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THE HISTOLOGICAL AND IMMUNOHISTOCHEMICAL APPEARANCE OF A VERY RARE ENTITY – BELLINI'S COLLECTING DUCT CARCINOMA

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Abstract: *The collecting Bellini's duct carcinoma is a very rare neoplasm that has the origin in the distal segment of the renal ducts. We present the case of a 64 female patient who underwent nephrectomy for a right renal mass. On the usual stain, the mass presented a tubular and solid architecture, with high pleomorphism. The diagnosis of collecting carcinoma was established with the help of immunohistochemistry. There are few cases described in the literature, most of them highlighting the difficulty in establishing the origin of this lesion, the variable immunohistochemical expression of the tumor and the high risk of metastasis and mortality.*

Key words: *Bellini, immunohistochemistry, rare neoplasia.*

1. Introduction

The Bellini carcinoma, also known as the collecting duct carcinoma (CDC), is a very rare entity with origins in the renal medulla, in the distal segment of the ducts. This tumor has a percent of appearance below 2% (some authors believe that below 1%) of all the neoplasms with renal origin. CDC has a poor prognosis and it is, according to some studies, the most aggressive tumoral lesion of the kidney. The median age of

appearance is around 62 years old and male patients are more often affected, with a ratio of 2:1 compared to female patients.

The first author who described this lesion briefly was Mason, back in 1955. The one who developed the description and added more details, such as mentioning the origins in the epithelia of the ducts is Jimenez, in 1976, while Fleming and Lewi, later in 1986, defined the criteria for the complete diagnosis [4, 5], [7].

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According to ISUP (International Society of Urological Pathology), Bellini carcinoma diagnosis should be established in lesions which have predominantly a tubular architecture, stromal reaction such as desmoplasia and cells with high pleomorphism which do not resemble any other tumor from the renal cell carcinoma or urothelial carcinoma spectrum [8], [13], [17].

When we encounter a tumoral entity that resembles CDC, it is important to consider several major differential lesions that might be more oftenly mistaken with Bellini. The most common neoplasms that are part of this category are the urothelial carcinoma with glandular differentiation, papillary renal cell carcinoma, medullary carcinoma of the kidney, the mucinous and spindle cell carcinomas, tubulocystic carcinoma. Other lesions with a high importance in this matter are hereditary leiomyomatosis RCC and metastatic carcinoma from GI tract or lung [9].

Unfortunately, due to the fact that this tumor is very rare and has a non specific symptomatology that occurs late in evolution, the patients are being diagnosed in advanced stages. It is mentioned that the improvement of the prognosis depends of an early diagnosis, yet because of the situations mentioned above, most of those involved are undergoing surgery and receive treatment when they are in advanced stages or even present metastasis. Some studies reported a very poor survival range, with a median of 11 months [2], [14].

2. Material and Methods

We present the case of a 64 years old female patient committed in the Urology Department of the Clinical County Hospital Târgu-Mureş, Mureş County. The patient presented a right renal mass and the tumoral stage established by the clinicians was cT1N0M0. Nephrectomy was performed and the sample was sent to the Pathology Department for diagnosing and stadialization. The tissue was fixed in formaline and processed according to the protocols.

3. Results

The patient presented in the Urology department for gross hematuria and flank pain. A CT scan was performed and a renal mass was seen at level of the right kidney.

On the gross examination, the nephrectomy specimen had dimensions of 150x80x60 mm, with renal parenchyma of 120x65 mm. We observed a tumoral mass involving both the medulla and the cortex, poorly circumscribed, with total dimensions of 26x23x22 mm. The color was yellow, with multiple hemorrhagic and necrotic areas.

Microscopically, on the Hematoxylin and Eosin stain, we observed an infiltrative tumoral mass which presented a tubular architecture, predominantly composed from a proliferation of tubular structures with different dimensions and forms. The majority of these structures were angulated, compressed, deformed and separated by a desmoplastic stroma in which we observed rare lymphocytes. The

tumoral tubular structures were lined by a single row of cubic cells with eosinophilic cytoplasm. The nuclei were increased in size and showed high pleomorfism. Nucleoli were also observed along with atypical mitosis. The grade of the tumor, based on the nuclei and nucleoli aspect, was 3 (according to the WHO/ISUP classification - nuclei visible at 100x magnification). Numerous areas of necrosis and hemorrhage were also present.

The tumor infiltrated the renal parenchyma, exceeded the renal capsule and extended into the perirenal lipomatous tissue, therefore the stage was set pT3aN0M0 (we had no information on

the lymph nodes and dissemination towards other sites). No invasion of the blood vessels of the renal hilum was visible [15], [18].

The adjacent renal parenchyma showed changes characteristic for the chronic nephritis: hyalinized glomeruli, thick blood vesseled, thyroidization of the renal tubes and chronic inflammation composed mostly by lymphocytes.

The surgical resection limits were not infiltrated by the tumoral cells. No other lesions were seen on gross or microscopical examination.

