42_Concorso Pubblico, per titoli ed esami, per la copertura a tempo determinato, della durata di cinque anni per n. 1 posto di RICERCATORE SANITARIO da assegnare alla SC NEUROLOGIA 5 - NEUROPATOLOGIA

PROVA 1

1. Tecniche di allestimento per microscopia elettronica

2. Con il termine "Firewall" si intende un software cha ha funzione di:
   a) proteggere i computer di una rete da accessi non autorizzati
   b) verificare la presenza di virus all'interno del computer
   c) consentire l'identificazione degli utenti all'avvio del computer

3. Leggere e tradurre il seguente testo

A Case of a Fumarate Hydratase Deficient Astrocytoma in Association With a Germline Fumarate Hydratase Mutation With Review of the Literature Considerations for Patients With Hereditary Leiomyomatosis and Renal Cell Cancer (HLRCC) Syndrome

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Abstract: Diffuse adult-type gliomas are delineated based on their molecular composition including the presence or absence of mutations in isocitrate dehydrogenase 1 or 2 (IDH1/2), a key enzyme in the citric acid cycle. IDH-mutant tumors are associated with better survival than IDH-wildtype counterparts and can be further subdivided into astrocytoma or oligodendroglioma. Rare gliomas with fumarate hydratase (FH) deficiency have been reported. Given that FH is also a critical enzyme in the citric acid cycle, such tumors seem to be epigenetically similar to IDH-mutant tumors and, despite meeting criteria as IDH-wildtype gliomas per the current recommendations set forth by the World Health Organization, may behave in a manner akin to IDH-mutant neoplasms. Hereditary leiomyoma and renal cell cancer syndrome is associated with cutaneous and uterine leiomyomas and renal cell carcinoma caused by a germline FH alteration. To date, only rare examples of patients with known germline FH mutation subsequently diagnosed with a glioma have been reported. We report a case of a young patient with a glioma harboring features of IDH-mutant astrocytoma without evidence of IDH1/2 alterations. After the identification of cutaneous FH-deficient leiomyomas, a retrospective analysis of his brain tumor revealed FH deficiency and a germline FH alteration was ultimately identified after further molecular studies. Although rare, we conclude that FH mutations seem to be part of the spectrum of alterations in diffuse gliomas.

Key Words: fumarate hydratase, glioma, isocitrate dehydrogenase, citric acid cycle, hereditary leiomyoma and renal cell cancer
(Am J Surg Pathol 2025;00:000–000)

The 2021 World Health Organization (WHO) Central Nervous System (CNS) Tumor Classification System stratifies adult-type diffuse gliomas into isocitrate dehydrogenase (IDH) wildtype and mutant varieties with IDH-mutant tumors demonstrating better overall survival.1 The category of IDH-mutant gliomas further diverges into astrocytomas and oligodendrogliomas, with the canonical IDH1 p.R132H mutation being the most commonly identified.1 IDH-mutant astrocytomas also characteristically harbor mutations in ATRX and TP53 without evidence of 1p/19q co-deletion, in contrast to oligodendrogliomas where this latter molecular finding is necessary for diagnosis.

ELISA MORESCO 02/03/1998 

PROVA ESTRATTA

18/12/2025

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PROVA 2

1. Utilità, principi e applicazioni delle colorazioni immunoistochimiche nella diagnostica istopatologica

2. In Excel cosa è una "funzione"?
   a) un algoritmo di calcolo precostituito che ci permette di elaborare un calcolo complesso sui dati contenuti nelle celle
   b) un comando che ci permette di stampare
   c) un comando che ci permette di creare un grafico

3. Leggere e tradurre il seguente testo

Meningioma classification by immunohistochemistry: A replicability study

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ARTICLEINFO Handling Editor: Dr W Peul
Keywords: Meningioma Molecular marker Recurrence Immunohistochemistry

ABSTRACT
Introduction: Meningiomas account for nearly 40% of intracranial tumors. Recently, the immunohistochemistry (IHC) markers S100B, SCGN, ACADL and MCM2 have been shown to be associated with underlying biological subtypes of meningioma (MG1-MG4). We aimed to evaluate these IHC markers in a clinical setting. Research question: Are the new proposed IHC markers clinically useful? Methods: In total, 244 patients with meningiomas with tissue in TMAs were included and the IHC markers S100B, SCGN, ACADL and MCM2 were analyzed. Two sets of analyses were performed; the first included all samples with any staining considered positive, the second only samples with >10% immunopositivity. PFS and OS were analyzed in correlation to immunopositivity in the second analysis set. Results: In the first set of analyses only 26.2% of samples could be to allocate to one group. No further analyses were performed with this selection. In the second set of analyses 52.0% could be allocated to a group. There was an enrichment of WHO grade 2 and 3 tumors in MG3 and MG4 as compared to MG1 (24.1% and 25.7% vs. 12.1%). Both the molecular group (p ¼ 0.032) and WHO grade (p ¼ 0.005) had significant impact on PFS, but only WHO grade predicted OS (p ¼ 0.033).
Conclusion: We studied the proposed new method of classifying meningiomas into groups MG1, MG2, MG3 and MG4 using IHC markers, but found difficulties applying the classification system in our material mainly due to lack of exclusivity of markers. Thus, in its present form the classification method lacks clinical applicability.

