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Melanotic Neuroectodermal Tumor of Infancy: the Use of Immunohistochemical Analysis

Melanotički neuroektodermalni tumor dojenačke dobi: primjena imunohistokemijske analize

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Abstract

The Melanotic Neuroectodermal Tumor of Infancy (MNTI) is an asymptomatic, pigmented neoplasm characterized by a fast and locally aggressive growth along with a rare tissue formation. In the diagnostic process, the use of imaging exams can suggest a local destruction suggestive of malignancy, a sign of bone remodeling and expansion. Therefore, as any early diagnosis minimizes risks and improves the prognosis of treatment for the patient, the aim of this study was, based on a clinical case report, to corroborate the use of histopathological analysis associated with immunohistochemistry. Thus, we conclude that the immunohistochemical exam is of great importance for a better complementation of the MNTI diagnosis process. In addition, it can reveal signs of possible aggressive growth.

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Introduction

The Melanotic Neuroectodermal Tumor of Infancy (MNTI) is an asymptomatic, pigmented neoplasm characterized by a fast and locally aggressive growth, in addition to a rare tissue formation (1-6).

It predominantly affects individuals in the first year of life, with 90% of the cases of this pathology occurring in the head and neck region, most commonly in the maxillary bone (3, 5-8).

This tumor originates from the neural crest, due to a biphasic population of neuroectodermal melanocytic, primitive cells and an epithelioid cell component with an abundance of pigments (1, 3, 4, 6, 8, 9).

In the diagnostic process, the use of imaging exams can suggest a local destruction, suggestive of malignancy, that is,

Uvod

Melanotički neuroektodermalni tumor dojenačke dobi (MNTI) asimptomatska je pigmentirana novotvorina koju obilježava brz i lokalno agresivan rast, uz rahlu formaciju tkiva (1 – 6).

Pretežno pogađa jednogodišnju djecu te se u 90 % slučajeva ta patologija pojavljuje u području glave i vrata, najčešće maksile (3, 5 – 8).

Taj tumor potječe iz neuralnoga grebena zbog dvofazne populacije neuroektodermalnih melanocitnih primitivnih stanica i epiteloidne stanične komponente s obiljem pigmenta (1, 3, 4, 6, 8, 9).

U dijagnostičkom procesu primjena slikovnih prikaza može pokazati lokalnu destrukciju, što upućuje na zloćudnost, znakove remodeliranja i ekspanziju kosti [8]. No uz te

signs of bone remodeling and expansion [8]. However, along with these tests, a histopathological analysis is needed and essential. Additionally, immunohistochemistry is useful in the diagnosis of MNTI (1, 2, 8, 9).

Therefore, since any early diagnosis minimizes the risks and increases the treatment prognosis for the patient, the objective of this study was, from a clinical case report, to corroborate the use of histopathological analysis associated with immunohistochemistry. The aim was also to briefly address the MNTI characteristics of the present clinical report in association with other studies in the literature.

Case Report

An 8-month-old male child was taken to a dental office with an expansive lesion in the oral cavity (Figure 1). The patient's mother reported the appearance of this alteration in the 3rd month after birth and of rapid growth. The patient had no previous serious pathologies. On physical examination, an increase in volume in the anterior region of the maxilla was observed, being characterized as a fixed nodular lesion with similarly colored mucosa in the surrounding area. In addition, its growth did not cause rigidity. Also, there was no pulsation, and no production of liquids.

An excisional biopsy was indicated. Subsequently, the histological sections revealed a fragment of mucosa covered by parakeratinized stratified pavement epithelial tissue. In the lamina, there was a neoplasm organized in nests, tubules and alveolar structures intermingled with dense stroma. Neoplastic cells presented a biphasic pattern. In areas, some nests of small and round cells were noted, exhibiting sparse hyperchromatic cytoplasm, while in other areas, epithelioid and cuboid cells were noted, exhibiting cytoplasm and light nuclei and dark brown granules of melanin pigment (Figure 2).

On immunohistochemical examination, neoplastic cells were moderately positive for anti-CD99 antibody, stromal cells were diffusely positive for anti-Vimentin antibody. The proliferative index was evaluated using, for this purpose, the Ki-67 antibody, which was shown to be less than 5%. Neoplastic cells were negative for anti-S100 and BRAF-V600E antibodies (Figure 3). Having combined clinical, morphological and immunohistochemical characteristics, a final diagnosis of melanotic neuroectodermal tumor of infancy (MNTI) was established.

