cognizancejournal.com
Seyyedabbas Pakmehr *et al*, Cognizance Journal of Multidisciplinary Studies, Vol.4, Issue.4, April 2024, pg. 157-164
(An Open Accessible, Multidisciplinary, Fully Refereed and Peer Reviewed Journal)
ISSN: 0976-7797
Impact Factor: 4.843
Index Copernicus Value (ICV) = 77.57

A Challenging Case of Primary Central Nervous System Lymphoma: Diagnostic Dilemmas and Therapeutic Insights

[1]Rozahabibi
Faculty of Pharmacy, Ahvaz Jondishapour University of Medical Science, Ahvaz, Iran
Rozahabibi72@yahoo.com

[2]Poorya Najjari Nabi
Faculty of Pharmacy, Tabriz University of Medical Sciences, Tabriz, Iran
Pooryann1993@gmail.com

[3]Mahsa Lotfi
Faculty of Pharmacy, Tabriz University of Medical Science Tabriz, Iran
Lotfimahsa24@gmail.com

[4]Reza Shah Hosseini
Istanbul Medipol University, Faculty of Medicine, Medical Student, Istanbul-TURKEY
rshahh93@gmail.com

[5]Negar Oliaei
Faculty of Pharmacy, Cyprus International University, Cyprus
negaroliaie@gmail.com

[6]Asma Hatami
Medical Chemistry Department, Faculty of Chemistry, University of Isfahan, Isfahan, Iran
Asma03198@gmail.com

[7*]Seyed Mohammad Nouri
Zanjan University of Medical Science, Zanjan, Iran
mvc2x@hotmail.com

[8*]SeyedAbbas Pakmehr
School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran
pakmehrabbas@yahoo.com

[9*]Sepideh Karkon Shayan
Student Research Committee, Faculty of Medicine, Gonabad University of Medical Sciences, Gonabad, Iran/ Social Development and Health Promotion Research Center, Gonabad University of Medical Sciences, Gonabad, Iran
sepidehshayan76@gmail.com

DOI: 10.47760/cognizance.2024.v04i04.008

cognizancejournal.com
Seyyedabbas Pakmehr *et al*, Cognizance Journal of Multidisciplinary Studies, Vol.4, Issue.4, April 2024, pg. 157-164
(An Open Accessible, Multidisciplinary, Fully Refereed and Peer Reviewed Journal)
ISSN: 0976-7797
Impact Factor: 4.843
Index Copernicus Value (ICV) = 77.57

Abstract:

Introduction: Primary Central Nervous System Lymphoma (PCNSL) is a rare malignancy primarily located in the brain, spinal cord, leptomeninges, and eyes. The origin of PCNSL is uncertain, but it is thought to arise from lymphocytes within the central nervous system. Diagnosis and treatment can be complex, especially in immunocompetent patients.

Case Report: A 65-year-old immunocompetent woman presented with symptoms including weight loss, severe weakness, and left hemiplegia. Initial brain MRI revealed an irregular mass with vasogenic edema in the right parietal lobe. Stereotactic biopsy confirmed large cell lymphoma (T-cell variant). The patient initially responded well to high-dose steroid treatment. Subsequent chemotherapy and radiotherapy were planned, but due to a positive PCR test, treatment was delayed.

Discussion: PCNSL presents with non-specific symptoms, making early diagnosis challenging. Diagnostic tools such as MRI, PET-CT, and immunohistochemistry play crucial roles. Steroid use before biopsy should be cautious, as it may affect tissue necrosis and diagnosis accuracy. Prompt diagnostic and therapeutic measures are essential for improved outcomes.

Conclusion: PCNSL is a rare and aggressive malignancy with a poor prognosis if left untreated. Early diagnosis and appropriate treatment, including chemotherapy and radiotherapy, are crucial for patient survival. Larger studies are needed to further understand and manage this challenging condition.

Introduction

Primary Central Nervous System Lymphoma (PCNSL) is a rare cancer confined to the brain, spinal cord, leptomeninges, and eyes. The origin of this type of lymphoma is often type B lymphocytes, and because the Central Nervous System (CNS) has no lymph nodes or lymphatic vessels, the cause of PCNSL is still uncertain (1). However, its source appears to be lymphocytes located in the CNS (2). This type of lymphoma has been reported in the context of congenital or acquired immune deficiency such as Wiskott-Aldrich syndrome, kidney transplantation, and in particular, AIDS (3).