To confirm the diagnosis of CDC, we performed a series of immunohistochemical reactions.

Table 1

Immunomarkers and the result of the reaction

Immunohistochemical marker	Result of the reaction
<i>Vimentin</i>	Positive, cytoplasm
<i>CK 7</i>	Positive, cytoplasm
<i>34BE12</i>	Positive, cytoplasm
<i>EMA</i>	Positive, membranous
<i>CK 8/18</i>	Positive, cytoplasm and membrane
<i>CK 19</i>	Positive, cytoplasm and membrane
<i>E-cadherin</i>	Positive, membranous
<i>Bcl2</i>	Negative on tumoral cells
<i>P 63</i>	Negative
<i>CD 117</i>	Negative
<i>P 53</i>	Negative

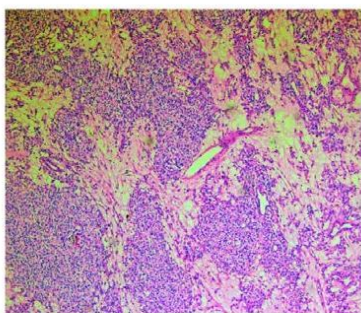


Fig. 1. *Bellini Duct carcinoma- Hematoxilin&Eosin stain, solid architecture*

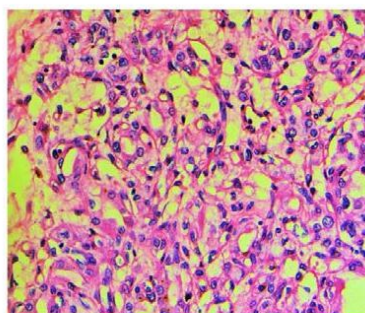


Fig. 2. *Bellini Duct carcinoma Hematoxilin&Eosin stain, high magnification*

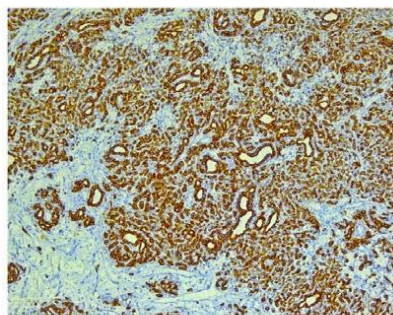


Fig. 3. *Immunohistochemistry- reaction with CK AE1/AE3*

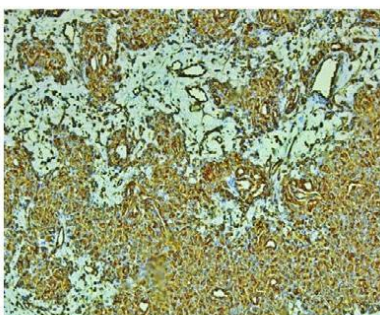


Fig. 4. *Immunohistochemistry- reaction with vimentin*

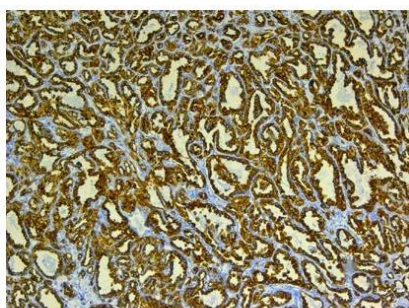


Fig. 6. *Immunohistochemistry- reaction with CK7*

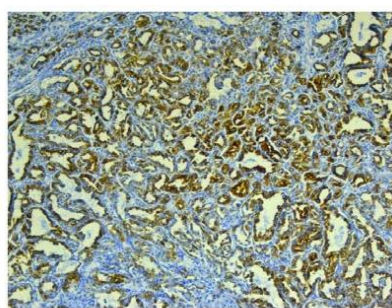


Fig. 7. *Immunohistochemistry- reaction with CK8/18*

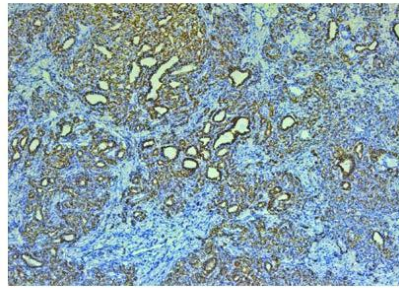


Fig. 7. Immunohistochemistry- reaction with *E-cadherin*

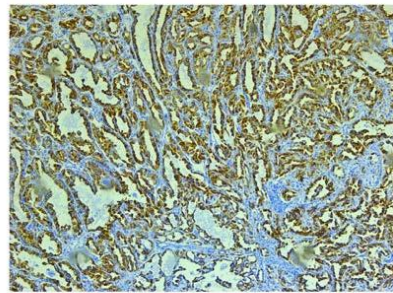


Fig. 9. Immunohistochemistry- reaction with 34BE12

4. Discussion

Collecting duct carcinoma (CDC) is a rare neoplasm, very hard to identify on the usual stain, that needs to be distinguished from all the other tumors with origins in the kidney. In literature, CDC is known to affect male patients mostly.