According to the literature, MNTI occurs more frequently in the gnathic bones, in younger patients, with a predilection for males and with some peculiar clinical features. Several studies in the literature have reported similar characteristics related to this neoplasm, as can be seen in Table 2:

Regarding the immunohistochemical peculiarities and the results of interactions with agents for the individual characterization of pathology, several studies in the literature have also reported the properties that are able to distinguish MNTI from other lesions, as can be seen in Table 3:

Discussion

As previously reported, MNTI, in several studies, shares similar characteristics, which were also present in this case re-

pretrage također je nužna patohistološka analiza. Ali i imunohistokemija je korisna u dijagnozi MNTI-ja (1, 2, 8, 9).

Budući da svaka rana dijagnoza smanjuje rizik i poboljšava prognozu liječenja, cilj ovog rada jest na temelju kliničkog prikaza slučaja potkrijepiti primjenu patohistološke analize povezane s imunohistokemijom, te ukratko istaknuti obilježja MNTI-ja u ovom kliničkom izvješću u vezi s ostalim studijama u literaturi.

Prikaz slučaja

Dječak od 8 mjeseci doveden je u stomatološku ordinaciju s ekspanzivnom lezijom u usnoj šupljini (slika 1.). Majka je prijavila tu promjenu u djetetovu 3. mjesecu i upozorila na njezin brzi rast. Prije toga kod pacijenta nije bila uočena neka značajna patologija. Fizikalnim pregledom uočeno je povećanje volumena u prednjem dijelu maksile, što se smatra fiksnom nodularnom lezijom sa slično obojenom sluznicom u okolnome području. Ali njezin rast nije prouzročio rigiditet, nije bilo pulsiranja i proizvodnje tekućine.

Indicirana je ekscizijska biopsija, pri čemu je histološkim rezovima otkriven ulomak sluznice prekriven parakeratiniziranim slojevitim epitelnim tkivom. U lamini se nalazila novotvorina organizirana u gnijezda, tubule i alveolarne strukture pomiješane s gustom stromom. Tumorske stanice imale su dvofazni uzorak. Na nekim područjima uočena su gnijezda malih i okruglih stanica s rijetkom hiperkromatskom citoplazmom, a u ostalima su zabilježene epiteloidne i kockaste stanice s citoplazmom i svijetlim jezgrama te tamnosmeđim granulama pigmenta melanina (slika 2.).

Na imunohistokemijskom pregledu tumorske stanice bile su umjereno pozitivne na anti-CD99 antitijela, a stromalne stanice bile su difuzno pozitivne na antivimentin antitijela. Indeks proliferacije procijenjen je korištenjem Ki-67 antitijela i pokazalo se da je manji od 5 %. Tumorske stanice bile su negativne na antitijela anti-S100 i BRAF-V600E (slika 3.). Kombinirajući klinička, morfološka i imunohistokemijska obilježja, konačna dijagnoza glasila je dječji melanotički neuroektodermalni tumor.

Prema literaturi, MNTI se češće pojavljuje s nekim osobujnim kliničkim značajkama u čeljusnim kostima mlađih pacijenata, uglavnom dječaka. U nekoliko istraživanja u literaturi autori izvješćuju o zajedničkim obilježjima te novotvorine (vidi tablicu 2.).

Kad je riječ o imunohistokemijskim obilježjima i rezultatima interakcija s agensima za individualnu karakterizaciju patologije, u nekoliko istraživanja u literaturi autori također izvješćuju o svojstvima koja mogu razlikovati MNTI od drugih lezija (vidi tablicu 3.).

Rasprava

Kao što je prije istaknuto u nekoliko istraživanja, MNTI ima zajednička obilježja, a u ovom slučaju spol pacijenta od-

