involved by relaps of primary tumor, brain tumor resection, and radiotherapy.

Keywords: ependymoma, radiation-induced malignancy, secondary malignancy, chemotherapy

Comparison of iron chelation effects of Deferoxamine, Deferasirox, and combination of Deferoxamine and Deferiprone on liver and cardiac T2* MRI in Thalassemia Major

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Background: Cardiac complications due to iron overload are the most common cause of death in thalassemia major. The aim of this study was to compare iron chelation effects of deferoxamine, deferasirox, and combination of deferoxamine and deferiprone on cardiac iron load in these patients measured by T2* MRI.

Methods: In this study, 108 patients aged over 10 years who had iron overload in cardiac T2* MRI, were studied. The first group received only deferoxamine, the second group only deferasirox, and the third group a combination of deferoxamine and deferiprone. Myocardial iron was measured at baseline and 12 months after the beginning of treatment through T2* MRI.

Findings: The three groups were similar in terms of age, gender, ferritin level, and mean myocardial T2* at baseline. In the deferoxamine group, myocardial T2* was increased from 12.0±4.1ms at baseline to 13.5±8.4ms at 12 months. Significant improvement was observed in myocardial T2* of the deferasirox group from 13.0±4.5ms to 17.5±7.1ms at 12 months(p<0.001). In the combined group, myocardial T2* was increased from 11.6±3.8ms to 16.8±9.9ms at 12 months (p<0.001). These differences between groups were not significant at 12 months. A significant improvement was observed in liver T2* at 12 months compared to baseline in the deferasirox group(p<0.01) and the combination group (p<0.005), while this was not significant in the deferoxamine group.

Conclusion: In comparison to deferoxamine monotherapy, combination therapy and deferasirox monotherapy had a significant improvement in myocardial and liver T2*.

Keywords: Thalassemia major, iron chelation, Deferoxamine, Deferasirox, Deferiprone

Why does the Iranian national program for screening of newborns for G6PD enzyme deficiency miss a large number of affected infants?

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Background: National neonatal screening for G6PD enzyme deficiency fails to detect all affected infants. In order to clarify the cause, this study has been done in Thalassemia Research Center, Sari, Iran.

Methods: This was a diagnostic study. The newborns born in a hospital in Sari were subjects for study. If both parents were born in the Mazandaran province and were accepted the study, the newborn was enrolled. After birth, cord blood from the placental side was collected. This sample was used for Decolorization test, quantitative enzyme assay(QEA) and DNA study. Then the parents advised to do the screening tests according to the routine procedure. They should take the newborn, 3-5 days after birth to the health center for blood sampling via a heel prick procedure. The laboratory method of screening was fluorescent spot test(FST). For male newborns, QEA was considered as the gold standard. The mean enzyme activity by QAE assay was 48±11.7U/g hemoglobin. Cases with <9.6 or 9.6-29.8 U/g hemoglobin enzyme activity was considered as total and partial deficient respectively. For females, DNA study was considered as the gold standard. Because of the X-linked characteristic of the disease, all rates calculated as gender specific. Sensitivity, specificity, positive and negative predictive values of the tests comparing the gold standards were calculated by SPSS software (V18).

Findings: A total of 365 neonates, including 191(52.3%) females, and 174(47.7%) males were studied. According to FST, 13 males(7.5%, CI 95%: 3.6-11.4) male newborns had G6PD deficiency. No female was detected. Decolorization test diagnosed 18(10.3%, CI95%: 7.2-13.4) males and one female newborns. QEA, diagnosed 19(10.9

%; CI 95%: 7.8-14) males and 28(14.6%; CI95% 9.6–19.6) females with G6PD enzyme deficiency, where 26 and 2 girls were partial and total deficient, respectively. DNA analysis could detect 14(8.0%; CI95%: 4.1-11.9) males as heterozygote and 34(17.8%; CI95%: 12.6-23) females as heterozygote.

Conclusion: FST is not sensitive enough for screening the newborns; so QEA is preferred.

Keywords: Neonatal Screening, G6PD Enzyme Deficiency, DNA Analysis, Fluorescent Spot Test, Decolorization Test, Quantitative Enzyme Assay, Iran

Acute severe hemolysis associated with Hepatitis A in patient with G6PD deficiency

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Background: G6PD(glucose 6 phosphate dehydrogenase) is the most important enzyme in glycolytic pathway that maybe leads to acute hemolysis after contact to special toxins(fava beans, drugs and infections) in patients who had enzyme deficiency. Intravascular hemolysis causes anemia, jaundice and hemoglobinuria. Hepatitis A in G6PD deficiency patients is one of the most important infections that lead to severe hemolysis which causes acute renal failure and severe anemia.

