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Diferencijalna dijagnoza bezbolne limfadenopatije: izazov u svakodnevnoj kliničkoj praksi sa prikazom slučaja i osvrtom na literaturu

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Sažetak

Uvod: Limfadenopatija se definiše kao abnormalni nalaz tokom fizikalnog pregleda pacijenta i odnosi se na limfne čvorove koji su abnormalni po veličini, konzistenciji ili broju. Pažljivo uzeta anamneza i detaljan fizikalni pregled omogućavaju lekaru da odabere adekvatan algoritam za postavljanje prave dijagnoze. Diferencijalna dijagnoza zahteva veliki oprez. Zbog širokog spektra mogućih uzročnika i često nespecifične kliničke slike, bezbolna limfadenopatija predstavlja veliki klinički izazov, naročito na nivou primarne zdravstvene zaštite.

Prikaz slučaja 1: Pacijentkinja, stara 54 godine, javila se na pregled zbog promene koju je napipala u levoj prepon. Detaljnim fizikalnim pregledom konstatovana je promena prečnika 25 mm, bezbolna na dodir. Ultrazvuk prepone pokazao uvećani limfni čvor sa perifernom vaskularizacijom. Biopsija uvećanog čvora pokazala metastatski karcinom porekla cerviksa. Na PET-CT je opisana solitarna promena uz gornju ivicu uterusa i depoziti u jetri. Onkološka komisija ordinirala hemioterapiju u tronedeljnom režimu. Pacijentkinja do sada prošla kroz 6 ciklusa hemioterapije.

Prikaz slučaja 2: Pacijent, star 76 godina, javio se na pregled zbog promene u desnoj pazušnoj jami koju ima nekoliko meseci unazad, bez drugih tegoba. Fizikalnim pregledom uočena je promena ispod desne pazušne jame, veličine jabuke, bezbolna na dodir. Biopsija promene govori u prilog metastatskog melanoma. Ultrazvuk abdomena pokazao metastaze na jetri. Dermatolog, pregledom kože, uočio lumbalno, leziju prečnika 1 cm, visoko suspektnu na melanom. Urađena je ekscizija lezije i PH nalaz potvrdio dijagnozu.

Zaključak: Bezbolna limfadenopatija je čest i dijagnostički izazovan nalaz, sa širokim spektrom uzroka od benignih stanja do maligniteta. Pravovremeno prepoznavanje i adekvatna obrada ključni su za ishod lečenja.

Ključne reči: maligni melanom, limfatičke metastaze, neoplazme grliča materice

Differental diagnosis of painless lymphadenopathy: challenges in everyday clinical practice with case report and literature overview

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Abstract

Introduction. Lymphadenopathy is defined as an abnormal finding during a physical examination, indicating that the lymph nodes are abnormal in size, consistency, and number. A thorough personal history and detailed physical examination allow the physician to formulate an appropriate diagnostic strategy. It is important to approach differential diagnoses with caution, as there is a wide range of potential causes and often nonspecific clinical presentations. Painless lymphadenopathy, in particular, presents a significant clinical challenge, especially in primary healthcare settings.

Case report 1. A 54-year-old female patient presented with a lump that she had noticed in her left groin. A detailed physical examination revealed a painless lump measuring 25 mm in diameter. An ultrasound of the groin showed an enlarged lymph node with peripheral vascularization. A biopsy of the lymph node confirmed the presence of metastatic cervical carcinoma. A PET-CT scan indicated a solitary lump along the upper uterine margin, along with liver metastases. The oncology team recommended three weeks of chemotherapy. The patient has since undergone six cycles of chemotherapy.

Case report 2. A 76-year-old male patient presented with a lump in his right armpit that had been present for several months, but he reported no other symptoms. A physical examination revealed a lump the size of an apple located under the right armpit, which was painless to the touch. A biopsy confirmed that it was a metastatic melanoma. An abdominal ultrasound showed the presence of liver metastases. A dermatological examination revealed a suspicious skin tumor in the lumbar area, measuring 1 cm in diameter, also highly suggestive of melanoma. After excising the lesion, the pathological findings confirmed the diagnosis.

Conclusion. Painless lymphadenopathy is a common finding that presents diagnostic challenges, with a broad range of causes that can vary from benign to malignant. Timely recognition and appropriate interventions are crucial for treatment outcomes.