Our case is presenting a female patient, age 64, with a tumoral mass in the right kidney. The age of the patient is very close to the median age of the patients reported to present this pathology, but since CDC has a very wide interval of appearance, age is not a reliable factor [3], [12].

Studies describe CDC as an infiltrative, poorly circumscribed tumor that usually extends below the renal capsule. In our case, on the gross examination, the tumor appears as a poorly circumscribed mass, involving both the medulla and the cortex.

The histology of the tumor is highly variable, but it shows an infiltrative pattern. It was mentioned that the

architecture of the neoplastic glands shows a tubular, papillar, solid or sarcomatoid pattern. Most authors described local or extended sarcomatoid transformation and tubulopapillar pattern. The number of mitoses is highly variable. According to Fuhrman grading system, most tumors were classified as grade III or IV, the lately WHO/ISUP classification also grades them as 3 or 4, depending on the sarcomatoid representation [1], [6], [10], [19, 20].

In our case, the tumor architecture was mostly tubular and no sarcomatoid transformation was observed. The cells presented high pleomorphism and were classified, according to WHO/ISUP, in grade 3. Desmoplasia is reported in most cases and also present in our sample, along with a low number of inflammatory cells - lymphocytes.

Immunohistochemistry is a very useful tool when facing CDC. In the past decades, there are several markers known to be expressed in this tumor, such as CTK

AE1/AE3 (a cocktail of keratins also known as pankeratin), CK7 (type II keratin with expression in a wide spectrum of epithelial tumors), 34BE12 (marker of urothelial origin), all of them positive in our case as well.

In time, more cases of CDC surfaced, therefore more markers were tested. It is stated that the tumoral cells express a larger number of markers than initially thought. However, many of these markers are not highly specific for this lesion and the diagnosis must be confirmed by using more than 2 or 3 antibodies. In our case, we chose a wide range of markers, most of them showing an intense expression. Besides the ones mentioned earlier, vimentin (mesenchymal marker), CK 8/18 (low molecular weight CK), CK 19 (smallest CK), EMA (epithelial membrane antigen) were also positive.

There are studies which mention the expression of p63 in 14% of CDC. Others describe an expression of bcl 2 in 4 out of 11 cases and a nuclear overexpression of p53. All these markers were negative in our case. CD 117 was also negative [4], [20]. Most studies sustain that E-Cadherin is usually negative in CDC, yet it can show positivity in rare occasions. In our case, E-Cadherin stain showed strong expression [11].

Regarding the follow-up of the patient, 6 months after the diagnosis her state was deteriorated. She began chemotherapy, the most used therapy method around the world. As mentioned before and proved in studies, this tumor has a high risk of mortality. The prognosis of the patient is very poor [16].

5. Conclusion

Collecting duct carcinomas are rare lesions, usually discovered in advanced stages. The diagnosis of these tumors requires a laborious work. It is important to exclude the other renal entities before raising the suspicion of Bellini and support the diagnosis with the use of immunohistochemistry. There is a limited number of cases described in the literature until now, all of them highlighting the particularities of CDC along with the tumor's heterogeneity in the usual staining with Hematoxylin & Eosin and in the immunohistochemical expression.

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Lucrari scanate si publicate

Andreea Tinca, Tivadar Bara, Ioan Jung, Simona Gurzu. Chylous ascites, induced by a pancreatic carcinoma, Virchow Archive volume 475, supplement 1, september 2019, E-PS-07-005, ISSN 1432-2307 (online)



E-PS-07-005

Chylous ascites, induced by a pancreatic carcinoma

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Background & Objectives: Chylous ascites is an uncommon condition of peritoneal cavity. The aim of the paper was to describe the case of a patient with ductal adenocarcinoma of the pancreatic body that presented as acute abdomen and chylous ascites.