Findings: we presented a 10 years old boy admitted to Madani hospital for acute jaundice and dark urine. He had no history of jaundice. In physical examination, he was pale and icteric. In lab tests he had severe anemia (Hb<4mg/dl) and hyperbilirubinemia(total Bili =12) and G6PD deficiency. Electrolytes, BUN and Cr were normal. We started treatment with sodium bicarbonate infusion and packed RBC cell but hemolysis continued and abdominal discomfort added to other symptoms. Liver function test checked and it showed elevated liver enzymes then we checked Hepatitis markers. We found elevated Hepatitis A antibody(IgM) which was upper than normal.

Conclusion: Acute hemolysis and acute renal failure may be trigger by Hepatitis A in patients with G6PD deficiency and leads to prolonged hospitalization. It is a good suggestion to all patients with G6PD deficiency to be vaccinate against Hepatitis A.

Keywords: G6PD Deficiency, Acute Hemolysis, Hepatitis

Reduced-intensity conditioning regimens for hematopoietic stem cell transplantation in children with primary immunodeficiency: IRAN experience

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Background: For decades, myeloablative regimen (MAC) was the only known preparative conditioning, applied to achieve a reliable immune reconstitution by suppressing recipient's immune system. However, application of MAC in Primary immunodeficiency diseases (PIDs) is challenged by increased rate of non-relapse mortality, probably due to higher risk of organ toxicity. Since 2006 an identical Reduced Intensity Conditioning (RIC) protocol has been employed in all PID patients referred to our center.

Methods: We prospectively analyzed the outcome of 53 pediatric patients (37 boys,16 girls) with LAD type-I

(n=17), SCID(n=8), Wiskott Aldrich(n=7), Chediak-higashi (n=6), Griscelli Syndrome type-II (n=6), Familial Erythrophagocytic Lymphohistiocytosis(n=5), CID(n=1), Hyper IgE (n=1), CGD(n=1) and Primary CD4 Deficiency (n=1) who had underwent HSCT from 2006 to 2013. The median age at transplantation was 3.5 years (range: 3 months-14years). Patients underwent transplantation from HLA-identical sibling donors (n=25), full matched other related donors (n=13), mismatched related donors (n=5),unrelated mismatched donor (n=8), and unrelated match donors (n=2). Sources of graft were from peripheral blood (n=29),bone marrow (n=14) or cord blood (n=10) of a healthy donor. All patients received RIC regimen with fludarabine, melphalan and ATG. Cyclosporine and methylprednisolone were used as Graft-versus-host disease (GvHD) prophylaxis regimen.

Findings: The median numbers of MNC and CD34 injected were 7.01×10^8 cell/kg, 4.12×10^6 cell/kg, respectively. Except two, all patients engrafted successfully. At the present time, 38 patients with median follow-up of 38 months are still alive and 36 of them are disease free without evidence of recurrent infection. The main causes of death were GvHD and infection.

Conclusion: Although HSCT is the therapeutic mainstay for rescuing PID patients, due to few cases of these diseases and various regimens used for HSCT, no definite conclusion has been reached over priority of using RIC vs. myeloablative conditioning in patients. With regard to the fact that PID patients at their presentation almost always have infectious diseases or history of different infections, we have used one identical RIC regimen since the establishment of the pediatric transplant unit in Iran. According to the results of the study, RIC regimen is found to be safe and feasible therapeutic approach in the treatment of PID patients.

Prevalence of early dental caries among children receiving Iron supplements

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Background: Iron deficiency is the most common form of micronutrient deficiency in the world. Supplementation of Iron at early age is considered to prevent iron deficiency malnutrition in Iran. In children, because of teeth staining after taking iron drops, parents are concerned about dental caries in their children and don't use this vital supplement in their children's diet properly. Hereby, we evaluated the effect of iron containing supplements on tooth caries in children.

Methods: This prospective cross-sectional study was carried out on the 50 children(6 months to 2-year-old) who received iron containing drops from health services centers in kerman. Children divided into two groups according to days per week taking iron (>4 and, 4 days per week) for at least 4 consequent weeks. Both groups compared for tooth staining and dental caries.

Findings: 10 out of 50 received iron containing drops more than 4 days a week. This study showed a relation between iron supplement application with tooth staining and its effect on dental caries, (80% vs. 60%).

Conclusion: The finding of this study indicates that parental concern about consumption of iron supplements by their children (6 months to 2-year-old) is serious.