Keywords: melanoma malignum, lymphatic metastases, Uterine Cervical Neoplasms

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Uvod

Limfadenopatija se definiše kao abnormalni nalaz tokom fizikalnog pregleda pacijenta i odnosi se na limfne čvorove koji su abnormalni po veličini, konzistenciji ili broju. Limfni čvorovi su deo limfnog sistema koji ima ulogu da štiti organizam od mikroorganizama, održava odgovarajući nivo telesnih tečnosti, apsorbuje hranljive materije i uklanja određene otpadne produkte. Ljudsko telo ima preko 600 limfnih čvorova. Jasno razumevanje njihove funkcije, anatomske lokalizacije, fizičkih karakteristika i uzroka njihovog uvećanja ključno je da bi se razlikovalo koje slučajeve treba hitno i agresivno obraditi, a koje samo pratiti. Obrazac, raspored i karakteristike limfadenopatije mogu pružiti dragocene kliničke informacije tokom dijagnostičkog procesa.

Postoje različite klasifikacije limfadenopatije, ali jednostavan i klinički koristan sistem je da se limfadenopatija klasifikuje kao:

- **Generalizovana** – ako su limfni čvorovi uvećani u dvema ili više nepovezanih regija
- **Lokalizovana** – ako je zahvaćena samo jedna anatomska regija

Patološki uvećani limfni čvorovi mogu biti bolni ili bezbolni, fiksirani ili pokretni, pojedinačni ili slepljeni.

Pažljivo uzeta anamneza i detaljan fizikalni pregled omogućavaju lekaru da odabere adekvatan algoritam za blagovremeno postavljanje prave dijagnoze, uključujući i odluku kada je bezbedno samo praćenje uvećanog limfnog čvora [1,2].

Prilikom uzimanja anamneze lekar treba obratiti pažnju na nekoliko ključnih pitanja:

- ima li lokalizovanih simptoma ili znakova koji mogu ukazati na postojanje infekcije ili neoplazme na određenom mestu
- ima li opštih simptoma (povišena telesna temperatura, gubitak telesne mase, umor, noćno znojenje) koji mogu sugerisati prisustvo tuberkuloze, limfoma i drugih neprepoznatih infekcija i maligniteta u slučajevima izostanka specifičnih znakova
- da li pacijent koristi neke lekove (penicilin, cefalosporini, sulfonamidi, fenitoin mogu izazvati limfadenopatiju) [2,3]

Tokom obavljanja fizikalnog pregleda treba opisati nekoliko karakteristika uvećanog limfnog čvora*: veličina* (normalni do 1cm u prečniku), *bol* (obično je rezultat upalnog procesa), *konzistencija* (tvrd kao kamen obično znak metastatskog karcinoma, mekši su znak infekcije), *lokalizacija* (supraklavikularna limfadenopatija nosi najveći rizik od maligniteta), *slepljenost* (grupa limfnih čvorova koja deluje povezano i kreće se kao celina).

Introduction

Lymphadenopathy is defined as an abnormal finding during a physical examination, indicating that the lymph nodes are abnormal in size, consistency, and number. Lymph nodes are integral components of the lymphatic system, playing a vital role in protecting the body from microorganisms, maintaining proper fluid levels, absorbing nutrients, and removing certain waste products. The human body contains over 600 lymph nodes. Understanding their functions, anatomical locations, physical characteristics, and the reasons for their enlargement is essential for distinguishing between cases that require urgent attention and those that can be monitored. The pattern, arrangement, and characteristics of lymphadenopathy can provide valuable clinical information during the diagnostic process.

Lymphadenopathy can be classified in different ways, but a straightforward and clinically useful system is as follows:

- **Generalized:** Enlarged lymph nodes are present in two or more unrelated areas of the body.
- **Localized:** Only one specific anatomical region is affected.

Enlarged lymph nodes can vary in several ways: they may be painful or painless, fixed in place or movable, and can occur as solitary nodes or in clusters.

A comprehensive personal history and thorough physical examination enable the physician to devise an appropriate diagnostic strategy, including deciding when it is safe only to monitor the enlarged lymph nodes.[1,2].