The frontal lobes are the most common site of involvement in the CNS. Although personality disorders and altered levels of consciousness are the hallmarks of the disease, the rate of seizures is lower compared to other types of brain tumors (3, 4). PCNSL grows rapidly, with clinical symptoms appearing a few weeks to several months before the diagnosis. If not treated, this disease can lead to death within one to three years. However, some studies have shown that if treated, 70% of the affected people can survive up to 5 years after the diagnosis (3). Meningiomas are often benign and slowly growing tumors that originate from the arachnoid cap cell of the meninges (4, 5). For B-cell CNS lymphoma, current therapies, such as high-dose chemotherapy, radiation, and some targeted therapy drugs, have shown little success in improving very poor patient outcomes (6).

Our aim in this study was to investigate a case of non-Hodgkin's lymphoma of the brain.

cognizancejournal.com
Seyyedabbas Pakmehr *et al*, Cognizance Journal of Multidisciplinary Studies, Vol.4, Issue.4, April 2024, pg. 157-164
(An Open Accessible, Multidisciplinary, Fully Refereed and Peer Reviewed Journal)
ISSN: 0976-7797
Impact Factor: 4.843
Index Copernicus Value (ICV) = 77.57

Case Report

A 65-year-old woman presented to our hospital while she had presented to another center before us, but there was no diagnosis. Patient symptoms include weight loss, extreme weakness, and left hemiplegia. The patient was examined, and the first MRI was performed on the brain with and without contrast material. MR studies of the brain with axial T1, T2, flair w, sagittal T2/w, and coronal T2 were performed. White and gray matter signal intensity, basal ganglia, cerebral ventricles, pituitary gland, and optic tract are normal. The midbrain, pons, medulla oblongata, both 7,8-neuro complexes, C.P. angle cisterns, and cerebellar hemispheres have a normal appearance. The ventricle system is seen normally without a midline shift. There is no evidence of restriction diffusion in DWI sequences. In the middle part of the right parietal lobe, there is a solid, hyperintense, irregular (42*40 mm) mass of vasogenic edema. Unlike gliomas, metastases, and tumefactive demyelinating lesions, which are T2-hyperintense, PCNSLs are hypointense on T2-weighted MRI signals due to a low intratumoral water content (Figure 1.2.).

Pre-Operation Images:

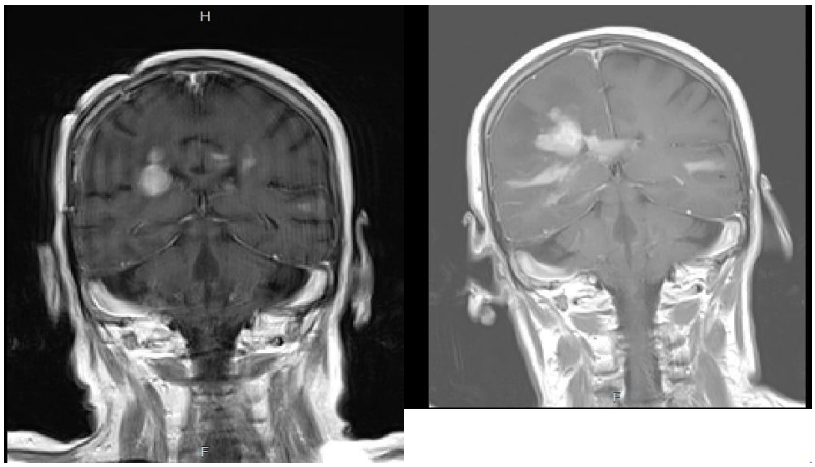

Figure 1. DWI and DWII in MRI, in the middle part of the right partial lobe, there is a solid, hyperintense, irregular diffusion.