Keywords: iron deficiency, dental staining, dental caries

Asymptomatic thrombocytopenia in TAR syndrome– A case report

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Background: TAR syndrome is rare congenital anomaly that present with hypo megakaryocytic thrombocytopenia and absence radius. Thrombocytopenia maybe presented at birth or early infancy with bleeding that leads to cranial hemorrhage and death. we present a 15 month infant with TAR syndrome. That hadn't past history of bleeding and hospitalization.

Case presentation: A 15 month's age infant admitted to Madany hospital for acute gastroenteritis. The infant was second child of unrelated parents that was born by c/s with short upper limbs. The infant had no symptoms(bleeding, petecia and echymous) until 15 months. In physical examination head, neck, heart and lungs were normal. The liver and spleen were not palpable. Both upper limbs were aplastic. The humerus bones were very short, the radius and ulna bones were absent. There were two hands with normal thumbs. Lower limbs were normal with shape and size. In laboratory study, WBC: 9700(Lymph 77%, Poly 23%), Hb= 11.6, Plt=79000, Mcv=74, Mch=34.2, CRP=positive, ESR=20 and electrolytes were normal.

Conclusion: Hypo megakaryocytic thrombocytopenia, absence radius(TAR syndrome) is very rare congenital hematologic and skeletal anomalies that Hall JG et al described in 1967. The hematologic symptoms were presented at birth or early infancy with thrombocytopenia and bleeding. The skeletal anomalies are absence radius bones with normal thumbs. Almost 90% of patients presented bleeding that maybe lead to life threatening cerebral hemorrhage. After early infancy thrombocytopenia improved but it will be relapsed with stress, infection and gastroenteritis. Genetic studies reveal micro deletions of long arm of first chromosome 1(q21-1). Pathophysiology of TAR syndrome is unknown, but serum thrombopoietin (TPO) is elevated in this syndrome that maybe due to no response of special receptor to TPO. Platelet transfusion is useful for thrombocytopenia, but IVIG and prednisolon are not effective.

Keywords: thrombocytopenia, absence radius, TAR syndrome, khorram Abad

پورپورای مادرزادی ترومبوسیتوپنیک

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زمینه: ترومبوسیتوپنیک ترومبوسیتوپنیک پورپورای مادرزادی (TTP مادرزادی) یک بیماری نادر است که بخاطر موتاسیون در ژن ADAMTS 13 که باعث کاهش تولید متالوپروتئیناز می شود ایجاد می گردد. کمبود متالوپروتئیناز باعث می شود مولتی مریهای بزرگ فاکتور ون ویل براند شکسته نشده و کم خونی میکرو آنژیوپاتیک همولیتیک ایجاد شود که با آنمی و ترومبوسیتوپنی و علائم کلیوی تظاهر پیدا میکند.

معرفی بیمار: مورد پسر ۹ ساله ای است که از ۳ سالگی دچار آنمی، ترومبوسیتوپنی، هماچوری، دوره هایی از افزایش اوره و کراتینین شده و با تشخیص هایی نظیر ترومبوسیتوپنیک پورپورای ایمیون، آنمی فانکونی، آنمی همولیتیک اتو ایمیون و سندروم اوانس تحت درمان ایمونوسپرسیو و تزریق مکرر فرآورده های خونی قرار گرفته است. بعد از ۶ سال برای بیمار TTP

مادرزادی بخاطر کمبود شدید ADAMTS13 و نرمال بودن آنتی بادی علیه آن مطرح شده و تحت درمان با تزریق منظم FFP قرار گرفته است. با توجه به نادر بودن TTP مادرزادی و تشابه علائم با بیماریهای خونی شایعتر امکان تاخیر در تشخیص بیماری وجود دارد و لذا توصیه می شود در کودکانی که با آنمی و ترومبوسیتوپنی مراجعه میکنند و دلیل واضحی برای آن پیدا نمیشود بررسی از نظر TTP مادرزادی انجام شود.

کلمات کلیدی: ترومبوسیتوپنیک ترومبوسیتوپنیک پورپورای مادرزادی، ADAMTS13، ترومبوسیتوپنی

بررسی نورپاتی ناشی از وین کریستین در کودکان مبتلا به لوسمی لنفوبلاستیک حاد و بیماران مبتلا به لنفوم غیر هوچکینی در بیمارستان البیرونی دانشگاه دمشق

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زمینه: وین کریستین که عامل کموتراپوتیک مفید در درمان لوسمی ها، لنفوم ها و دامنه وسیعی از تومورهای جامد می باشد بالقوه یک نوروتوکسین قوی است و نورپاتی حسی _ حرکتی، شایعترین سمیت این داروست.