When gathering a patient's personal history, a physician should focus on several important questions:

- Are there localized symptoms or signs that indicate an infection or neoplasm in a specific area?
- Are there general symptoms, such as fever, weight loss, malaise, and night sweats, that may indicate the presence of tuberculosis, lymphoma, or other unrecognized infections and malignancies, particularly when specific signs are missing?
- Does the patient take any medications (e.g., penicillin, cephalosporins, sulfonamides, phenytoin) that may cause lymphadenopathy?[2,3]

When performing a physical examination of enlarged lymph nodes, several characteristics should be evaluated: *size* (normal lymph nodes are typically up to 1 cm in diameter), *pain* (lymph nodes that are painful usually indicate an inflammatory process), *consistency* (a lymph node that feels hard like a stone may be a sign of metastatic carcinoma, whereas softer lymph nodes are more likely associated with infection), *localization* (lymphadenopathy in the supraclavicular region carries the highest risk for malignancy), *confluency* (a group of lymph nodes that appear connected and move as a single unit may indicate a more serious condition). These characteristics can help in distinguishing the underlying causes of lymphadenopathy.

Kada je limfadenopatija lokalizovana, lekar treba da pregleda regiju koju dreniraju zahvaćeni limfni čvorovi, u potrazi za znacima infekcije, kožnih promena ili tumora. Takođe, treba pažljivo pregledati i druge regije sa limfnim čvorovima, kako bi se isključila mogućnost da se ipak radi o generalizovanoj, a ne samo lokalizovanoj limfadenopatiji. Ovo je važan aspekt kliničkog pregleda, jer je jedna studija pokazala da su lekari primarne zdravstvene zaštite prepoznali generalizovanu limfadenopatiju kod samo 17% pacijenata kod kojih je ona zapravo bila prisutna[2]

Laboratorijska i imidžing dijagnostika mogu biti od velike pomoći u evaluaciji limfadenopatije i postavljanju diferencijalne dijagnoze. U proceni se koriste sledeći dijagnostički protokoli:

- KKS, kompletan metabolički panel, laktat dehidrogenazu (LDH), serologije na gljivične infekcije (histoplazmoza, blastomikoza, kokcidiomikoza, kriptokokoza), laboratorijsko ispitivanje na sifilis, HIV, CMV, EBV, HSV, HBV, kao i QuantiFERON test za tuberkulozu
- RTG grudnog koša može biti od pomoći u razjašnjavanju medijastinalne limfadenopatije i osnovnih bolesti koje zahvataju pluća, uključujući tuberkulozu, kokcidioidomikozu, limfome, histiocitoze
- Ultrazvuk može biti koristan za dokumentovanje obima zahvaćenosti limfnih čvorova i eventualnih promena u njima.
- CT grudnog koša, abdomena i karlice može pomoći u preciznijem određivanju lokalizacije limfadenopatije, njenog obrasca i veličine. Takođe, može poslužiti kao vodič za biopsiju ukoliko je potrebna.
- Biopsija limfnog čvora (eksciziona biopsija kao zlatni standard, *fine needle* aspiracija i *core needle* biopsija) omogućava imunohistohemijsku, genetsku, molekularnu analizu[2,4]

Diferencijalna dijagnoza zahteva veliki oprez. Dok bolna limfadenopatija najčešće ukazuje na akutne, inflamatorne procese, bezbolna limfadenopatija predstavlja poseban dijagnostički izazov jer može biti prvi znak ozbiljnih i potencijalno životno ugrožavajućih bolesti. Bezbolna limfadenopatija može se javiti u svim uzrastima, ali njeno kliničko značenje varira u zavisnosti od starosti pacijenta, anamneze, trajanja i lokalizacije. U pedijatrijskoj populaciji češće je benigne etiologije, dok kod odraslih, naročito starijih osoba, postoji veći rizik od maligniteta.[1,2,4]

Postoji čitav etiološki spektar bezbolne limfadenopatije.

- Maligne bolesti (ALL, Hodgkin, non-Hodgkin limfom, metastatski karcinomi…)
- Infektivne bolesti (HIV, EBV, CMV, tuberkuloza, sifilis…)

When lymphadenopathy is localized, the physician should examine the area drained by the affected lymph nodes, checking for signs of infection, skin lesions, or tumors. Additionally, other lymph node regions must be thoroughly assessed to rule out the possibility of generalized lymphadenopathy. This step is crucial because a study found that primary healthcare physicians recognized generalized lymphadenopathy in only 17% of affected patients.[2]

Laboratory and imaging techniques can be very helpful in evaluating lymphadenopathy and making a differential diagnosis. The assessment includes various diagnostic protocols:

- Complete blood count (CBC), complete metabolic panel, lactate dehydrogenase (LDH), serology for fungal infections (histoplasmosis, blastomycosis, coccidioidomycosis, cryptococcosis), laboratory testing for syphilis, HIV, CMV, EBV, HSV, HBV, as well as the QuantiFERON test for tuberculosis.
- Chest X-ray can help differentiate mediastinal lymphadenopathy from other lung diseases, including tuberculosis, coccidioidomycosis, lymphomas, and histiocytosis.
- Ultrasound is effective in documenting the size of affected lymph nodes and any changes in their structure.
- CT scans of the chest, abdomen, and pelvis can provide more accurate localization of lymphadenopathy, including its pattern and size. They can also serve as guidance for biopsy if needed.
- Excision biopsy of the lymph node (the golden standard), fine needle aspiration, and core needle biopsy ensure immunohistochemical, genetic, and molecular analyses.[2,4]

Differential diagnosis requires careful consideration. While painful lymphadenopathy typically indicates acute inflammatory processes, painless lymphadenopathy presents a more complex diagnostic challenge, as it may be the first sign of serious and potentially life-threatening condition. Painless lymphadenopathy can occur at any age, but its clinical significance varies based on the patient's age, medical history, duration, and location of the lymphadenopathy. In the pediatric population, painless lymphadenopathy is mostly benign, while in adults, particularly in older individuals, there is a higher risk of malignancy.[1, 2, 4]

There is a broad spectrum of causes for painless lymphadenopathies:

- Malignant diseses (ALL, Hodgkin, non-Hodgkin lymphoma, metastatic carcinoma…)
- Infectious diseases (HIV, EBV, CMV, tuberculosis, syphilis…)

- Autoimune bolesti (sistemski lupus, reumatoidni artritis, sarkoidoza…)
- Lekovi (penicilini, cefalosporini…) [2,4]

Zbog širokog spektra mogućih uzročnika i često nespecifične kliničke slike, bezbolna limfadenopatija predstavlja veliki klinički izazov naročito na nivou primarne zdravstvene zaštite.

Prikaz slučaja 1

Pacijentkinja, stara 54 godine, javila se na pregled u ambulantu opšte prakse zbog promene koju je napipala u predelu leve prepone. Negirala prehlade i povišenu temperaturu, subjektivno bila bez tegoba. Urađen je detaljan fizikalni pregled u toku kojeg je konstatovana ovalna promena u levoj preponi, prečnika oko 25 mm, pokretna i bezbolna na dodir, imponuje kao uvećan limfni čvor. Pacijentkinji su indikovani laboratorijski nalazi (Se 10, CRP 4.3, Le 9.3, neutrofili 56.8, limfociti 34, Er 5.05, Hgb 150, Htc 0.45, trombociti 301), ultrazvuk prepone i pregled ginekologa. Na ultrazvuku prepone opisan je uvećan limfni čvor, dimenzija 29x16 mm, cistično degenerisan sa diskretnom perifernom vaskularizacijom. Ginekološki nalaz uredan (uterus u normalnom položaju, dimenzija 46x35 mm, kavum prazan, endometrijum 3.5 mm, adneksa b.o. Douglas prostor prazan). Iz ginekološke anamneze dobijeno da je imala 3 trudnoće i 1 porođaj, prva menstruacija sa 15 godina, poslednja sa 47 godina. Pacijentkinja je poslata na Kliniku za abdominalnu hirurgiju gde je nakon hirurškog pregleda načinjena biopsija uvećanog čvora, koja je pokazala promenu koja ide u prilog metastatskom karcinomu ginekološkog porekla, na prvom mestu porekla cerviksa. Na Klinici za ginekologiju i akušerstvo načinjeni su biopsija cerviksa koja je pokazala prisustvo hronične upale i eksplorativna kiretaža kojom su dobijeni komadići strome bez žlezda. U brisu cerviksa izolovana je ureaplazma. Načinjen je i PET-CT na kome je opisana solitarna lezija prečnika 8.5 mm uz gornju ivicu uterusa levo. Uz lateralni zid abdomena levo, intraperitonealno, uočena su dva patološki izmenjena limfna čvora i sekundarni depoziti u parenhimu jetre. Na Institutu za onkologiju Vojvodine urađena je dijagnostička laparoskopija sa *ex tempore* biopsijom promene koja potvrđuje dijagnozu karcinoma porekla cerviksa. Onkološka komisija je predložila hemioterapiju (Taxol i Carboplatin uz Avastin u tronedeljnom režimu). Pacijentkinja je do sada prošla kroz 6 ciklusa hemioterapije.

