Seminario de Patología Quirúrgica
Dr. César Morán Moran

Caso 1 (1s7213B)

Hombre de 43 años presento con dificultad para respirar y dolor toracico. Al examen radiologico se le encontro una masa en el lobulo superior del pulmon derecho.

Diagnosis:

PRIMARY MONOPHASIC SYNOVIAL SARCOMA

This tumor represents a relatively new entity within the spectrum of pulmonary mesenchymal tumors. In 1995 we described our experience with 25 cases of pulmonary neoplasms showing the features of monophasic synovial sarcoma without previous history of neoplasia elsewhere (1). This tumor essentially represents the counterpart of monophasic synovial sarcoma of soft tissue and its histopathological features when arising in the lung are similar to those described in other locations. Therefore, it is necessary to exclude the possibility of a metastatic tumor by clinical means prior to establishing a diagnosis of primary synovial sarcoma of thelung.

In our study there were 14 women and 11 men between the ages of 16 and 77 years (mean age: 38.5 years). Clinically, the most common symptoms were hemoptysis, cough, shortness of breath, and chest pain. However, a few patients were completely asymptomatic and their tumor was discovered on chest X-rays during a routine examination. The tumors ranged in size from 0.6 to 20 cm in diameter. Areas of necrosis and/or hemorrhage as well as cystic changes were observed. The histologic features of the tumors recapitulated those seen in monophasic synovial sarcomas of soft tissues, namely the presence of a proliferation of oval to spindle cells with pointed nuclei and scant, inconspicuous cytoplasm. Areas showing epithelioid, hemangiopericytic, myxoid, and neural-like growth patterns were all present in our lesions. Immunohistochemically, all the tumors showed positive reaction with epithelial markers, namely low-molecular weight keratins (23/25 cases) and EMA (25/25 cases). Ultrastructurally, these tumors displayed desmosome-type cell junctions, strands of rough endoplasmic reticulum, occasional dilated mitochondria, and scattered ribosomes.

The differential diagnosis of primary monophasic synovial sarcoma of the lung essentially involves other mesenchymal tumors which, although unusual, may also present as primary pulmonary neoplasms, as well as spindle cell carcinomas. The most important differential diagnosis therefore includes leiomyosarcoma, rhabdomyosarcoma, fibrosarcoma, neurogenic sarcoma, and pleomorphic (spindle cell) carcinoma of the lung.

REFERENCES

1. Zeren H, Moran CA, Suster S, Fishback NF, Koss MN: Primary pulmonary sarcomas with features of monophasic synovial sarcoma: a clinicopathological, immunohistochemical and ultrastructural study of 25 cases. Hum Pathol 1995; 26:474-480.

2. Ramanathan T: Primary leiomyosarcoma of the lung. Thorax 1974; 29:482-489.
3. Wick MR, Scheithauer BW, Piehler JM, et al: Primary leiomyosarcoma: a light and electron microscopic study. Arch Pathol Lab Med 1974; 106:510-514.
4. Moran CA, Suster S, Abbondanzo SL, Koss MN: Primary leiomyosarcomas of the lung: a clinicopathologic and immunohistochemical study of 18 cases. Mod Pathol
5. Przygodski RM, Moran CA, Suster S, Koss MN: Primary pulmonary rhabdomyosarcomas. Mod Pathol 1995; 8:658-661.
6. Eriksson A, Thunnel M, Lundquist G: Pedunculated endobronchial rhabdomyosarcoma with fatal asphyxia. Thorax 1982; 37:390-391.
7. Moran CA, Suster S, Koss MN: Primary malignant "triton" tumour of the lung. Histopathology
8. Suster S: Primary sarcomas of the lung. Semin Diag Pathol 1995; 12:140-157.
9. Otis C, Carter DL:
10. Roviaro G, Montorsi M, Varoli F, et al: Primary pulmonary tumors of neurogenic origin. Thorax 1983; 38:942-945.
11. Unger PD, Geller SA, Anderson PJ: Pulmonary lesions in patients with neurofibromatosis. Arch Pathol Lab Med 1984; 108:654-657.
12. Fishback NF, Travis WD, Moran CA, et al: Pleomorphic carcinoma (spindle/giant cell) carcinoma of the lung. Cancer 1994; 73:2936-2945.
13. Suster S, Huczar M, Herczeg E: Spindle cell squamous carcinoma of the lung. A light microscopic, immunohistochemical and ultrastructural study of a case. Histopathology 1987; 11:871-878.