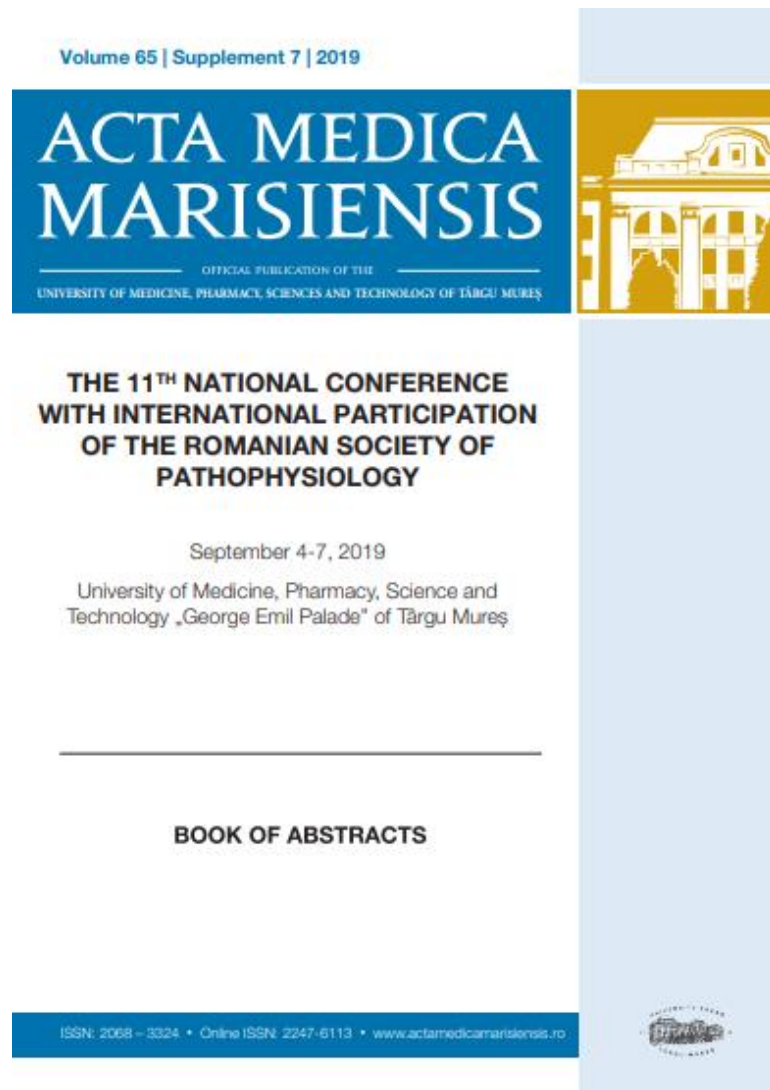
Methods: A 76-year old previously healthy male presented with acute abdomen and suspicion of pancreatic body cancer, with associated ascites, was done. Emergent surgery consisted on splenopancreatectomy with dissection of the peripancreatic lymph nodes. The fluid from abdominal cavity had a milky aspect and was proved having lymphatic origin.

Results: The 50x40x20 mm pancreatic tumour involved the pancreatic body and tail and showed direct infiltration of the spleen hilum, being diagnosed as pT3N1 ductal adenocarcinoma. Most of the lymph vessels showed tumour emboli, which induced blockage of the lymphatic flow. The patient died at three weeks after surgery.

Conclusion: In patients with pancreatic cancer, chylous ascites can indicate an aggressive carcinoma with lymphatic flow blockage.

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Andreea Cătălina Tinca , Mihaela Şincu , Sabin Turdean , Mihai Turcu, Robert J. Bartha , Ovidiu S. Cotoi
-A rare case of verrucous carcinoma, Acta medica marisiensis, Volume 65 | Supplement 7 | 2019, p37-37.
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A RARE CASE OF VERRUCOUS SQUAMOUS CELL CARCINOMA-CASE REPORT

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Introduction: Verrucous carcinoma is a rare and well differentiated variant of the cutaneous squamous cell carcinoma and it was described first by Ackerman (also called Ackerman tumour). It can appear on both skin -especially palm and soles- and oral cavity and it's more common in older men (>60 years old). This type of carcinoma is characterised by slow growth, minimal local invasion and rare metastases, on a long term having a better prognosis than the other types of squamous carcinoma.

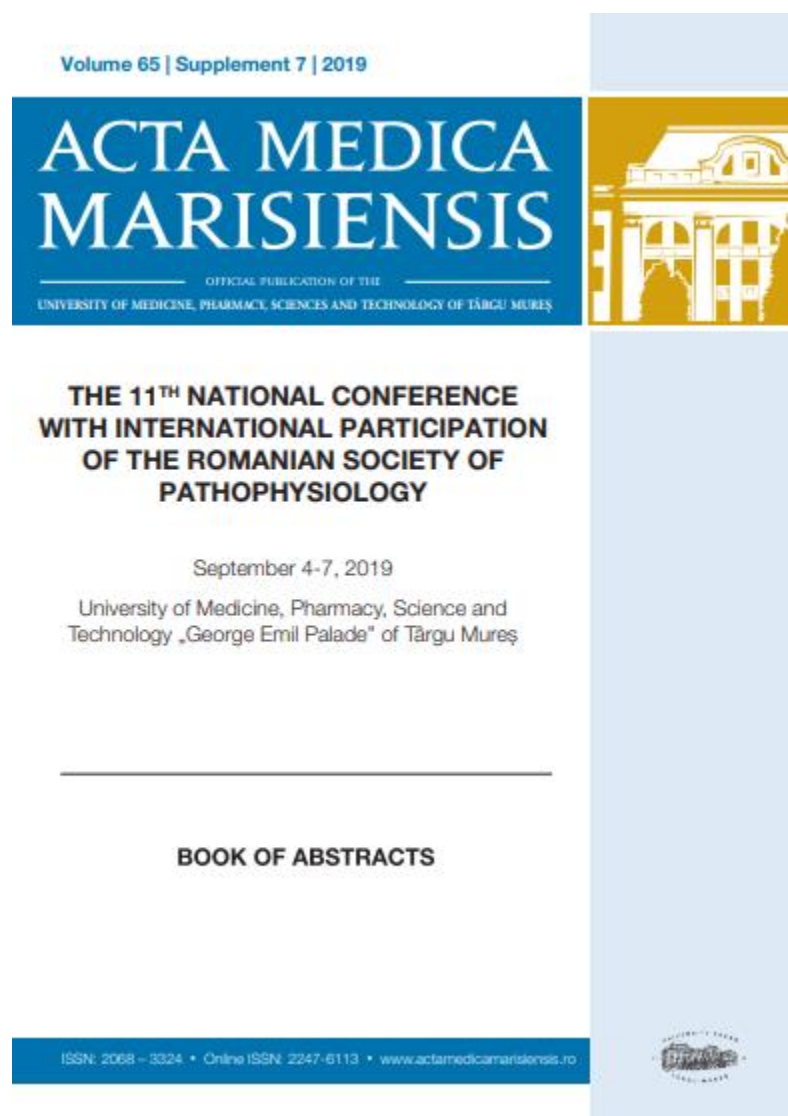
Case report: We present a case of verrucous carcinoma located on the sacral region in a 54 year old female patient with no medical background.