- Autoimmune diseases (systemic lupus, rheumatoid arthritis, sarcoidosis…)
- Medications (penicillin, cephalosporins…)[2, 4]

Painless lymphadenopathy presents a significant clinical challenge, particularly at the primary healthcare level, due to its wide range of causes and often nonspecific clinical presentation.

Case report 1

A 54-year-old female patient presented to the primary healthcare center with a lump she had noticed in her left groin. She reported no history of cold or fever and was otherwise healthy. A detailed physical examination revealed an oval lump in the left groin measuring approximately 25 mm in diameter. The lump was movable, painless to touch, and appeared to be an enlarged lymph node. We ordered laboratory tests for this patient, which showed the following results: ESR 10, CRP 4.3, leukocytes 9.3, neutrophils 56.8%, lymphocytes 34%, erythrocytes 5.05, hemoglobin 150, hematocrit 0.45, and platelets 301. Additionally, we scheduled a groin ultrasound and a gynecological examination. The ultrasound of the groin revealed an enlarged lymph node measuring 29 x 16 mm in diameter, with cystic degeneration and discrete peripheral vascularization. The gynecological exam was normal, showing that the uterus was in the correct position, measuring 46 x 35 mm in diameter. The uterine cavity was empty, the endometrium measured 3.5 mm, the adnexa appeared non-specific, and the Douglas pouch was empty. The gynecological history revealed that the patient had experienced three pregnancies and one delivery. She had her first period at the age of 15 and her last at 47. The patient was referred to the clinic for abdominal surgery, where a biopsy of an enlarged lymph node was performed. The results indicated a tumor consistent with metastatic carcinoma of gynecological origin, likely derived from the cervix. A biopsy of the cervix was conducted at the clinic for gynecology and obstetrics, which showed signs of chronic inflammation. An exploratory curettage was performed, resulting in the collection of stromal tissue, but without any glandular components. A cervical swab revealed the presence of Ureaplasma. A PET-CT scan was performed, which showed a solitary lesion measuring 8.5 mm in diameter along the upper left margin of the uterus. Additionally, two pathologically altered lymph nodes were found in the peritoneum, near the left lateral abdominal wall, along with secondary deposits in the liver. At the Institute for Oncology of Vojvodina, a diagnostic laparoscopy with an ex tempore biopsy was conducted, confirming the diagnosis of carcinoma of cervical origin. The oncology team recommended a chemotherapy regimen consisting of Taxol and Carboplatin, with Avastin, scheduled over three weeks. The patient has completed six cycles of chemotherapy so far.

Prikaz slučaja 2

Pacijent, star 76 godina, javlja se u ambulantu opšte prakse zbog promene ispod pazuha za koju navodi da je prisutna unazad nekoliko meseci. Subjektivno se osećao dobro, negirao prisustvo bilo kakvih tegoba. U toku fizikalnog pregleda uočena je promena veličine jabuke ispod desne pazušne jame, nepokretna, bezbolna na dodir. Pacijent se upućuje hematologu koji isključuje hematološka oboljenja i predlaže ultrazvuk pazušne jame i limfnih čvorova vrata. Na ultrazvuku desne pazušne jame opisana je hipoehogena fokalna promena dimenzija 60x40 mm. Urađena je biopsija promene koja je pokazala fragmente vezivno-masnog tkiva delom infiltrisani atipičnim poligonalnim ćelijama eozinofilne citoplazme, delom ispunjene melaninskim pigmentom povećanog nukleocitoplazmatskog odnosa. U okolnom vezivnom tkivu prisutan i slobodan melaninski pigment. Uočavaju se široka područja nekroze. Nalaz ide u prilogu metastatskog melanoma. Ultrazvuk abdomena je pokazao tumore jetre tipa metastaza. Pacijent je sa ovim nalazima poslat na Kliniku za kožno-venerične bolesti. Dermatolog je pregledom kompletne kože uočio nodularnu leziju prečnika 1 cm, lumbalno desno sa dermoskopski pozitivnim blue-black fenomenom i chrysalis strukturama zbog čega je visoko suspektna na melanom. Urađena je ekscizija lezije, a PH nalaz je potvrdio dijagnozu.

