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Prostate carcinomas mimicking a digestive malignancy

SORIN DEMA[1)], ALIS LILIANA CARMEN DEMA[2,3)], SORINA TĂBAN[2,3)], BIANCA ROXANA NATARÂŞ[3)], LIVIUS COSMIN DAMINESCU[4)], CIPRIAN CONSTANTIN DUŢĂ[5)], ALIN-ADRIAN CUMPĂNAŞ[4,6)], TIBERIU RĂZVAN BARDAN[4,6)]

[1)]*Service of Radiotherapy, Emergency City Hospital, Timişoara, Romania*

[2)]*Discipline of Morphopathology, Department of Microscopic Morphology, Victor Babeş University of Medicine and Pharmacy Timişoara, Romania*

[3)]*Department of Pathology, Pius Brînzeu Emergency County Hospital, Timişoara, Romania*

[4)]*Clinic of Urology, Pius Brînzeu Emergency County Hospital, Timişoara, Romania*

[5)]*Department of Surgery II, Victor Babeş University of Medicine and Pharmacy, Timişoara, Romania*

[6)]*Department of Urology, Victor Babeş University of Medicine and Pharmacy, Timişoara, Romania*

Abstract

Aim: To report our experience with specific cases of prostate cancer (PC) in which patients presented digestive symptoms, cases that represent a challenge and a source of error regarding the clinical and morphological diagnosis. *Methods*: The most important clinical and pathological data were collected from three patients with PC which presented symptoms and/or investigations that initially suggested a digestive malignant tumor. *Results*: We identified three patients with PC where the prostate tumor was not suspected based on the clinical-imagistic data, the correct diagnosis being the prerogative of the morphological investigation: in the first case, PC was detected during the microscopic examination of the lymph nodes (LN) in the intestinal resection specimen performed for suspected rectal cancer (RC), in the second case, in which the PC was synchronous with a RC, the dominant symptomatology was gastrointestinal, and in the third case, initially, the patient presented a widely disseminated PC, with pleural and bone metastases, as well as LN metastases, and apparent peritoneal involvement. *Conclusions*: Unusual forms of PC presentation are not as rare as expected and should be acknowledged by all those involved in diagnosing this neoplasm. PC should always be considered in the differential diagnosis of a rectal tumor. The immunohistochemical (IHC) investigation is essential for establishing the diagnosis in difficult cases. An integrated approach of the interpretation of clinical manifestations, imagistic and serological changes would shorten the diagnostic time and help reduce diagnostic errors.

Keywords: prostate carcinoma, digestive malignancy mimicker, immunohistochemistry.

Introduction

Prostate cancer (PC) is the second most common cancer affecting men worldwide, after lung cancer [1], occupying the third place in Romania, after lung and colorectal cancer [2]. Most cases of PC fall into one of the three major presentation patterns: (*i*) a tumor detected in a prostate core-needle biopsy (CNB) performed for an abnormal digital rectal examination (DRE), abnormal imagistic findings or for an increased value of serum prostate-specific antigen (PSA) [3]; (*ii*) a clinically manifest cancer, which is a tumor that has clinical signs [4], causing lower urinary tract symptoms and sometimes manifestations directly linked to the presence of metastases; (*iii*) an incidental, clinically inapparent tumor that is neither palpable nor visible by imaging, detected by the microscopic examination of the transurethral resection specimen of the prostate (TURP) [4, 5], or of the adenomectomy specimen [4, 6] and not so rare, of the cystoprostatectomy specimen performed for a urinary bladder tumor [7].

Some authors include malignant prostate tumors discovered during the autopsy in a patient who was not diagnosed with PC in his lifetime in the category of incidental PC [8], while others prefer to categorize these tumors as latent carcinomas [4, 9].

PC is considered occult when there are clinical manifestations caused by metastases or elevated tumor markers, but the primary tumor cannot be identified [4]. Very rarely does PC presents with symptoms suggestive of a primary tumor of the digestive tract as first manifestations [10–12], in this situation establishing the prostate origin of the tumor represents a challenge for both the clinician and the pathologist.

Aim

This study describes three cases of PC in which the presentation of the prostate tumor was unusual, initially suggesting a tumor of the digestive tract.

Patients, Materials and Methods

The study was approved by the Ethical Committee of Pius Brînzeu Emergency County Hospital, Timişoara, Romania (Approval No. 215 from 15.12.2020).

Cases were selected from the database and archives of the Clinic of Radiotherapy, Emergency City Hospital, Timişoara, the Department of Urology and from the Department of Pathology, Pius Brînzeu Emergency County Hospital, Timişoara, from the period of 1998 to 2020. There were selected the cases of PC that showed a symptomatology

and/or imagistic changes that suggested a digestive neoplasm initially. All relevant clinical, imagistic, and pathological information were extracted from the clinical record and the databases of the two Hospitals, *i.e.*, age at diagnosis, the type of specimen in which the tumor was diagnosed, serum PSA, the pathological data evaluated in each case and data regarding the evolution of the disease.