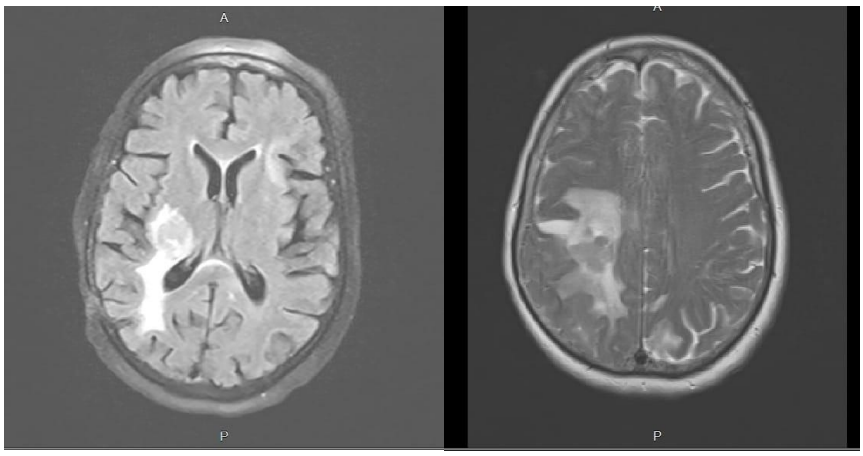

Figure 2. DWI and DWII in MRI, in the middle part of the right partial lobe, there is a solid, hyperintense, irregular diffusion.

cognizancejournal.com
Seyyedabbas Pakmehr *et al*, Cognizance Journal of Multidisciplinary Studies, Vol.4, Issue.4, April 2024, pg. 157-164
(An Open Accessible, Multidisciplinary, Fully Refereed and Peer Reviewed Journal)
ISSN: 0976-7797
Impact Factor: 4.843
Index Copernicus Value (ICV) = 77.57

It was evident that a mass with less enhancement and diffused around the thalamus in the depth of the parietooccipital lobe was not surgically available due to the specific location of the mass, and the patient underwent further examination and a stereotactic biopsy with suspected lymphoma. The patient underwent high-dose steroid treatment before a definitive diagnosis. As a result of management, the patient's left hemiplegia improved and he was able to walk, and the edema and mass volume decreased, and the patient responded well to the steroid.

After stereotactic biopsy, small pieces of cream with soft consistency were sent to the pathology department in total dimensions of 1.5*1*0.2, which were identified after examining a brain mass with lymphoproliferative disorder. Atypical lymphocytes around the arteries were seen in the pathology slide. Immunohistochemical (IHC) staining shows CD3+, CD20-, and LCA+, so the final diagnosis is large cell lymphoma (T cell variant), because in IHC, T cell markers are positive. The chest X-ray showed no evidence of masses in the chest, mediastinum, or pleura, so the presence of metastases in this patient is ruled out.

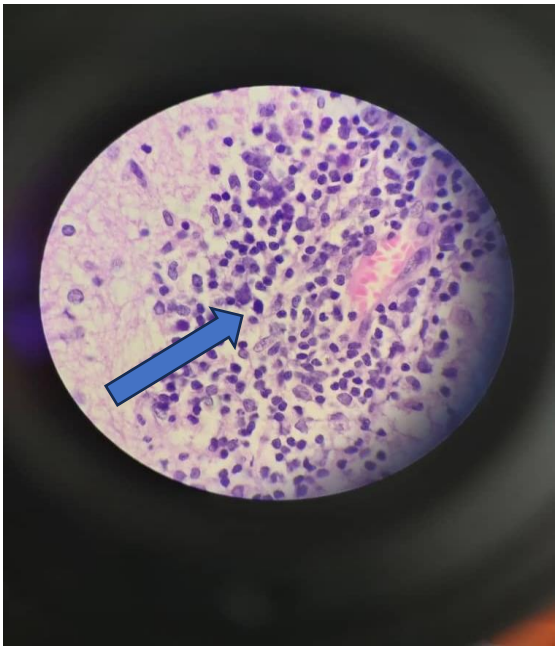

Figure 3. atypical lymphocyte

The patient was a candidate for chemoradiotherapy and was referred to another center, but due to a positive PCR test, chemoradiotherapy was delayed, and the patient was still receiving moderate-dose steroid treatment, including dexamethasone 4 mg daily. The patient is now well and has undergone one dose of chemoradiotherapy, but due to a delay in chemoradiotherapy, the mass has spread throughout the brain. *The patient was started on the MATRix regimen (methotrexate, cytarabine, and rituximab) with a 20-gram (Gy) dose of radiation.*

The important thing is that the surgery was not performed to resect the mass because the patient might be paralyzed by it.