Diskusija

Lekari opšte prakse se, tokom svog rada, najviše susreću sa jednom vrstom limfadenopatije, a to je cervikalna. Cervikalna limfadenopatija je najčešće lokalizovana i povezana sa inflamatornim procesima u vratu ili okolnim regijama. Na primer, infekcija grla, prehlada, karijes, infekcija uha, bronhitis, konjunktivitis i infekcije pljuvačnih žlezda mogu biti uzročni faktori. Pored infekcija, određeni karcinomi glave i vrata, mogu izazvati lokalizovanu cervikalnu limfadenopatiju. Takvi tumori najčešće zahvataju nos, paranazalne šupljine, usnu duplju, glasne žice, pljuvačne žlezde i štitastu žlezdu. Cervikalna limfadenopatija može biti i generalizovana zbog sistemske bolesti koja zahvata organe udaljene od regije vrata. Najčešće se javlja kao posledica hronične infekcije, malignih bolesti i autoimunih poremećaja. Hronične infekcije kao što su AIDS, infektivna mononukleoza i plućna tuberkuloza često se prezentuju uvećanjem cervikalnih limfnih čvorova [5].

Rosai-Dorfmanova bolest (RDD) je retki histiocitni poremećaj. Prvi put je identifikovana 1960-ih godina kao benigno, samoograničavajuće stanje koje se karakteriše izraženom limfadenopatijom. Od tada postignuti su značajni pomaci u razumevanju faktora koji dovode do ove bolesti. Prema klasifikaciji hematopoetskih maligniteta Svetske zdravstvene organizacije, RDD se danas svrstava u neoplastične bolesti.

Case report 2

A 76-year-old male patient presented to a primary healthcare center with a lump in his right armpit that had been present for several months. He reported feeling fine overall and denied having any other health issues. During the physical examination, a lump the size of an apple was observed beneath the right armpit. The lump was immovable and painless to the touch. The patient was referred to a hematologist, who ruled out hematological diseases. The hematologist also recommended an ultrasound of the armpit and neck lymph nodes. The ultrasound of the right armpit revealed a hypoechoic focal lump measuring 60 x 40 mm in diameter. A biopsy was performed, and the results indicated fragments of reticular-fatty tissue that were partially infiltrated with atypical polygonal cells. These cells displayed eosinophilic cytoplasm and were partly filled with melanin pigment. Additionally, there was an increased nucleocytoplasmic ratio observed. Free melanin pigment was also present in the surrounding reticular tissue, and extensive areas of necrosis were noted. These findings suggest a diagnosis of metastatic melanoma. An abdominal ultrasound revealed liver tumors that were consistent with metastases. The patient was referred to the dermatology clinic. During a full skin examination, the dermatologist observed a nodular lesion measuring 1 cm in diameter located in the right lumbar area. The lesion exhibited a positive dermoscopic *blue-black* phenomenon and *chrysalis* structures, raising strong suspicion for melanoma. An excision of the lesion was performed, and the histopathologic findings confirmed the diagnosis.

Discussion

Cervical lymphadenopathy is the most common condition encountered in a general practitioner's practice. It is primarily associated with inflammatory processes in the neck and nearby regions, such as throat infections, colds, dental caries, ear infections, bronchitis, conjunctivitis, and infections of the salivary glands. In addition to infections, certain head and neck carcinomas can cause localized cervical lymphadenopathy. These tumors typically affect the nasal passages, paranasal cavities, oral cavity, vocal cords, salivary glands, and thyroid gland. Cervical lymphadenopathy can also be generalized due to systemic diseases that impact organs distant from the neck. This is often a result of chronic infections, malignancies, or autoimmune diseases. Chronic infections, such as AIDS, infective mononucleosis and pulmonary tuberculosis often present with enlarged cervical lymph nodes[5].