Results: The H&E stains revealed a lesion characterized by endophytic and exophytic architecture with prominent hyperkeratosis. The microscopy of the carcinoma showed the "rete ridges" which are bulbous, with "bulldozing" pattern that invade in the depth of the skin. The epidermis is also interested by papillomatosis, hypergranulosis and acanthosis of the squamous layer. The cytologic changes were minimal, these tumors don't usually show significant anaplasia. A chronic inflammatory cell dermal infiltrate was also present, but due to the fact that the lesion was fragmented during excision we couldn't evaluate the edges of the tumor.

Conclusion: Verrucous carcinoma is more common in the oral cavity, soles and palms, it can rarely appear in any other skin area. It has a better prognosis than the classic type of squamous carcinoma.

Keywords: verrucous carcinoma, immunoprofile, squamous cell carcinoma

Tinca, Andreea Cătălina; Şincu, Mihaela; Turdean, Sabin; Turcu, Mihai; Bartha, Robert J.; Cotoi, Ovidiu
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PRIMARY OVARIAN ENDOMETRIOID CARCINOMA ASSOCIATED WITH SIMPLE ENDOMETRIAL HYPERPLASIA-CASE REPORT

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Introduction: The endometrioid carcinoma of the ovary is a rare ovarian tumor which represents 10-25% of the primary ovarian carcinomas and can be associated in around 30% of the cases with endometrial, benign or even malignant, lesions. It can occur in patients with a wide range of ages, from 26 to 87 years old, but it is more common in the 50-70 range.

Case report: we report the case of ovarian endometrioid carcinoma in a 44 year old female patient who underwent surgery for a left ovarian tumor.

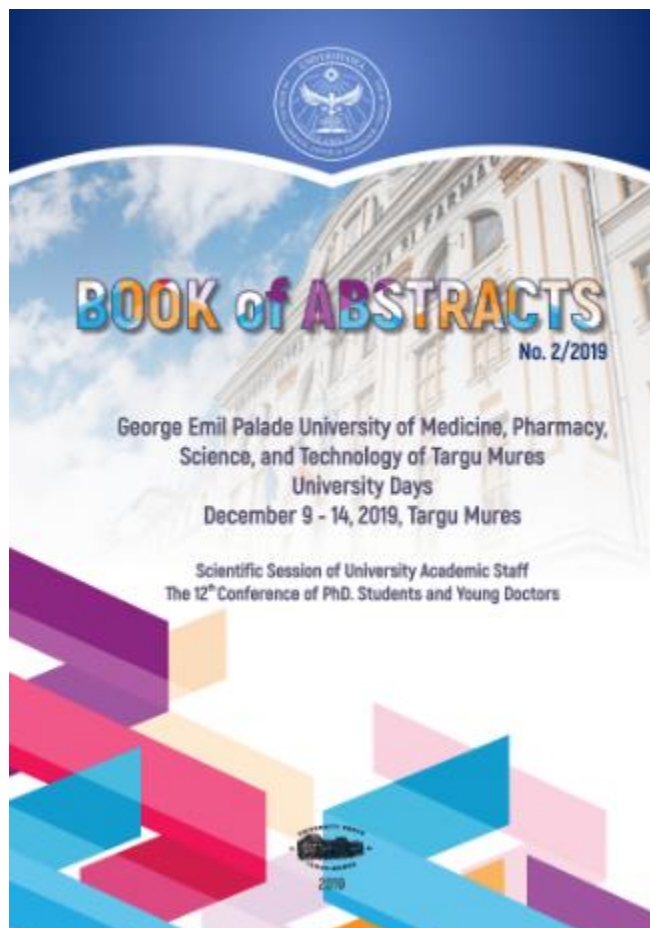
Results: In the ovary, H&E stains revealed a proliferation of glandular structures with different sizes and aspects, some of them presenting cystic dilatations and villoglandular pattern. The glands were surrounded by a reduced stroma and their epithelium was columnar and displayed moderate cytological atypia: prominent nucleoli, typical and atypical mitotic figures and pleomorphism. Squamous metaplasia, areas of necrosis and inflammation were present in the tumoral area. The pathological stage was pT1c2NxMx. Immunohistochemistry exhibits diffuse positivity for CK7, and focal positivity for WT1 and CDX2.