After initial administration of high-dose corticosteroids, an MRI was taken. There is a sign of surgery at the right parietal bone and lobe with subdural effusion and hematoma; there is a round extra-axial 15*15 mm hypointense lesion in T1 without enhancement; there is extensive white matter vasogenic edema and hyperintense bright lesion in T2 in the cortical and subcortical areas of the right frontal lobe; there is a 2 ring enhancement in the deep white matter of the right frontal lobe and isointense to the cortex mass with mild peripheral edema in the superior sub-tentorial area of the right cerebellum.

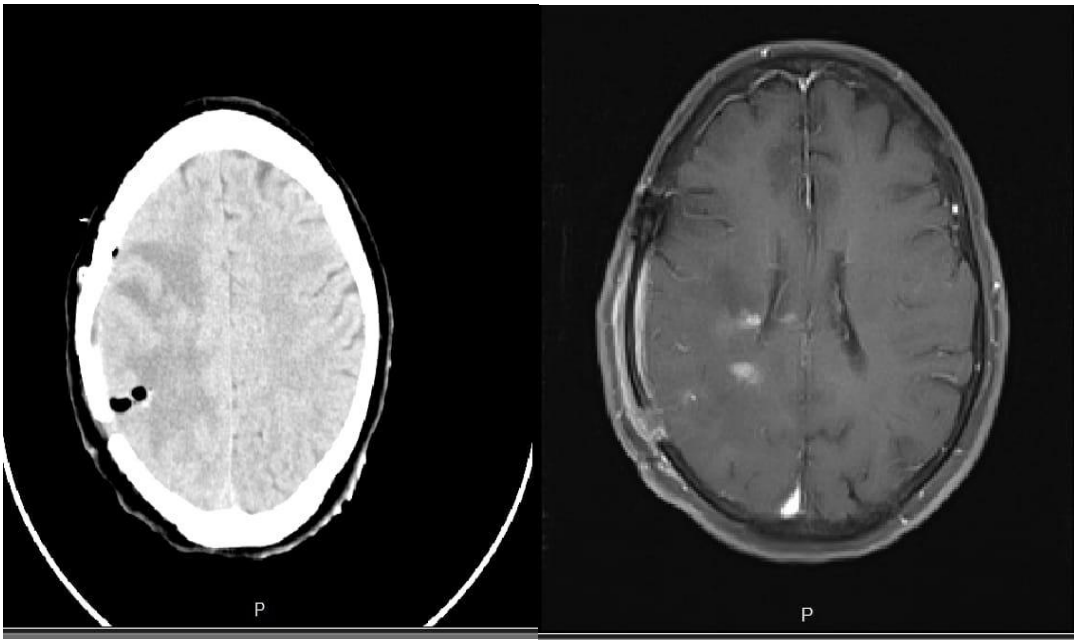

Figure 4. Post-operation DWI and DWII imaging (After initial administration of high-dose corticosteroids)

Discussion

PCNSL is a malignant NHL. It was first described by Bailey in 1929 as perivascular sarcoma (7). The vast majority (90%) of cases are diffuse large B-cell lymphomas. Less common variants include Burkitt, T-cell, immunoblastic, or low-grade malignant B-cell lymphomas (7,8,9). PCNSL can arise in the brain, spinal cord, eyes, cranial nerves, or meninges (14). The aggressive parenchymal involvement of PCNSL almost always invades only locally, rarely metastasizing outside the nervous system. PCNSL itself is rare, comprising only 2–6% of all primary brain tumors and 1–2% of all NHLs (15).

The location of the PCNSL determines the clinical picture. The most common presentation, seen in 70% of patients, is focal neurological symptoms. Forty percent present with neuropsychiatric symptoms, followed in

ISSN: 0976-7797
Impact Factor: 4.843
Index Copernicus Value (ICV) = 77.57

frequency by signs of increased intracranial pressure such as headache, nausea, and vomiting in 33%, seizure in 14%, and ocular symptoms in 4% of cases (16).