Rosai-Dorfman disease (RDD) is a rare histiocytic disorder that was first identified in the 1960s. Initially considered a benign and self-limited condition, it is characterized by prominent lymphadenopathy. Since then, significant ad-

RDD se obično prezentuje bilateralnom cervikalnom limfadenopatijom. Klinički tok varira od samoograničavajućeg stanja do diseminovanog oblika sa povećanim mortalitetom. Prema našim saznanjima, do sada su u literaturi opisana i četiri slučaja gde je izolovano zahvatanje aksilarnih limfnih čvorova predstavljalo jedini znak nodalne forme RDD [6]. Iako retko oboljenje, RDD treba ostati na listi diferencijalne dijagnoze cervikalne limfadenopatije, naročito kod starijih pacijenata. Opisani su slučajevi gerijatrijskih pacijenata gde je cervikalna limfadenopatija bila jedini znak RDD-a udružene sa Hodgkin limfomom [7].

Retki uzročnik cervikalne limfadenopatije je i Kikuči-Fudžimatova bolest (Kikuchi-Fujimoto disease) poznata i kao histiocitni nekrotizirajući limfadentitis. Benigno je, samoograničavajuće stanje koje se karakteriše uvećanjem limfnih čvorova vrata i najčešće pogađa mlade žene. U najvećem broju slučajeva prolazi samo, bez terapijskog tretmana. Među ređe, ali ipak prisutne uzročnike u praksi, spadaju i Gošeova bolest, Niman-Pikov sindrom i amiloidoza [5].

Cervikalna limfadenopatija, sama po sebi, nije ozbiljno stanje. Najčešće je znak akutne infekcije. Međutim, može biti znak ozbiljnih hroničnih oboljenja. Vrlo često predstavlja nespecifičan klinički znak osnovne bolesti i zahteva temeljno ispitivanje. Ukoliko pacijent uz klinički nalaz uvećanih limfnih čvorova vrata navodi i simptome poput gubitka telesne težine, konstantnog umora, noćnog znojenja i neobjašnjive temperature, to može ukazivati na ozbiljna stanja kao što su maligna oboljenja, autoimune bolesti, ozbiljne hronične infekcije. Stoga je neophodno sprovesti dodatnu dijagnostiku uključujući laboratorijske i radiološke pretrage, kao i biopsiju uvećanog limfnog čvora, radi blagovremenog postavljanja tačne dijagnoze i adekvatnog lečenja [5,8].

Procena limfadenopatije ima poseban značaj i u reumatologiji, s obzirom na to da je uvećanje limfnih čvorova čest nalaz u kliničkom spektru nekoliko poznatih reumatoloških bolesti, uključujući reumatoidni artritis, sistemski lupus i Sjögrenov sindrom. Opisano je nekoliko slučajeva gde je generalizovana bezbolna limfadenopatija bila jedini znak sistemskog lupusa. Pored toga, limfadenopatija može predstavljati početnu ili izraženiju manifestaciju retkih reumatoloških oboljenja, kao što su IgG4-relacionisana bolest i Castlemanova bolest, čije komplikacije mogu biti potencijalno životno ugrožavajuće [9,10]. Diferencijalna dijagnoza bezbolne limfadenopatije mora ići i u pravcu reumatoloških oboljenja, naročito ako pacijent daje podatak da postoji porodična predispozicija za ove bolesti. Pravilno uzeta anamneza može biti od velike pomoći u određivanju dijagnostičkog pravca i bržem postavljanju adekvatne dijagnoze.

Broj plastičnih hirurških intervencija, kao što su ugradnje grudnih implantata, vrtoglavo raste. Silikonski grudni implantati postali su osnovna metoda i u estetskoj i u rekonstruktivnoj hirurgiji dojke. Oko 80% rekonstruktivnih operacija dojke, nakon mastektomije, zasniva se na ugradnji

vancements have been made in understanding the factors that lead to this disease. According to the World Health Organization's classification of hematopoietic malignancies, RDD is now categorized as a neoplastic disease. Typically, RDD presents as bilateral cervical lymphadenopathy. The clinical course of the disease can range from self-limited to a disseminated form, which is associated with a higher mortality rate. Notably, our research has uncovered four published case reports in which only the axillary lymph nodes were affected, representing a nodal form of RDD[6]. Though it is a rare disease, Rosai-Dorfman disease (RDD) should still be considered in the differential diagnosis of cervical lymphadenopathy, particularly in older patients. There have been reported cases of geriatric patients who exhibited cervical lymphadenopathy as the sole symptom of RDD, along with cases of Hodgkin lymphoma[7].