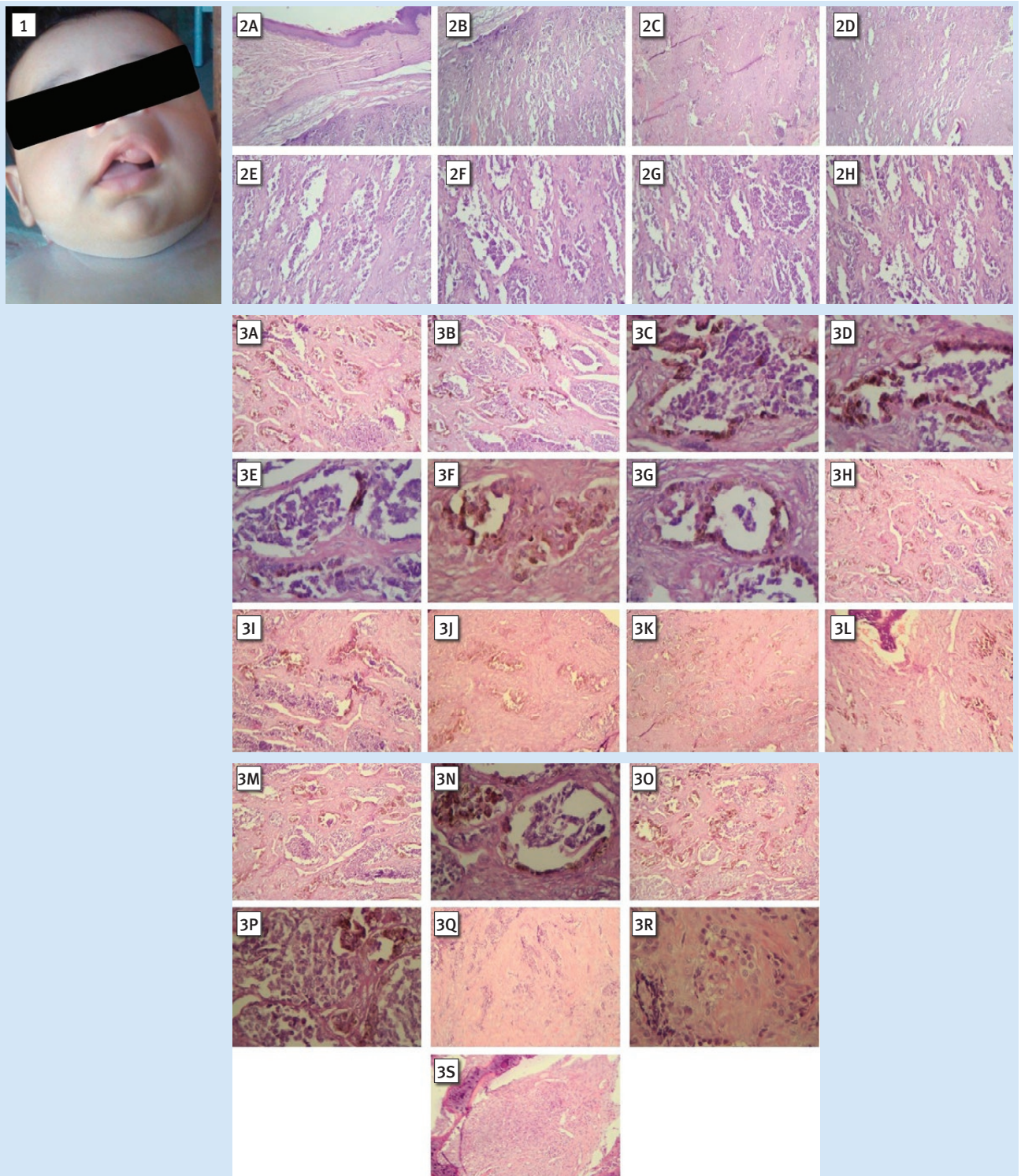


Figure 1 Photo showing a lesion in the oral cavity. Source: personal archive.

Slika 1. Lezija u usnoj šupljini (izvor – osobni arhiv)

Figure 2 Histological sections in hematoxylin and eosin showing a neuroectodermal lesion.

Slika 2. Histološki rezovi u hematoksilinu i eozinu koji pokazuju neuroektodermalnu leziju

Figure 3 Anti-CD99 immunohistochemical test with moderately positive labeling (A – G), diffusely positive for anti-Vimentin (H – M), proliferative index less than 5% with Ki-67 (N – P) and negative cell labeling for anti-S100 and BRAF-V600E (Q – S).

Slika 3. Anti-CD99 imunohistokemijski test s umjereno pozitivnim označavanjem (A – G), difuzno pozitivnim na antivimentin (H – M), proliferativnim indeksom manjim od 5% s Ki-67 (N – P) i negativnim označavanjem stanica za anti-S100 i BRAF-V600E (Q – S)

Table 1 Immunohistochemical Result
Tablica 1. Imunohistokemijski rezultati

Antibodies • Antitijela	Result • Rezultati
Anti-CD99	+
Anti-Vimentin • Antivimentin	++
Anti-S100	-
BRAF-V600E	-

Source: Done by the author. • Izvor – autori

port. Furthermore, the patient's sex fits the predilection for a gender reported in the literature, with involvement in the first year of life. Also, regarding the characteristics of the lesion in the present study, these were similar to the literary findings, such as rapid and expansive growth with regional anatomical deformation; rigid and fixed lesion; in addition to the predilection for the maxillary bone (Table 2). However, it was observed that there was no pigmentation of the adjacent tissues surrounding the tumor lesion.