The median age at diagnosis is 53–57 years in immunocompetent patients, as in our case, the patient was immunocompetent when he was diagnosed with a 1.2:1 male-to-female sex distribution, whereas in immunocompromised patients, the median age at diagnosis is 31–35 years with a clear male predominance (male-to-female ratio of 7.38:1) (17).

Immunocompromise in these patients is typically secondary to HIV, organ transplants, or a primary immunodeficiency syndrome (18).

The clinical manifestations of PCNSL are non-specific, with the most common symptoms being cognitive decline and gait disturbance (10).

In the case of our study, the symptoms of hemiplegia, severe weakness, and excessive thinness were observed. Therefore, no specific manifestation can be considered a hallmark of the disease, and a set of diagnostic tools is needed. Several diagnostic methods are mentioned in the articles, including MRI, CT scan, PET-CT, IHC, X-ray, and pathological examination.

In our case, we have used MRI, pathology examination, and IHC (immunohistochemistry). PET-CT is more accurate than MRI for diagnosing PCNSL. Statistical analyses have found that 18-FDG PET-CT imaging is helpful for the differential diagnosis of PCNSLs and other tumors and that this test is superior to MRI (13) as well PET-CT that was performed early in the course of the disease suggested the possibility of lymphoma, so we believe that PET-CT is of greater value than MRI for the early diagnosis of PCNSLs (12) Unfortunately, this method has not been used in our study for diagnosis.

The MRI appearance of PCNSL is characterized by iso- or hypointense signals on T1-weighted images, iso- or slightly hyperintense signals on T2-weighted images, hyperintense signals on fluid-attenuated inversion recovery images, and plaque enhancement (11). As well, we have observed in MRI study a solid hyperintense irregular (42* 40 mm) mass vasogenic edema in the centrum semi ovale of the right parietal lobe. It was evident that a mass with less enhancement and diffused around the thalamus in the depth of the parietooccipital lobe was not surgically available due to the specific location of the mass, and the patient underwent further examination and a stereotactic biopsy with suspected lymphoma. Because of the low incidence of PCNSL in immunocompetent patients and the lack of specific clinical manifestations and positive auxiliary examinations, the disease was easily missed and misdiagnosed (12).

We used high-dose steroids to control symptoms due to a suspicion of lymphoma in the patient. Corticosteroids should be used with caution before the diagnosis of central nervous system diseases because, in patients with PCNSL, corticosteroid therapy may inhibit tumor growth or even cause the tumor to subside (12) .Steroid use can reduce the accuracy of the biopsy, so we should delay the use of steroids until after the biopsy. In a study, histopathological interpretation was difficult because dexamethasone treatment resulted in tumor tissue necrosis, and an accurate histopathological diagnosis took 2 weeks in this case (12) There is not much diagnostic

ISSN: 0976-7797
Impact Factor: 4.843
Index Copernicus Value (ICV) = 77.57

evidence for steroid administration, and it can be prescribed, which has received good feedback for early administration in both our study and other studies.

In the pathology slide, as in other studies, lymphocytic infiltration was evident, but the final diagnosis was completed by IHC examination, and the type of mass was identified as non-Hodgkin's lymphoma T cells, according to special tumor markers.

In this study, we used X-rays to rule out metastasis, but PET-CT can also be used to look for metastatic lesions (12).

To treat the patient, different chemotherapy regimens as well as radiotherapy can be used. In this study, our patient was started on the MATRix regimen (methotrexate, cytarabine, and rituximab) with a 20 Gray (Gy) dose of radiation.

The important point is that diagnostic and therapeutic measures should be taken quickly, and delay in each stage can lead to a poor prognosis for the patient. For example, in this study, due to delays in treatment (chemotherapy and radiotherapy), patient prognosis.