Caso 2 (s01. 3388)

Mujer de 47 años con dolor en el flanco derecho se le efectuó un examen radiológico encontrándose una masa en el riñón derecho.

Diagnosis:

Spindle and Cuboidal Renal Cell Carcinoma (Loopoma)

This is an unusal neoplasm that has been coded under different names. In the majority of cases reported in the literatura, the behavior of these tumors has been that of a low grade malignant neoplasm. Nevertheless, documented cases to lymph nodes have been described. Clinically, patients may present with symptoms of hematuria, general fatigue, flank pain, and weight loss, and nephrolithiasis. Currently, the classification of renal tumors does not allow much space to depart from the convencional carcinoma. Tus, the descriptive form in which these neoplasms are presented.

The most important sigue is to be able to separate these tumors from other benign and more malignant tumors of the kidney. Among the benign lesions that may enter in the differential diagnosis are: metanephric adenoma, papillary renal cell carcinoma, and sarcomatoid renal cell carcinoma. Nevertheless, the features of "Loopoma" are rather characteristic, due to its bland appearance, presence of myxoid stroma, lack of marked pleomorphism and high mitotitc activity.

By immunohistochemistry, these tumors have been described as showing positive staining for EMA, S-100 protein, and CAM5.2. On the other hand, HMB-45 and smooth muscle actin have been reported negative.

Selected Referentes

1. Hes O, Hora M, Perez-Montiel DM, et al. Spindle and cuboidal renal cell carcinoma: a tumour having frequent association with nephrolithiasis: report of 11 cases. Histopathology 2002; 41:549-55
2. Rakozy C, Storkel S. Tubulo-mucinous renal neoplasms show consistent morphologic, immunohistochemical, and genetic findings: is it time to define a new renal tumor entity? Mod Pathol 2001; 14:190[a]
3. Srigley JR, Reuter V. Phenotypic molecular, and ultrastructural studies of a novel low grade renal epithelial neoplasm possibly related to the loop of Henle. Mod Pathol 2002; 15:182[a]
4. Nagashima Y, Arai N, Tanaka Y, et al. Two cases of a renal epithelial tumour resembling inmature nephron. Virch Arch A Pathol Anat Histopathol 1991; 418:77-81.
5. Lloreta J, Corominas JM, Munne A, et al. Low-grade spindle cell carcinoma of the kidney. Ultrast Pathol 1998; 48:416.

Caso 3 (s02.190071)

Hombre de 38 años con dolor al orinar referido al flanco derecho. Se le efectuaron exámenes radiológicos encontrándose una masa en el riñón derecho.

Diagnosis:

PRIMITIVE NEUROENCTODERMAL TUMOR (PNET)

Extra-osseous round cell tumors bearing features similar to those described in skeletal neoplasms designated as Ewing's sarcoma are rare. Over the years, these tumors have been known by a variety of names including extraskeletal Ewing's sarcoma, malignant small cell tumor of the thoracopulmonary region, Askin's tumor, paravertebral round cell tumor, and primitive neuroectodermal tumor. Today most of those tumors have been grouped into a single family - PNET.
The existence of a group of soft tissue neoplasms characterized by round cells with scanty cytoplasm, moderate amounts of chromatin in the nuclei, inconspicuous nuclei, mitosis, rosettes, hemorrhage and necrosis was first recognized by Angerval and Enzinger in their description of 39 cases, and all of them with a distinctive feature of intracellular glycogen. At that time this latter feature was considered to be a feature observed in extra-skeletal Ewing's sarcoma but not in other neoplasm including neuroblastoma. However, it is well known that some neuroblastomas may also contain glycogen in their cytoplasm. Thus, the finding of glycongen alone in the cytoplasm of these tumors does not indicate a particular neoplasm. Ultrastructural studies have also been controversial stating that the features of extra skeletal Ewing's sarcoma are distinctive enough to allow separation from other small cell tumors while others consider that the ultrastructure of these tumors is broad with some overlapping features.
The clinical and radiological features of this tumor when it occurs in the renal parenchyma do not allow differentiation from other more common renal cell neoplasms.