The diagnosis of MNTI can be performed mainly by radiological characteristics in association with histopathological examinations (4, 5). However, immunohistochemical analyses and molecular studies are useful and can contribute to the diagnosis of this neoplasm, especially in difficult cases and particularly in small biopsies with the possibility of differentiating this pathological change from other tumors present in childhood (6-9, 16).

Thus, some immunohistochemical characteristics have been described by several researchers by exposing pathological MNTI tissue to some reagents, such as cytokeratin, HMB45, S100, Ki-67 and others (Table 3) (12-14).

Positive anti-CD99 and anti-vimentin antibodies were observed in the present study and are reported in the literature as immunohistochemical characteristics of MNTI, in addition to anti-S100 antibody negativity (7-9, 12, 14, 17, 18) (Table 1 and 3). Besides, the prophylactic index with the use of the ki-67 antibody observed was similar to the study by Cui, Mao and Liao (14), with the value lower than 5%, but different from the study by Moreu et al. (3), with a mean value of 18%, in a survey of 11 patients (0 to 30%).

According to Souza et al. (12), positivity for the Ki-69 and anti-CD99 antibody, which was also observed in the present clinical case, may suggest an aggressive tumor growth, thus, giving a possible plausible explanation for the rapid growth of the tumor, usually in about 3 months.

Although histological evaluation is important for the final diagnosis of a pathological lesion, in cases of MNTI it is a poor indicator of clinical behavior (11). However, immunohistochemical analysis provides some information about the aggressiveness of these tumors (17).

Thus, with the rapid growth of MNTI, its malignant potential, in addition to recurrence rates, an early diagnosis is essential (12). Therefore, immunohistochemical analyses have become important because they can help confirm a melanotic neuroectodermal tumor of infancy diagnosis (12, 19, 20).

govara jednoj od sklonosti navedenoj u literaturi, s uključenošću u dobi od godinu dana. Kad je riječ o obilježjima lezije, u ovom istraživanju bile su slične nalazima u literaturi, što obuhvaća brz i ekspanzivan rast s regionalnom anatomskom deformacijom, rigidnu i fiksnu leziju i sklonost prema maksilarnoj kosti (tablica 2.). No uočeno je da nije bilo pigmentirano susjedno tkivo koje okružuje tumorsku leziju.

Dijagnoza MNTI-ja može se postaviti uglavnom na temelju radioloških snimki u kombinaciji s patohistološkim pretragama (4, 5). Ali korisne su i imunohistokemijska analiza te molekularne pretrage jer mogu pridonijeti dijagnostici te novotvorine, posebno u teškim slučajevima, a osobito u malim biopsijama s mogućnošću razlikovanja te patološke promjene od drugih tumora koji se pojavljuju u djetinjstvu (6 – 9, 16).

Zato je nekoliko istraživača opisalo neka imunohistokemijska obilježja izlažući patološko tkivo MNTI-ja reagensima, kao što su citokeratin, HMB45, S100, Ki-67 i drugi (tablica 3.) (12 – 14).

Positivni nalazi antitijela na CD99 i vimentin uočeni su u ovom istraživanju i navedeni su u literaturi kao imunohistokemijska obilježja MNTI-ja, uz negativnost na antitijela S100 (7 – 9, 12, 14, 17, 18) (tablice 1. i 3.). Profilaktični indeks primjenom antitijela Ki-67 bio je sličan istraživanju Cuija, Maoa i Liaoa (14), s vrijednošću nižom od 5 %, ali različit od istraživanja Moreua i suradnika (3) s prosjekom od 18 % u anketi u kojoj je sudjelovalo 11 pacijenata (0 – 30 %).

Prema Souzi i suradnicima (12), pozitivnost na Ki-69 i antitijela CD99, također uočena u ovom kliničkom slučaju, može upućivati na agresivan rast tumora. To može biti uvjerljivo objašnjenje za brzi rast tumora, obično oko tri mjeseca.

Iako je histološka procjena važna za konačnu dijagnozu patološke lezije, u slučajevima MNTI-ja ona je loš pokazatelj kliničkoga ponašanja (11). No imunohistokemijska analiza daje neke informacije o agresivnosti tih tumora (17).