The overall incidence of PCNSL has recently increased, and the 5-year and 10-year survival rates for PCNSL are 29.9% and 22.2%, respectively (19). Unfortunately, PCNSL is an aggressive tumor with high rates of recurrence after treatment. It has a poor prognosis without treatment, with an expected survival of only 3–6 months. Chemotherapy alone or combined with radiation can boost the estimated survival time up to 25–60 months (20). Relapses occur in the first and second years in 30–60% of patients, with survival after relapse averaging 2–4 months (21).

References

1. Lukas RV, Stupp R, Gondi V, Raizer JJ. Primary central nervous system lymphoma-PART 1: Epidemiology, diagnosis, staging, and prognosis. Oncology. 2018; 32(1):17-22. [PMID]
2. Cantwell L, Ramakrishnan A, Shaughnessy PJ, Bachier CR, Selby G, Bhushan V, et al. Autologous stem cell transplant in patients with primary central nervous system lymphoma: A multicenter analysis from the Sarah cannon blood cancer network. Biology of Blood and Marrow Transplantation. 2018; 24(3):S259-60. [DOI:10.1016/j.bbmt.2017.12.238]
3. Li V, Levine AB, Gooderham PA, Yip S, Chew J. Case of primary central nervous system lymphoma arising at site of remote herpes encephalitis. World Neurosurgery. 2018; 113:217-22. [DOI:10.1016/j.wneu.2018.01.143] [PMID]
4. Baldi I, Engelhardt J, Bonnet C, Bauchet L, Berteaud E, Grüber A, et al. Epidemiology of meningiomas. Neurochirurgie. 2018; 64(1):5-14. [DOI:10.1016/j.neuchi.2014.05.006] [PMID]
5. Zouaoui S, Darlix A, Rigau V, Mathieu-Daudé H, Bauchet F, Bessaoud F, Fabbro-Peray P, et al. Descriptive epidemiology of 13,038 newly diagnosed and histologically confirmed meningiomas in France: 2006-2010. Neurochirurgie. 2018; 64(1):15-21. [DOI:10.1016/j.neuchi.2014.11.013] [PMID]
6. Bromberg JEC, Issa S, Bakunina K, Minnema MC, Seute T, Durian M, et al. . Rituximab in patients with primary CNS lymphoma (HOVON 105/ALLG NHL 24): a randomised, open-label, phase 3 intergroup study. Lancet Oncol. (2019) 20:216–28. 10.1016/S1470-2045(18)30747-2
7. Kuker W, et al. Primary central nervous system lymphomas (PCNSL): MRI features at presentation in 100 patients. J Neurooncol. 2005;72(2):169–77.
8. Mohile NA, Abrey LE. Primary central nervous system lymphoma. Neurol Clin. 2007;25(4):1193–207.
9. Miller DC, et al. Pathology with clinical correlations of primary central nervous system non-Hodgkin's lymphoma: the Massachusetts General Hospital experience 1958–1989. Cancer. 1994;74(4):1383–97.
10. Izquierdo, C, Velasco, R, Vidal, N, et al. Lymphomatosis cerebri: a rare form of primary central nervous system lymphoma. Analysis of 7 cases and systematic review of the literature. Neuro Oncol 2016; 18: 707–715.