The examination of the endometrium showed features of simple endometrial hyperplasia without atypia of the glandular epithelium.

Conclusion: Our case captures the coexistence of these two lesions: primary ovarian endometrioid carcinoma and simple endometrial hyperplasia, both favored by hyperestrogenism.

Keywords: ovarian endometrioid carcinoma, endometrial hyperplasia, immunoprofile.

Andreea Tinca, Mihaela Sincu, Turcu M, Bartha R, Cotoi OS, Turdean S– A rare case of paratesticular liposarcoma, Acta medica marisiensis, Book of abstracts No. 2/2019, pg 53, ISSN 2602-1609, ISSN-L 2602-1609.



diagnosis of follicular hyperplasia was made. After two months the patient developed a new enlarged lymph node in the same site, removed surgically and examined histologically. **Results:** The architecture of the second lymph node is partially effaced by large geographic, follicular structures lacking mantle zone, with back to back configuration, with monotonous cellular composition and prominent starry sky pattern. The aberrant follicles are composed of lymphocytes expressing B-cell associated antigens and the germinal center markers. Bcl-2 and MUM1 stains are negative. The high proliferative rate outlines the seipiginous pattern. IgD shows absence of mantle cuffs around most of the follicles. This case adrees the borderline between florid follicular hyperplasia and PTFL. **Conclusions:** Differentiation between reactive and neoplastic lymphoid follicles of PTFL is often problematic. Morphology is important especially in PTFL with partial involvement, that lack of the t(14; 18) and is most bcl-2 protein negative. We proposed this case for FISH and PCR studies. Interesting features of this case are represented by three important aspects: age of patient and possibility of partial involvement of lymph node by B-cell proliferation with alarming histological features.

Keywords: florid follicular hyperplasia, pediatric-type follicular lymphoma, follicular lymphoma

A RARE CASE OF PARATESTICULAR LIPOSARCOMA

Tinca Andreea¹, Sincu Mihaela¹, Turcu M¹, Bartha R¹, Cotoi CS¹, Turdean S¹

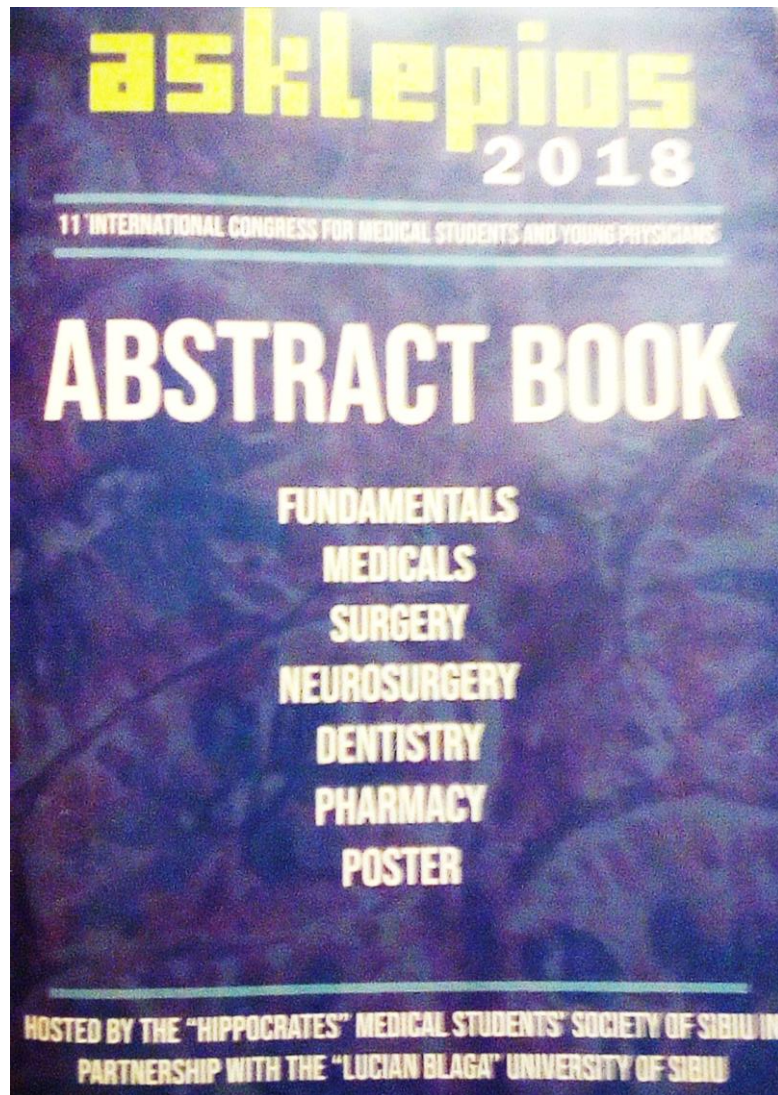
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Backgrounds: Liposarcoma is a rare mesenchymal tumor that arises from the lipoblasts and has an unknown cause of appearance. Histologically, the major types of liposarcoma according to the latest morphological features are: well differentiated liposarcoma, dedifferentiated liposarcoma, myxoid-round cell liposarcoma and pleomorphic liposarcoma. Pleomorphic liposarcoma is a lesion that appears in less than 10% of the total of lipomatous tumors and it is considered to have the highest malignant grade with significant risks of metastasis, recurrence and invasion. **Material and methods:** We intend to present the case of a 66 year old male patient with the clinical diagnosis of orchi-epididymitis that undergo surgery. Orchiectomy was performed. **Results:** Microscopically, the lesion described above consisted of a proliferation of lipoblasts with bizarre, hyperchromatic nuclei, with marked pleomorphism. There were also numerous multinucleated giant cells along with fusiform and round cells. Myxoid areas with thin, branched vessels were also described. Necrosis was absent and the number of mitosis, mostly atypical, was 7/10 HPF. The tumoral process infiltrated tunica albuginea but the testicular parenchyma was not involved. The surgical resection limit was negative. The immunohistochemical stains showed positivity for protein S100, CD34 and K67 and was negative for CD68. **Conclusions:** liposarcoma is a neoplasm that appears usually in sites like retroperitoneum and lower extremities. The pleomorphic liposarcoma is an extremely rare type with a high grade of malignancy and paratesticular location is exceptionally. There are only around 200 cases described in the literature at the moment.