روش: در این مطالعه که بصورت گذشته نگر و توصیفی انجام شده است به بررسی نورپاتی وین کریستین در ۱۵۲ بیمار مبتلا به ALL و NHL که از ۲۰۰۷/۶/۱ لغایت ۲۰۰۹/۶/۳۰ به بیمارستان البیرونی شهر دمشق سوریه مراجعه داشته اند (سرپاتی و بستری) پرداخته شده است. بررسی بیماران بصورت Consecutive بوده است و انتخابی در مورد آنان صورت نگرفته است. تمام این بیماران دارو را در دوز مجاز دریافت کرده بودند و چگونگی ارتباط علائم عصبی بیماران با وین کریستین صرفا بر اساس نحوه درگیری و خصوصیات بالینی و رد سایر علل بوده است و نیز ارتباط سیر علائم با قطع یا کاهش دوز وین کریستین بررسی گردیده است.

یافته ها: از ۱۵۲ بیمار فوق الذکر ۸۱ نفر مبتلا به AHL و ۷۱ نفر مبتلا به ALL بوده اند (۹۳ مرد و ۵۹ زن). سن متوسط بیماران ۳۳/۶ سال بوده است (حداقل ۹ و حداکثر ۷۹ سال). ۶۹ نفر از بیماران دچار نورپاتی وین کریستین شده اند (۴۳/۱٪). نورپاتی حسی عمدتا بصورت هیپراستزی قرینه دست یا پا هر دو بوده که در ۵۲ مورد شدید و آزار دهنده و در ۳۵ مورد مختصر بوده است. ۳۸ نفر (۱۲/۷٪) نورپاتی احشایی بصورت ایلئوس و یبوست و ندرتا اسهال پیدا کرده بودند که در ۲۶ مورد شدید و در ۱۱ مورد خفیف و گذرا بوده است. ۶۰ نفر از بیماران (۵/۹٪) نورپاتی حرکتی پیدا کرده بودند که در ۵ نفر شدید بوده است که بصورت کاهش رفلکسهای وتری، ضعف عضلانی، تحلیل عضلانی عمدتا در اندام تحتانی و به همراه foot drop تظاهر کرده و در یک مورد با همین علائم در اندام فوقانی و در یک نفر با علائم خفیف تر همراه بوده است. یک نفر از بیماران Bell's palsy و یک نفر خشونت صدا داشته است. تنها یک نفر دچار درد فک شده است. ۴۰ نفر از بیماران (۱۴/۷٪) چندین نوع عارضه را با هم داشته اند. سن متوسط بیماران دچار نورپاتی ۳۸/۷ و سن متوسط بیماران بدون این عارضه ۲۹/۷ بوده است. سن متوسط بیماران دچار نورپاتی حرکتی ۱۸/۲ و سن بیماران دچار نورپاتی احشایی بطور متوسط ۵۲/۳ بوده است. مسئله دیگر نحوه برخورد با این عارضه بوده است. در موارد نورپاتی حسی خفیف (گرید ۱) در تمام موارد ادامه درمان تشدید علائم را در بر نداشته است. در نورپاتی حسی شدید (گرید ۲) ابتدا دوز دارو نصف شده است که تنها در ۵ مورد عارضه پیشرفت داشته و سبب قطع کامل وین کریستین شده است. در نورپاتی احشایی خفیف (گرید ۳) دوز دارو نصف شده است که در دو مورد سبب بهبودی عارضه شده است و در یک مورد عارضه پیشرفت داشته و نهایتا دارو قطع شده است. در نورپاتی احشایی شدید (گرید ۴) دارو کاملا قطع شده است که در تمام موارد علائم برطرف شده است. در نورپاتی حرکتی

(گرید ۵) دارو کاملاً قطع گردیده که در تمام موارد علیرغم بهبودی تدریجی عارضه، بهبودی کامل حاصل نشده است.

نتیجه گیری: نوروپاتی ناشی از وین کریستین عارضه نسبتاً شایعی است که با افزایش سن بر میزان بروز آن افزوده می شود. نوروپاتی احشایی عمدتاً در افراد بالای ۵۰ سال و نوروپاتی حرکتی عمدتاً در افراد زیر ۲۰ سال دیده می شود. در موارد بروز نوروپاتی احشایی یا حرکتی قطع کامل دارو لازم است ولی در موارد نوروپاتی حسی می توان در موارد خفیف مدارا کرد و یا آنکه دوز دارو را به نصف تقلیل داد.

کلمات کلیدی: وین کریستین، نوروپاتی، لوسمی لنفوبیدی حاد، لنفوم غیر هوچکین