11. Sutherland, T, Yap, K, Liew, E, et al. Primary central nervous system lymphoma in immunocompetent patients: a retrospective review of MRI features. J Med Imaging Radiat Oncol 2012; 56: 295–301.
12. Zeng X, Lu X, Li X, Peng L, Chen L. A case report of primary central nervous system lymphoma. J Int Med Res. 2020 Jul;48(7):300060520937839. doi: 10.1177/0300060520937839. PMID: 32660288; PMCID: PMC7361490.
13. Lewerenz, J, Ding, XQ, Matschke, J, et al. Dementia and leukoencephalopathy due to lymphomatosis cerebri. BMJ Case Rep 2009; 2009: r8-r2008. DOI: 10.1136/bcr.08.2008.0752.
14. Saini M, et al. A new xenograft model of primary central nervous system lymphoma. J Neurooncol. 1999;43(2):153–60.
15. Haldorsen IS, et al. CT and MR imaging features of primary central nervous system lymphoma in Norway, 1989–2003. AJNR Am J Neuroradiol. 2009;30(4):744–51.
16. Mohammadi M, Fazilat A, Mamalo AS, Ojarudi M, Hemmati-Dinarvand M, Beilankouhi EA, Valilo M. Correlation of PTEN signaling pathway and miRNA in breast cancer. Molecular Biology Reports. 2024 Dec;51(1):221.
17. Mohammadi M, Fazilat A, Mamalo AS, Ojarudi M, Hemmati-Dinarvand M, Beilankouhi EA, Valilo M. Correlation of PTEN signaling pathway and miRNA in breast cancer. Molecular Biology Reports. 2024 Dec;51(1):221.
18. Mansour A, et al. MR imaging features of intracranial primary CNS lymphoma in immune competent patients. Cancer Imaging. 2014;14:22.
19. Ostrom, QT, Gittleman, H, Fulop, J, et al. CBTRUS statistical report: primary brain and central nervous system tumors diagnosed in the United States in 2008-2012. Neuro Oncol 2015; 17: iv1–iv62.
20. Juergens A, et al. Long-term survival with favorable cognitive outcome after chemotherapy in primary central nervous system lymphoma. Ann Neurol. 2010;67(2):182–9.
21. McFarlin BL, Villegas-Downs M, Mohammadi M, Han A, Simpson DG, O'Brien Jr WD. Enhanced identification of women at risk for preterm birth via quantitative ultrasound: a prospective cohort study. American Journal of Obstetrics & Gynecology MFM. 2023 Dec 7:101250.
22. Entezami M, Havaeji H. Green Drug Supply Chain Investigation by Time-Market Balance and Risk. World Journal of Engineering and Technology. 2023 Aug 29;11(3):611-31.
23. Shakerimoghaddam A, Moghaddam AD, Barghchi B, Sanani MG, Azami P, Kalmishi A, Sabeghi P, Motavalli F, Khomartash MS, Mousavi SH, Nikmanesh Y. Prevalence of Pseudomonas aeruginosa and its antibiotic resistance in patients who have received Hematopoietic Stem-Cell Transplantation; A globally Systematic Review. Microbial Pathogenesis. 2023 Sep 27:106368.
24. Kiarashi M, Mahamed P, Ghotbi N, Tadayonfard A, Nasiri K, Kazemi P, Badkoobeh A, Yasamineh S, Joudaki A. Spotlight on therapeutic efficiency of green synthesis metals and their oxide nanoparticles in periodontitis. Journal of Nanobiotechnology. 2024 Jan 5;22(1):21.
25. Ghahjavarestani AM, Martin MD, Gavalda JM. Study of marital satisfaction in autistic families. Journal of Autism and Developmental Disorders. 2020;18(2):21-31.
26. Shoeibi M, Baghbadorani PR. Moving Toward Resiliency in Health Supply Chain. International journal of industrial engineering and operational research. 2023 Oct 18;5(3):63-74.
27. Pourali G, Kazemi D, Chadeganipour AS, Arastonejad M, Kashani SN, Pourali R, Maftooh M, Akbarzade H, Fiuji H, Hassanian SM, Ghayour-Mobarhan M. Microbiome as a biomarker and therapeutic target in pancreatic cancer. BMC microbiology. 2024 Jan 5;24(1):16.
28. Bagi M, Amjad F, Ghoreishian SM, Sohrabi Shahsavari S, Huh YS, Moraveji MK, Shimpalee S. Advances in technical assessment of spiral inertial microfluidic devices toward bioparticle separation and profiling: A critical review. BioChip Journal. 2024 Jan 22:1-23.
29. Kiarashi M, Bayat H, Shahrtash SA, Etajuri EA, Khah MM, Al-Shaheri NA, Nasiri K, Esfahaniani M, Yasamineh S. Mesenchymal Stem Cell-based Scaffolds in Regenerative Medicine of Dental Diseases. Stem Cell Reviews and Reports. 2024 Feb 3:1-34.
30. Jalaledin G, Mehrnaz M, inventors. Method for producing rod-shaped and branched metallic nano-structures by polyol compounds. United States patent application US 12/870,792. 2011 Apr 21.
31. Ghanavi J, Mostafavi M, Ghanavi Z, inventors. Method for the synthesis of metallic nano products. United States patent US 9,487,399. 2016 Nov 8.