Zato je, uz brzi rast MNTI-ja, njegov zloćudni potencijal, uz stopu recidiva, ključna rana dijagnoza (12). Stoga je imunohistokemijska analiza postala važna jer pomaže i potvrđuje dijagnozu (12, 19, 20).

Table 2 Epidemiological data and clinical characteristics**Tablica 2.** Epidemiološki podatci i klinička obilježja

Author • Autor	Case Report • Prikaz slučaja	Epidemiology • Epidemiologija	Clinical Characteristics • Klinička obilježja
Wu et al. (10)	Case report of a 3-month-old newborn with remarkable tumor growth in 4 days without previous trauma. • Prikaz slučaja tromjesečnoga novorođenčeta sa značajnim rastom tumora u 4 dana bez prethodne traume.	70% of cases are located in the maxilla, followed by the cranial, mandibular and cerebral regions. • 70 % slučajeva nalazi se u maksili, zatim u kranijalnoj, mandibularnoj i cerebralnoj regiji.	Fast growing, pigmented, firm, sessile tumor with malignant potential. • Brzo rastući, pigmentirani, solidni, sesilni tumor sa zloćudnim potencijalom.
Moreu et al. (3)	Clinical research with 11 patients aged (months) ranging from 0 to 5 months and mean age of 3.18 months. • Kliničko istraživanje sa sudjelovanjem 11 pacijenata od 0 do 5 mjeseci i prosječne dobi od 3,18 mjeseci.	Prediction for the head and neck area, especially in the jaw bone. • Područje glave i vrata, posebno čeljust.	Painless, sessile, pigmented (black or blue) and non-ulcerated lesion. • Bezbolna, sesilna, pigmentirana (crna ili plava) i neulcerirajuća lezija.
Unsal; Yançin (9)	A 6-month-old male child with increased mandibular volume. • Dječak od 6 mjeseci s povećanim volumenom mandibule.	It affects more the head and neck region. And it predominantly affects the maxilla (70 to 80%), skull (10%), mandible (6%) and brain (4%). In addition to the predominance in babies. • Više utječe na regiju glave i vrata te pretežno zahvaća maksilu (70 do 80 %), lubanju (10 %), mandibulu (6 %) i mozak (4 %). Prevladava kod novorođenčadi.	It presents as a rapidly growing, locally destructive, painless, immobile, black, brown, or blue pigmented swelling. • Prikazuje se kao brzo rastuća, lokalno destruktivna, bezbolna, nepokretna, crna, smeđa ili plavo pigmentirana oteklina.
Pontes et al. (5)	Literature review. • Pregled literature.	Greater predominance in gnathic bones and slightly affect males (1.32: 1). • Prevladava u čeljusnim kostima s većom pojavnosću kod muškaraca (1,32 : 1).	More satisfactory prognosis in younger patients, due to the size of the pathology and less chance of metastasis. • Zadovoljavajuća prognoza za mlađe pacijente zbog veličine patološkog procesa i manje vjerojatnosti metastaziranja.
Santos et al. (2)	Anterior maxillary growth in a 6-month-old girl • Prednji maksilarni rast kod šestomjesečne djevojčice.	Prevalence in gnathic bones (maxilla) in males and occurs in the first year of life, especially in the first months. • Prevalencija u čeljusnim kostima (maksili) kod dječaka, pojavljuje se u prvoj godini života, osobito u prvim mjesecima.	Rapid growth, invasive and causing deformities. Possibly malignant transformation and bone metastasis. • Brzi rast uzrokuje invazivne deformitete. Moguća zloćudna transformacija i metastaze u kosti.
Soles et al. (8)	Literature review. • Pregled literature.	Greater predominance in craniofacial bones (maxillary) and male predilection. • Veća sklonost u maksili i sklonost kod muških.	Firm, lobulated change, well-defined mass, bluish-black hue. In addition to showing rapid growth and local infiltration into adjacent tissues. • Firm, lobulated change, well-defined mass, bluish-black hue. In addition to showing rapid growth and local infiltration into adjacent tissues.
Ren et al. (4)	Literature review. • Pregled literature.	Higher prevalence in cranial bones, observed in men and women, in addition to being diagnosed in the first years of life. • Veća prevalencija u kostima lubanje uočena kod muškaraca i žena, obično se dijagnosticira u prvim godinama života.	Progressive, asymptomatic growth and firm edema, with an intact epithelial surface. • Progresivan, asimptomatski rast i čvrsti edem s intaktnom površinom epitela.
Tiwari; Yadav (6)	3-month-old girl with intraoral swelling and progressive growth and firm consistency. • Tromjesečna djevojčica s intraoralnom oteklinom, progresivnim rastom i čvrstom konzistencijom.	More commonly in the craniofacial region, mainly the maxillary bone, followed by the skull, mandible and predilection in children under 1 year of age. • Češće u kraniofacijalnoj regiji, uglavnom u maksilarnoj kosti, zatim u lubanji i mandibuli, predilekcija kod djece mlađe od godinu dana.	Pigmented and benign neoplasm, with high potential for rapid growth and locally destructive. • Pigmentirana i benigna novotvorina s visokim potencijalom za brzi rast i lokalno destruktivna.
Ebel et al. (1)	Case report of a 4-month-old boy with MNTI in the skull and 2-week rapid growth • Prikaz slučaja četveromjesečnog novorođenčeta s MNTI-jem u lubanji i brzim rastom u dva tjedna	Greater involvement in the maxillary region, followed by the cranial region. • Veća zahvaćenost maksilarne regije, a zatim i kranijalne.	Rapid development, without symptoms, pigmentary and invasive edema. • Brz razvoj, bez simptoma, pigmentiran i invazivan edem.
Mengide et al. (11)	Extra-axial growth in the skull of an 8-year-old boy complaining of headache for about 3 months. • Ekstraaksijalni rast u lubanji 8-godišnjega dječaka koji se oko tri mjeseca žalio na glavobolju.	The most common location of the tumor is the craniofacial region, although other regions are described. Mainly in patients under 1 year of age. • Najčešća lokacija tumora je kraniofacijalna regija, iako su opisana i druga područja. Uglavnom nastaje kod mladih od 1 godine.	Solid and painless lesion, in addition to being pigmented and is a neoplasm causing deformity in regions of appearance. • Čvrsta i bezbolna lezija, osim što je pigmentirana – novotvorina koja uzrokuje deformitet u regijama u kojima se pojavljuje.