Histologically, these tumors are characterized by the presence at low magnification of a neoplastic cellular proliferation which can be separated in lobules by thin fibroconnective tissue while in other areas the cellular proliferation is distributed in sheets of neoplastic cells, cords or nests. Areas showing cystic areas filled with blood and pools of blood may also be seen. At higher magnification, the neoplastic cellular population is rather homogenous composed of round cells with indistinct cell borders, scanty cytoplasm, round to elongated nuclei and inconspicuous small nucleoli. In some areas the tumor cells have a tendency to be distributed around vessels. Mitotic activity can be brisk and necrosis and hemorrhage are invariably present. In better-differentiated tumors, the presence of rosettes helps in the diagnosis; however, rosettes are not always present in these tumors. In some cases the presence of necrosis and/or hemorrhage can be so prominent that the tumor cells are difficult to visualize. In other tumors, the so-called Azzopardi phenomenon may be seen. Histochemical stains using periodic acid-Schiff (PAS) may help in the diagnosis; however, not only this histochemical stain may be negative but also positive staining may be seen in other type of neoplasms in that particular anatomic location.

The use of immunohistochemistry has shaped to some extent our views regarding these tumors. Initially, the use of neuron specific enolase (NSE) was consider specific for the neural derivation of these tumors; however, that notion faded rapidly after NSE was known to

stain several other tumor which were not necessarily of neural origin. Another marker that has been used with partial results in the evaluation of these tumors is S-100 protein; however, the results obtained have been controversial. More recently, the use of CD-99 (HBA-71 or the MIC2 gene product) (Ewing's Marker) was view as an important immunohistochemical tool for the diagnosis of these tumors; however, CD-99 may also show positive staining in other tumors of epithelial and mesenchymal origin. One important immunohistochemical markers that can be of help in the proper clinical setting is synaptophysin which is more widely use as a neuroendocrine marker. However, these latter immunohistochemical markers appear to be more consistent in the staining of these tumors.

Recent advances in molecular techniques have established a closer relationship between Ewing's sarcoma/PNET. Today there is very little doubt that those tumors are closely related. Chromosome translocations t(11;22) (q24;q12) and t(21;22) (q22;1q12) and their oncoproteins have been found in cases of Ewing's sarcoma/PNET.

The differential diagnosis of PNET can be quite difficult since there are other types of epithelial, mesenchymal, and/or neural tumors that may share similar histopathological features. By far the most difficult diagnostic considerations include rhabdomyosarcoma, neuroblastoma, lymphoma/leukemia, and more unusual metastatic small cell carcinoma or metastatic sarcoma from an osseous primary. The two latter conditions can be dealt with by a careful clinical history and radiological evaluation. However, with the two former ones a careful histological and immunohistochemical analysis is required.

In cases of rhabdomyosarcoma the presence of rhabdomyoblast in better-differentiated tumors may lead to a correct interpretation. In cases in which the histology is not so characteristic, the use of a panel of immunohistochemical studies including muscle markers can solve the problem. The problem with neuroblastoma can be more difficult to solve since these tumor also vary in their immunohistochemical profile. NSE, S-100 protein may show positive staining in both tumors; however, the presence of synaptophysin and CD-99 positivity couple with the histology of the tumor will lead more towards a PNET. In cases of lymphoma or leukemia the histological features and the presence of positive staining in tumor cells with LCA and B or T markers should lead to a correct interpretation.