Keywords: liposarcoma, pleomorphic, paratesticular, rare, neoplasm

Lucrari scanate si publicate

Tinca Andreea Catalina, Moldovan Loredana, Roman Mihaela-Andreia, Moreh Zsuzsanna, Therapeutic options for acute cough in children, Book of Abstracts Asklepios 2018, 11th international congress for medical students and young physicians, Sibiu ISSN 1843-0406, date of congress 3-6 May 2018.



POSTER – THERAPEUTIC OPTIONS FOR ACUTE COUGH IN CHILDREN

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Scientific coordinator: Lecturer Moreh Zoriana, MD, PhD

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Introduction: Cough is one of the most common symptoms that occurs during the course of the disease in pediatric patients, being a self-defeating reflex of the organism against harmful agents. Its role is to remove the foreign bodies, mucus and microbes from the respiratory tract. It is more common in pre-school children than in other categories.

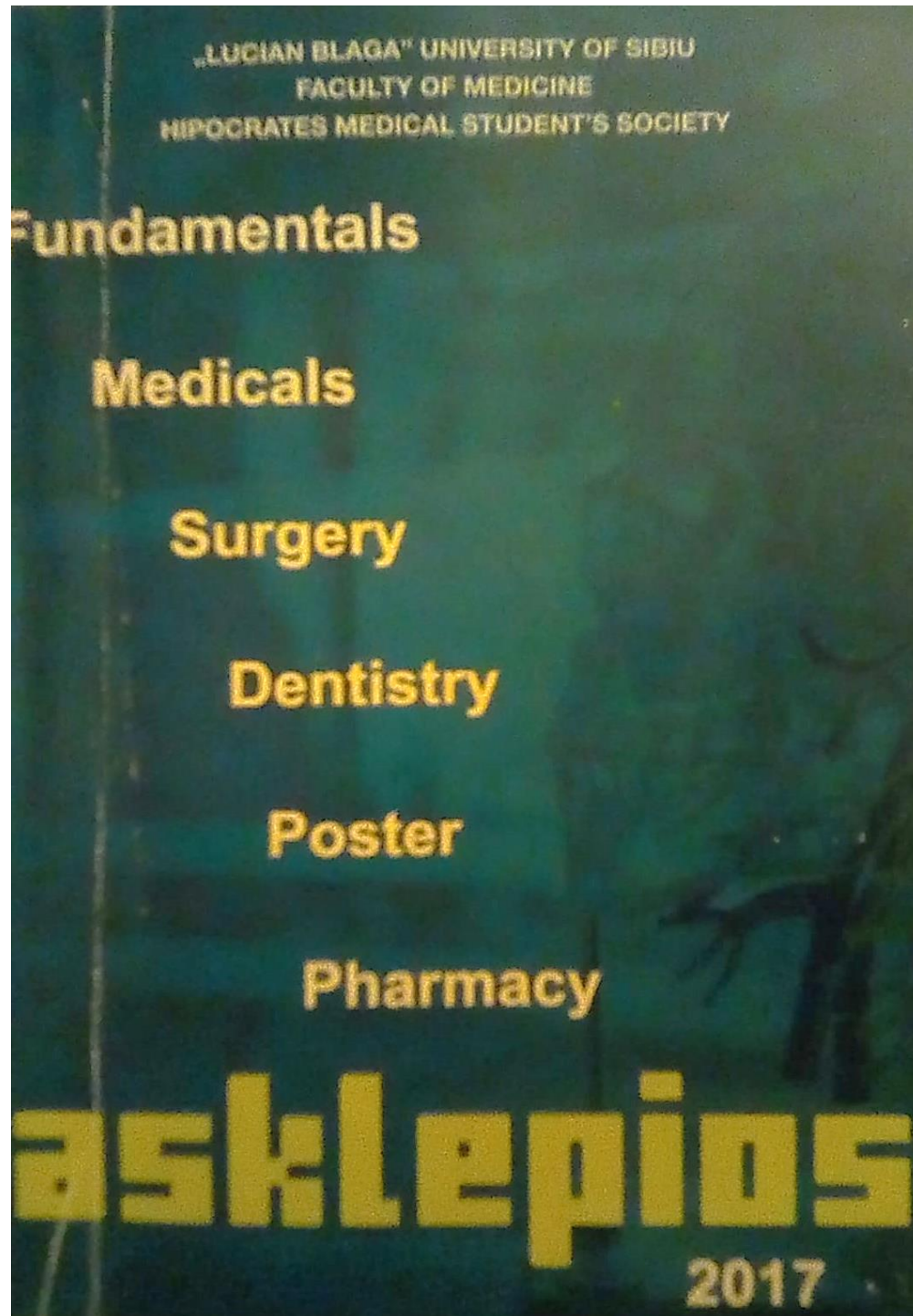
Material and methods: We conducted a clinical trial based on a questionnaire between 2017-2018, comprising a total of 23 questions addressed to parents who have children between 0 and 4 years of age, admitted to the Pediatrics II Clinic of the Mures County Clinical Hospital. In this study, I followed the next parameters: sex, age, disturbing symptoms, medication used for cough, who prescribed it, what are the parents' expectations, the frequency of cough, if the child had complications after the cough and which were those and others. We tried to see which are the options of treatment and if those are efficient or not, to be able to determine if there is indeed a need to treat this symptom.