A rare cause of cervical lymphadenopathy is Kikuchi-Fujimoto disease, also known as histiocytic necrotizing lymphadenitis. This condition is benign and self-limiting, characterized by enlarged lymph nodes, and it primarily affects younger women. In most cases, it resolves on its own without the need for therapeutic intervention. Other uncommon causes of cervical lymphadenopathy include Gaucher disease, Niemann-Pick syndrome, and amyloidosis[5].

Cervical lymphadenopathy, while not usually a serious condition, often indicates the presence of an acute infection. However, it can also be a sign of serious chronic diseases. Frequently, it serves as a nonspecific clinical indicator of an underlying condition, necessitating a thorough examination. If a patient experiences symptoms such as weight loss, persistent malaise, night sweats, and unexplained fever, along with already enlarged cervical lymph nodes, it could indicate a serious condition, including malignancies, autoimmune diseases, or severe chronic infections. Therefore, it is essential to conduct further diagnostic procedures, including laboratory tests, X-rays, and a biopsy of the enlarged lymph nodes, to arrive at an accurate diagnosis and provide appropriate treatment[5, 8].

The evaluation of lymphadenopathy is particularly important in rheumatology because enlarged lymph nodes are commonly observed in several rheumatic diseases, including rheumatoid arthritis, systemic lupus erythematosus, and Sjögren's syndrome. There are numerous cases in the literature where generalized, painless lymphadenopathy has been the only indication of systemic lupus. Additionally, lymphadenopathy can be an initial or prominent manifestation of rare rheumatic conditions, such as IgG4-related disease and Castleman's disease, which may lead to potentially life-threatening complications[9,10]. The differential diagnosis of painless lymphadenopathy can often involve rheumatologic diseases, particularly if the patient has a family history of such conditions. A thorough personal history is crucial and can significantly assist in determining the appropriate diag-

implantata. Silikonska limfadenopatija je retka komplikacija koja nastaje nakon ugradnje silikonskih implantata. Ovo stanje se obično javlja kada silikon iz oštećenih implantata migrira u okolna tkiva i akumulira se u limfnim čvorovima. Takvo nagomilavanje izaziva perzistentnu reakciju na strano telo, što dovodi do, najčešće, bezbolnog uvećanja limfnih čvorova, najčešće aksilarnih. Stanje se neretko otkriva slučajno tokom rutinskog pregleda pacijenata. Kod pacijentkinja sa istorijom karcinoma dojke, a nakon rekonstruktivne operacije, procena limfadenopatije je od suštinskog značaja kako bi se isključilo prisustvo maligniteta [11].

Zaključak

Bezbolna limfadenopatija je čest i dijagnostički izazovan nalaz, sa širokim spektrom uzroka od benignih stanja do maligniteta. Pravovremeno prepoznavanje i adekvatna obrada ključni su za ishod lečenja. Preporuke za praksu jesu sledeće:

- Uvek proceniti da li je limfadenopatija lokalizovana ili generalizovana
- Obratiti pažnju na sistemske simptome
- Pravovremeno uputiti pacijenta na biopsiju pri sumnji na malignitet
- Izbegavati nepotrebnu dijagnostiku bez jasnog kliničkog opravdanja

nostic pathway and achieving an accurate diagnosis.

The number of plastic surgery procedures, such as breast implants, is increasing. Silicone breast implants have become a standard option in both aesthetic and reconstructive breast surgery. Approximately 80% of reconstructive breast surgeries following mastectomy involve the use of these implants. Silicone lymphadenopathy is a rare complication that can occur after the placement of silicone implants. This condition arises when silicone from the implants migrates into surrounding tissue and accumulates in the lymph nodes. As a result, patients may experience a persistent reaction to the foreign material, leading to painless enlargement of the lymph nodes, primarily in the axillary region. Silicone lymphadenopathy is often discovered during routine check-ups. For patients with a history of breast cancer, it is crucial to assess lymphadenopathy after reconstructive surgery to rule out the possibility of malignancy[11].

Conclusion

Painless lymphadenopathy is a common and diagnostically challenging finding with a wide range of causes, from benign to malignant. Timely recognition and appropriate management are key to treatment outcome. Practical recommendations include:

- Always evaluate whether the lymphadenopathy is localized or generalized.
- Pay attention to the existence of systemic symptoms.
- Refer a patient promptly for a biopsy if malignancy is suspected.
- Avoid unnecessary diagnostic procedures if there's no clear clinical justification.

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