Regarding the prognosis and treatment of PNET, it appears that the treatment of choice of chemotherapy.

REFERENCES

1. Angerval L, Enzinger FM: Extra skeletal neoplasms resembling Ewing's sarcoma. Cancer 1977; 101:446-449.
2. Askin FB, Rosai J, Sibley R, Dehner LP, et al: Malignant small cell tumors of the thoracopulmonary region in children. Cancer 1979; 43:2438-2451.
3. Gould V, Jannson D, Warren W: Primitive neuroenctodermal tumors (PNET) of the chest wall in adults. Modern Pathology 1991; 4:115A, Abstract 681.
4. Hashimoto H, Enjoji M, Nakajima T, et al: Malignant neuroepithelioma (peripheral neuroblastoma). Am J Surg Pathol 1983; 7:309-318.
5. Lane S, Ironside JW: Extraskeletal Ewing's sarcoma of the nasal fossa. J Laryngol Otol 1990; 104:570-573.
6. Soule EH, Newton W, Moon TE, et al: Extraskeletal Ewing's sarcoma. A preliminary review of 26 cases encountered in the intergroup rhabdomyosarcoma study. Cancer 1978; 42:259-264.
7. Suster S, Ronnen M, Huczar M: Extraskeletal Ewing's sarcoma of the scalp. Pediatr Dermatol 1988; 5:126-128.
8. Tefft M, Vawter GF, Metus A: Paravertebral "round cell" tumors in children. Radiology 1969; 92:1501-1509.
9. Wigger JH, Salazar G, Blanc WA: Extraskeletal Ewing's sarcoma. Arch Pathol Lab Med 1977; 101:446-449.
10. Fujii Y, Hongo T, Nakagawa Y, et al: Cell culture of small round cell tumor originating in the thoracopulmonary region, evidence for derivation from a primitive pluripotential cell. Cancer 1989; 64:43-51.
11. Yunis EJ, Agostini RM, Walpusk JA, et al: Glycogen in neuroblastomas. Am J Surg Pathol 1979; 3:199-208.
12. Guillespie JJ, Roth LM, Wills ER, et al: Extraskeletal Ewing's sarcoma. Am J Surg Pathol 1979; 3:99-108
13. Schmidt D, Mackay B, Ayala A: Ewing's sarcoma with neuroblastoma like features. Ultrastructural Path 1982; 3:99-108
14. Linnoila RI, Tsokos M, Triche TJ, et al: Evidence for neural origin and PAS-positive variants of the malignant small cell tumor of thoracopulmonary region ("Askin's tumor"). Am J Surg Pathol 1986; 10:124-133.
15. Tsokos M, Linnoila RI, Chandra RS, et al: Neuron-specific enolase in the diagnosis of neuroblastoma and other small, round cell tumors in children. Hum Pathol 1984; 15:575-584.
16. Gonzales-Crussi F, Wolfson SL, Misugi K, et al: Peripheral neuroectodermal tumors of the chest wall in childhood. Cancer 1984; 54:2519-2527.
17. Ordonez NG: Application of immunohistochemistry in the diagnosis of soft tissue sarcomas: a review and update. Adv Anat Pathol 1998; 5(2):67-85.
18. Batsakis JG, El-Nagar A: Ewing's sarcoma and primitive neuroectodermal tumors: Cytogenetic cynosures seeking a common histogenesis. Adv Anat Pathol 1997; 4(4):207-220.

Caso 4 (s04. 16696)

Mujer de 53 años con dificultad para respirar y dolor toráxico. Estudios radiológicos demostraron una masa en el lóbulo inferior del pulmón derecho.

Diagnosis:

Rhabdoid tumor del pulmón, primario

Since the initial description by Beckwith and Palmer of a renal neoplasm resembling rhabdomyosarcoma, similar tumor has been described in several anatomic areas including thorax. The name given to this tumor is that of rhabdoid tumor due to its resemblance to rhabdomyosarcoma. Although initially thought to be exclusively a renal neoplasm, the tumor does have a ubiquitous distribution and the named that has been coined when these tumors are outside the kidney is extrarenal rhabdoid tumor.