1. Introduction

Meningiomas make up as many as 40% of primary intracranial tumors in the adult population. Meningiomas are classified as grade 1–3 according to the World Health Organization (WHO) Classification of Tumors in the Central Nervous System (CNS) (Louis et al., 2021). The WHO classification from 2016 was the first to include molecular markers for diagnosis of intracranial tumors, such as gliomas (Louis et al., 2016). In 2021, the WHO classification was again revised with major changes, and new tumor types were introduced that exemplify the role of molecular diagnostics in CNS tumor classification (Louis et al., 2021). However, meningiomas are still considered a single tumor type with 15 subtypes based on morphological criteria. Several molecular biomarkers, among others SMARCE1, BAP1, KLF4/TRAF7, have been associated with specific subtypes of meningioma, whilst TERT promotor mutation, homozygous deletion of CDKN2A/B, and H3K27me3 loss of nuclear expression are considered associated with grading of these tumors (Louis et al.,2021).

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PROVA NON ESTRATTA

18/12/2025

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PROVA 3

1. Utilità, principi e applicazioni dell'immunofluorescenza nella diagnostica istopatologica

2. Per SPAM si intende:
   a) l'invio non richiesto di messaggi di posta elettronica con fini commerciali o offensivi
   b) un programma che permette di scrivere messaggi di posta elettronica
   c) una truffa bancaria on line

3. Leggere e tradurre il seguente testo

Immunohistochemical Approach to the Differential Diagnosis of Meningiomas and Their Mimics

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Abstract
The differential diagnosis between meningioma and others tumors can be challenging. This study aimed to evaluate different immunohistochemical markers for the differential diagnosis between meningioma and their morphological mimics. Immunohistochemistry was performed on tissue microarray with antiepithelial membrane antigen (EMA), progesterone receptor, somatostatin receptor 2A (SSTR2A), CD34, STAT6, S100, SOX10, HMB45, MelanA, GFAP, inhibin, and BCL2 antibodies. One hundred and twenty-seven meningiomas, 26 solitary fibrous tumor/hemangiopericytomas (SFT/HPC), 39 schwannomas, 17 hemangioblastomas, 21 melanomas, 9 gliosarcomas, 5 neurofibromas, 9 peripheral primitive neuroectodermal tumors, 7 synovial sarcomas, and 5 malignant peripheral nerve sheath tumors were included in the microarray. SSTR2A was the most sensitive (95.2%) and specific (92%) marker of meningiomas. In combination, SSTR2A and/or EMA positivity reached maximal sensitivity (100%). Coexpression of SSTR2A and EMA was the most specific (94.8%) for the diagnosis of meningioma, regardless of the grade or subtype, with the exception of the differential diagnosis with synovial sarcoma. All synovial sarcomas were EMApositive and 6/7 SSTR2A-positive. STAT6 showed optimum sensitivity and specificity (100%) for SFT/HPC. SOX10 was the most sensitive (94.3%) and specific (100%) marker to discriminate meningiomas from schwannomas. In conclusion, SSTR2A, STAT6, and SOX10 were the most sensitive and specific markers to distinguish meningiomas from their morphological mimics.

Key Words: Epithelial membrane antigen, Immunohistochemistry, Meningioma, Schwannoma, Solitary fibrous tumor, SOX10, SSTR2A, STAT6.

INTRODUCTION
Meningiomas are common neoplasms that originate from archnoidal cells and most often attach to the inner surface of the dura mater. They account for 13%–30% of primary intracranial tumors and 25% of intraspinal tumors; they occur in adults with a median age of 65 years and are predominantly observed in females. The vast majority of meningiomas arise in intracranial, intraspinal, or orbital locations. Intraventricular and epidural meningiomas are uncommon (1, 2). Rare primary extradural meningiomas have been reported outside the neural axis (2, 3). According to the World Health Organization (WHO) criteria, meningiomas are classified into 3 grades (2). Grade I meningiomas are the most frequent and are considered as benign with a low risk of recurrence. Grade II meningiomas are less common and have a higher rate of recurrence, and grade III tumors are rare, and are associated with poor overall survival rates. Meningiomas exhibit a wide range of histological appearances. Among the different WHO subtypes, the most commonly encountered are the meningothelial, fibrous, and transitional meningiomas (2). While the majority of cases are diagnosed on routine hematoxylin and eosin-stained sections, certain cases can show overlapping morphology with other less common intracranial, intraspinal, or orbital neoplasmsthat require different treatments. The most common differential diagnoses are schwannomas and other rare meningeal tumors, such as solitary fibrous tumor/hemangiopericytoma (SFT/HPC), predominantly with the fibrous variant of meningioma. Microcystic or clear cell variants of meningioma can overlap morphologically with hemangioblastomas. Anaplastic meningioma can be difficult to differentiate from sarcoma, melanoma, or carcinoma.

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PROVA NON ESTRATTA

18/12/2025