The table summarizes some clinical cases with the epidemiological and clinical characteristics of MNTI reported by the corresponding authors. • U tablici su sažeti neki klinički slučajevi s epidemiološkim i kliničkim obilježjima MNTI-ja koje su prijavili odgovarajući autori.

Source: Done by the authors • Izvor – autori

Table 3 Immunohistochemical characteristics described in the literature.**Tablica 3.** Imunohistokemijska obilježja opisana u literaturi

Author • Autor	Anatomopathology / Immunohistochemistry Characteristics • Anatomopatologija/imunohistokemijska obilježja
Souza et al. (12)	The immunohistochemical profile of MNTI is generally positive for cytokeratin and HMB45 and negative for S100. And Ki-67 and CD99 expressions are quite uncommon and may be related to more aggressive tumor growth. • Imunohistokemijski profil MNTI-ja općenito je pozitivan na citokeratin i HMB45, a negativan na S100. Ekspresija Ki-67 i CD99 dosta je rijetka i može biti povezana s agresivnijim rastom tumora.
Albuquerque et al. (13)	Small cells of neural origin are confirmed by positivity for NSE, synaptophysin and chromogranin. And cells of ectodermal origin can be confirmed by the positivity of EMA, CK, HMB-45. • Za male stanice neuralnoga podrijetla potvrđeno je da su pozitivne na NSE, sinaptofizin i kromogranin. A stanice ektodermalnog podrijetla mogu se potvrditi kao pozitivne na EMA, CK, HMB-45.
Cui; Mao; Liao (14)	Smaller round cells were melanoma-associated antigen 45 (HMB45) / vimentin / epithelial membrane antigen (+), no significant glial fibrillary acid protein staining (GFAP) / neuron-specific enolase (NSE) / synaptophysin (+), and the largest cells were cytokeratin (CK) / S-100. Scattered cells exhibited desmin immunoreactivity and ~2% of cells were Ki-67 (+). • Manje okrugle stanice bile su antigen 45 povezan s melanomom (HMB45)/vimentin/antigen epitelne membrane (+), bez značajnoga bojenja proteina glijalne fibrilarne kiseline (GFAP)/ neuron-specifična enolaza (NSE)/sinaptofizin (+), a najveće stanice bili su citokeratin (CK)/S-100. Raspršene stanice pokazale su desmin-immunoreaktivnost i ~2 % stanica je Ki-67 (+).
Batta et al. (7)	Larger epithelioid cells stain positively with cytokeratin, vimentin and HMB-45, reflecting epithelial and melanocytic differentiation, in addition to generally not reacting with S-100 protein, helping to differentiate tumors such as melanoma. Smaller cell nests in MNTI are often positive for neurogenic markers such as synaptophysin, neuron-specific, enolase, and glial fibrillary acidic protein. • Veće epitelioidne stanice pozitivno se boje citokeratinom, vimentinom i HMB-45, odražavajući diferencijaciju epitela i melanocita, osim što općenito ne reagiraju s proteinom S-100, pomažući u razlikovanju tumora kao što je melanom. Manja stanična gnijezda u MNTI-ju često su pozitivna na neurogene biljege kao što su sinaptofizin, neuron-specifična enolaza i glijalni fibrilarni kiseli protein.
Strieder et al. (15)	Larger cells express cytokeratins (CKs), epithelial membrane antigen (EMA), glial fibrillary acidic protein (GFAP), S100 and HMB45 protein, and smaller cells express CD56 and synaptophysin; both cells express neuron-specific enolase (NSE), PGP 9.5 and chromogranin A. • Veće stanice ekspimiraju citokeratine (CKs), antigen epitelne membrane (EMA), glijalni fibrilarni kiseli protein (GFAP), proteine S100 i HMB45, a one manje CD56 i sinaptofizin; obje stanice ekspimiraju neuron-specifičnu enolazu (NSE), PGP 9.5 i kromogranin A.
Wu et al. (10)	The epithelioid component of large cells shows a small to moderate amount of eosinophilic cytoplasm and is positive with pancytokeratin and HMB45 immunostaining. The small blue primitive cell component does not show appreciable cytoplasm and is positive for synaptophysin. • Epitelioidna komponenta velikih stanica pokazuje malu do umjerenu količinu eozinofilne citoplazme i pozitivna je na pancitokeratin i HMB45. Komponenta male plave primitivne stanice ne pokazuje značajnu citoplazmu i pozitivna je na sinaptofizin.