Tumor with similar histology have been described in the thorax – mediastinum and luna. However, when these tumor have been described in luna, they usually are in association with another convencional non-small cell carcinoma. The occurrence of these tumors in its pure form is rather inusual. However, we also relieve that the name rhabdoid tumor, at least when these tumors occur in the luna is rather misleading, since ultrastructural studies (personal experience) point in the dirrection of an epithelial neoplasm. Tus, we prefer the term "rhabdoid carcinoma" for these tumor. In addition, we consider that the prognosis of these cases while in the luna may be determined by the clinical stage at the time of diagnosis.

Rhabdoid carcinomas of the luna may show similar immunohistochemical features as those described elsewhere. Tumor cell may be positive for vimentin, cytokeratin and epithelial membrana antigen. In some cases the tumor cell may show positive reaction for neurofilament protein and desmán.

The differential diagnosis in this type of tumor is with a primary rhabdomyosarcoma or pleomorphic carcinoma of the luna. In the former, the tumor cells will show positive staining for desmán and myoglobin and negative staining for keratin (some cases of rhabdomyosarcoa may show positive staining for keratin) while in the latter, even though epithelial markers may show positive stianing, the tumor may show much more pronounced pleomorphism componed of malignant giant cells admixed with a malignant spindle cell proliferation.

<u>Selected Referentes</u>

1. Dervan PA, et al. Malignant rhabdoid tumor of sofá tissue. Histopathology 1987; 11:183-190.
2. Weeks DA, Beckwith JB, et al. Rhabdoid tumor. An entity of a phenotype? Arch Pathol Lab Med 1989; 113:113-114.
3. Vogel AM, Gown AM, et al. Rhabdoid tumors of the kidney contain mesenchymal specific and epithelial specific intermediate filament protein. Lab Invest 1984; 50:232-38.

Caso 5 (s02. 13085)

Mujer de 57 años con dolor en el flanco derecho se le encontró una masa en el riñón derecho la cual fue extirpada encontrándose un Carcinoma de células claras de riñón. Durante el procedimiento se le encontró una masa en el Hígado la cual fue extirpada. La muestra patológica es de la masa en el hígado.

Diagnosis: Angiomiolipoma del hígado

Primary angiomyollipomas of the liver are rare. The same as when tese tumors occur in other more common areas, the histology is similar and consist on the formation of well formed vessels, adipose tissue , and polygonal to spindle cell proliferation. Hematopoeitic elements and foam cell may also be present. Although cellular atypia may be present, the tumor does not mitotic activity.

The tumor occur in any age group without predilection for a particular sex. Tuberous sclerosis has been associated with this tumor; however, in no more than 10% of the cases. Grosssly, the tumors are solitary in the great majority of cases and the histology is characteristic with the presence of thick wall vessels, adipose tissue and spindle cells, which represent smooth muscle. Occasionally the tumor may show larger cells with round nuclei and prominent nucleol, with a hybernoma-like appearance. Immunohistochemically, the tumor cells are positive for smooth muscle actin and for HMB-45.

The differential diagnosis of angiomyolipoma in the liver Hill incluye a metastatic neoplasm or a primary hepatic tumor such as a smooth muscle tumorw, namely when the tumor is componed predominantly of smooth muscle. On the other hand, a small gipsy can be interpreted as fatty change in samples in which the smooth muscle proliferation is not apparent.

Surgical resection of the tumor is curative in these patients.

Selected Referentes

1. Goodman ZD, Isaac KG. Angiomyolipoma of the liver. Am J Surg Pathol 1984; 8:745.50
2. Nonomura A, Mizukami Y, Kodaya N. Angiomyolipoma of the liver: a collective review. J Gastroenterol 1994; 29:95-105.