Results and discussions: from a total of 60 patients, 37 were from the urban area and 23 from the rural area. The most disturbing symptom was the nasal obstruction for the urban area and cough for the rural. The treatment used for all children was syrup. ACC in 25% of the cases. The treatment was prescribed in 62% of the cases by the family physician. The most common cough was productive. From the most popular methods in fighting cough, excepting the prescribed medication, we found honey, but a big number of parents said they use no other method. Even if the cough was treated, the amelioration was shown only in 17% of the cases, after 2-3 days of treatment. Regarding complications, those were present in 10% of the cases (nausea), showing that the mother's fears regarding the symptom are not justified.

Conclusions: Parent's fear regarding cough are pneumonia, pulmonary lesions, suffocation and perturbation of sleep, but none of the patients showed these complications. Also, only a small number of children showed amelioration after the treatment.

Keywords: children, cough, treatment

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CASE REPORT – THE CLINICAL SPECTRUM AND COMPLICATIONS OF VERTEBROBASILAR STROKE AND PONTINE INFARCTION

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Introduction: The ischemic stroke is known as an acute loss of cerebral function due to an abnormal perfusion of the brain tissue after an arterial obstruction. The perfusion of the brainstem is maintained by the vertebral/basilar artery system which is rarely affected by ischemia. Pontine strokes have less than 10% of all ischemic events but they can be associated with severe disabilities.

Case report: This presentation shows the case of a 51 year old woman with no medical record, hospitalized in January for nausea, vomiting and lethargy that appeared suddenly, with progressive evolution towards worsening. No lesion was visible on the computer tomography scan. The neurological exam after 24 hours showed left facial palsy and hyposthenia, ptosis and exotropia in the left eye, dysphagia, hyporeflexia on the left ear, the patellar reflex decreased on the left side, ataxic and thermic hypoesthesia on the right side and ataxia. The blood tests showed a high glucose level, and ESR with a value of 52, the blood count test and blood chemistry panel were normal. The blood pressure was 168/96. After these investigations the patient was diagnosed with stage 2 hypertension and type 2 diabetes mellitus, diabetes with a high risk for stroke. Later in evolution, as a complication of the facial palsy, the patient developed corneal ulcer and amblyopia.

Management and Results: The magnetic resonance imaging scan in T2 weighted sequences showed an 12/10mm area resembling a stroke on the left side of the pons, medulla and cerebellar left middle peduncle. The contrast MRI of the brain showed a hypersignal T2 lesion in the left side of the pons, without edema or invasion, which enhances Gadolinium in the middle cerebellar peduncle. In the light of the symptoms and investigations we are not certain about the origin of the lesion (tumor or stroke) and a new MRI will be performed after 3 months.

Conclusions: Patients with pontine infarct can present a wide range of symptoms, depending on the affected region and the size of the lesion. This presentation discusses the clinical signs of a pontine stroke and its complications.

Keywords: vertebral/basilar, pons, stroke