Moreau et al. (3)	In HE staining, a fibrocollagenous stroma surrounding an epithelioid and neuroblastic component organized in lobules or alveolar structures. And the neuroblastic component was discrete and masked by a large melanin-rich epithelioid component. Epithelioid cells expressed epithelial and melanocytic markers (AE1/AE3; and melan A, PS 100 and HMB 45, respectively). • U HE bojenju fibrokolagena stroma okružuje epitelioidnu i neuroblastičnu komponentu organiziranu u lobule ili alveolarne strukture. Neuroblastična komponenta bila je diskretna i maskirana velikom epitelioidnom komponentom bogatom melaninom. Epitelioidne stanice ekspimiraju epitelne i melanocitne biljege (AE1/AE3; melan A, PS 100 i HMB 45).
Nicosia et al. (16)	They are usually positive for cytokeratin, vimentin, epithelial membrane antigen, HMB-45, glial fibrillary acidic protein, and specific neuronal enolase. • Obično su pozitivni na citokeratin, vimentin, antigen epitelne membrane, HMB-45, glijalni fibrilarni kiseli protein i specifičnu neuronsku enolazu.
Unsal; Yalçın (9)	The largest fraction of epithelioid cells expressed a number of cytokeratins - in most patients HMB-45, but rarely S-100.8 protein. Neuroblast-like cells are positive for neuron-specific enolase, CD 56, glial fibrillary acidic protein and synaptophysin, and melanogenic cells are positive for HMB-45, epithelial antigen membrane antigen, cytokeratin and vimentin. • Najveća frakcija epitelioidnih stanica ekspimirala je niz citokeratina - kod većine pacijenata HMB-45, ali rijetko protein S-100.8. Stanice slične neuroblastima pozitivne su na neuron-specifičnu enolazu, CD 56, glijalni fibrilarni kiseli protein i sinaptofizin, a melanogene stanice pozitivne su na HMB-45, antigen membrane epitelnoga antigena, citokeratin i vimentin.
Emmerling; York; Caccanese (17)	There is identification of immunohistochemical markers, such as cell population frequently expressing cytokeratins, HMB-45 and vimentin, while S100 is much less common. And the small cell population usually expresses synaptophysin but is negative for another neuroendocrine marker, chromogranin A. • Postoji identifikacija imunohistokemijskih biljega kao što je stanična populacija s čestom ekspresijom citokeratina, HMB-45 i vimentin, a S100 mnogo je rjeđi. Populacija malih stanica obično ekspimiraju sinaptofizin, ali je negativna na drugi neuroendokrini biljeg - kromogranin A.
Santos et al. (2)	Other markers, such as HMB45, Melan A, cytokeratin, and neuroblastic markers, such as synaptophysin and neuron-specific enolase, can help in diagnosis. • Drugi biljezi poput HMB45, melana A, citokeratina i neuroblastičnih biljega kao što su sinaptofizin i enolaza specifična za neurone, mogu pomoći u dijagnozi.
Soles et al. (8)	The cells present are positive for vimentin and neuron-specific enolase and negative for S100. Larger melanogenic epithelioid cells are commonly positive for cytokeratins and some differentiating markers of melanocytes (HMB-45, dopamine b-hydroxylase, etc.). Smaller neurogenic cells are positive for synaptophysin and negative for cytokeratin, in addition to being positive for glial fibrillary acidic protein (GFAP), but rarely for neurofilament and CD99. • Prisutne su stanice pozitivne na vimentin i neuron-specifičnu enolazu, a negativne na S100. Veće melanogene epitelioidne stanice obično su pozitivne na citokeratine i neke diferencirajuće biljege melanocita (HMB-45, dopamin b-hidroksilaza, itd.). Manje neurogene stanice pozitivne su na sinaptofizin i negativne na citokeratin, osim što su pozitivne na glijalni fibrilarni kiseli protein (GFAP), ali rijetko na neurofilament i CD99.
Atarbashi-Moghadam Et Al. (18)	Epithelioid cells are positive for cytokeratin, HMB-45 and NSE. Smaller cells are generally positive for NSE and CD56 and sometimes synaptophysin. Furthermore, MNTI are not expressed in the S-100 protein. Larger epithelioid cells express MDM-2, cyclin D1 and A. • Epitelioidne stanice pozitivne su na citokeratin, HMB-45 i NSE. Manje stanice općenito su pozitivne na NSE i CD56, a katkad i na sinaptofizin. Nadalje, nisu izraženi proteini S-100. Veće epitelioidne stanice ekspimiraju MDM-2, ciklin D1 i A.
Ebel et al. (1)	Immunohistochemically positive staining for markers such as HMB-45, synaptophysin and cytokeratin strengthens the diagnosis. A marker to differentiate between benign and malignant tumors does not exist so far. • Imunohistokemijski pozitivno bojenje na biljege kao što su HMB-45, sinaptofizin i citokeratin jača dijagnozu. Biljeg za razlikovanje benignih i malignih tumora zasad ne postoji.

The table summarizes some histopathological and immunohistochemical characteristics of MNTI based on studies in the literature. • Tablica sažima neka patohistološka i imunohistokemijska obilježja MNTI-ja na temelju istraživanja u literaturi.

Source: Done by the authors. • Izvor – autori

Conclusion

In conclusion, the immunohistochemical exam is of great importance for a better complementation of the MNTI diagnosis process. In addition, it can help detect any serious signs and symptoms of potentially aggressive growth.

Authors' contribution: A.S. B. P. and V.A.M.M. – the idealization of the study was carried out; A.L.A.S., W.C.A.A., J.P.M., A.S.B.P. - The writing and planning of the pre-project were produced. Finally, the assistance, production and revision of the manuscript were realized by all authors.

Zaključak

Zaključujemo da je imunohistokemijski pregled veoma važan za bolju nadopunu dijagnostičkoga postupka MNTI-ja jer dodatno upozorava na znakove mogućega agresivnoga rasta.

Doprinos autora: S. B. P. i V. A. M. M. – idealizacija studije/ predložili temu za studiju; A. L. A. S., W. C. A. A., J. P. M., A. S. B. P. – planirali i pisali predprojekt. Svi su autori pisali i revidirali tekst.

Sažetak

Melanotički neuroektodermalni tumor dojenačke dobi (MNTI) asimptomatska je pigmentirana novotvorina koja brzo i lokalno agresivno raste, uz rahlu formaciju tkiva. U dijagnostičkom procesu primjena slikovnih prikaza može pokazati lokalnu destrukciju, što upućuje na zloćudnost, znakove remodeliranja i ekspanziju kosti. Zato, kako svaka rana dijagnoza smanjuje rizike i poboljšava prognozu liječenja, cilj ovoga rada je na temelju kliničkoga prikaza slučaja potkrijepiti primjenu patohistološke analize povezane s imunohistokemijom. Stoga zaključujemo da je imunohistokemijski pregled veoma važan za nadopunu dijagnostičkog procesa u slučaju MNTI-ja. Dodatno upozorava na znakove mogućega agresivnoga rasta.

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