For the immunohistochemical (IHC) investigation, additional sections from the selected paraffin blocks, with a thickness of 3–4 μm, were placed on Super Frost Ultra Plus slides. We used the following primary antibodies: anti-cytokeratin 7 (CK7) [clone OV-TL12/30 – DAKO, ready to use (RTU)], anti-cytokeratin 20 (CK20) (clone, Ks20.8 – DAKO, RTU), anti-PSA (polyclonal – DAKO, RTU), anti-prostate specific membrane antigen (PSMA) (clone 1D6 – Novocastra, 1/50 dilution), anti-NKX3.1 (clone EP356 – Cell Marque, RTU), anti-synaptophysin (Syn) (clone DAK-Synap, RTU) and anti-chromogranin A (CgA) (clone LK2H10 – Immunologic, 1/3000 dilution). Antigen retrieval was performed by heat-induced epitope retrieval (HIER) in target retrieval solution pH 6 (for CK20, PSMA, NKX3.1, CgA) and pH 9 (for CK7, PSA, Syn) 20 minutes, at 98°C. After the incubation with primary antibodies (15–30 minutes), we used a Horseradish peroxidase (HRP)–polymer detection system (Novolink) – 30 minutes, visualization with 3,3'-Diaminobenzidine (DAB) (5 minutes), followed by counterstaining with Hematoxylin (3 minutes).

Results

Case No. 1

A 57-year-old patient without a urological history was admitted in the Hospital for abdominal discomfort, alternating diarrhea and constipation, and was subsequently evaluated with colonoscopy that identified three polyps in the descending colon, sigmoid and rectum [a 1.5 cm polyp situated at 7 cm from the external anal orifice (EAO), a 3 cm polyp situated at 20 cm from the EAO and one measuring 1 cm, situated at 40 cm from the EAO], which were biopsied in another institution that did not provide access to the histopathological (HP) diagnosis. The patient underwent surgical intervention. Intraoperatively, a rigid rectal mass was identified, located at 7 cm from the EAO, with a diameter of approximately 3 cm, without expression on the serosa. An anterior rectal resection (ARR) with termino-terminal anastomosis was performed. The pathological report of the ARR specimen described two predominantly tubular adenomatous polyps with low (Figure 1A) and high-grade dysplasia; 11 lymph nodes (LN) were identified, two of them with metastatic involvement (Figure 1B) by a malignant proliferation composed of glands lined by a single row of cells with pale eosinophilic cytoplasm, relatively uniform, vesicular nuclei, with prominent nucleoli and rare mitotic figures, with the following IHC profile: CK7-, CK20-, and PSA+ (Figure 1C). Based on the IHC results, a diagnosis of LN metastasis from a prostatic primary tumor was established. The postoperatively measured serum PSA level showed a value of 5.8 ng/mL, with subsequent DRE detecting a small, hard prostate with a nodule in the right lobe.

The transrectal CNB of the prostate confirmed PC (Figure 1D), with a Gleason score of 7 (3+4), with an obvious extraprostatic extension [infiltration of the adipose tissue in ≥2/high-power field (HPF)] (at least pT3a, LV1). Treatment was initiated with Zoladex and Bicalutamide with good outcome of the prostatic disease.

At one year, two years and four years after surgery, the patient returned to the Hospital complaining of the recurrence of transit disorders – defecation difficulties, multiple stools of normal consistency, that were reduced in quantity. The local examination showed stenosis of colorectal anastomosis. Initially dilatation of the stenosis was performed, followed by the resection of the colorectal anastomosis and amputation of the rectum by abdomino-perineal route, with a permanent left iliac colostomy. The patient died four years after the diagnosis of PC.

Case No. 2

A 71-year-old patient without a uropathological history was admitted to the Hospital for rectal bleeding. DRE detected a vegetant, friable, hemorrhagic tumor, painful to the touch, with traces of blood on the gloved finger, situated on the anterior rectal wall, at about 5 cm from the EAO. A recto-sigmoidoscopy revealed a polypoid, ulcerated, friable bleeding rectal tumor. Computed tomography (CT) showed an eccentric thickening of the rectal wall up to 1.2 cm and a prostate measuring 4.4/3.5/4.4 cm, that centrally was slightly inhomogeneous. The endoscopic biopsy of the rectal wall tumor showed an intestinal-type adenocarcinoma. Anterior resection of the rectum with low termino-terminal anastomosis was performed for a clinically staged rectal tumor cT4N2M0 (IIIC). During the surgical intervention, a tumor mass of approximately 8/6 cm was detected in the distal 1/3 of the rectal ampulla. At the dissection of the sphincter and the anal canal, the suspicion of prostate invasion by the rectal cancer (RC) was raised, and partial prostate resection was performed.

HP examination of the resection specimen revealed synchronous tumors: (*i*) intestinal adenocarcinoma G2pT2 N0LV0 (Figure 2, A and B), (*ii*) prostatic adenocarcinoma with a Gleason score of 9 (4+5), grade group 5, invading the outer layers of the bowel (Figure 2, C and D), presenting predominantly poorly formed/fused glands and individual infiltrative cells, with a foamy/pale or amphophilic cytoplasm and large, vesicular nuclei, with eosinophilic macronucleoli, perineural invasion with two perirectal LN presenting PC metastases – pT4N1LV1Pn1. The patient is alive after two years and nine months/two years and six months after the diagnosis of RC and PC, respectively.

Case No. 3

A 59-year-old patient, with no significant personal or familial pathological history, except for a grandmother with breast cancer, athletic, with no previous determinations of serum PSA level, presented to the Hospital in June 2020, complaining of decreased appetite, constipation, and significant weight loss (approximately 10 kg in two months), lower back pain, and marked asthenia.

At the time of admission, the first set of laboratory tests performed detected microcytic hypochromic anemia [hemoglobin (Hb) 9.4 g/dL], an increased alkaline phosphatase (ALP) 335 U/L, and a low quantity of fluid accumulated in the left pleural cavity detected during an exploratory transcutaneous ultrasound of the abdominal cavity.

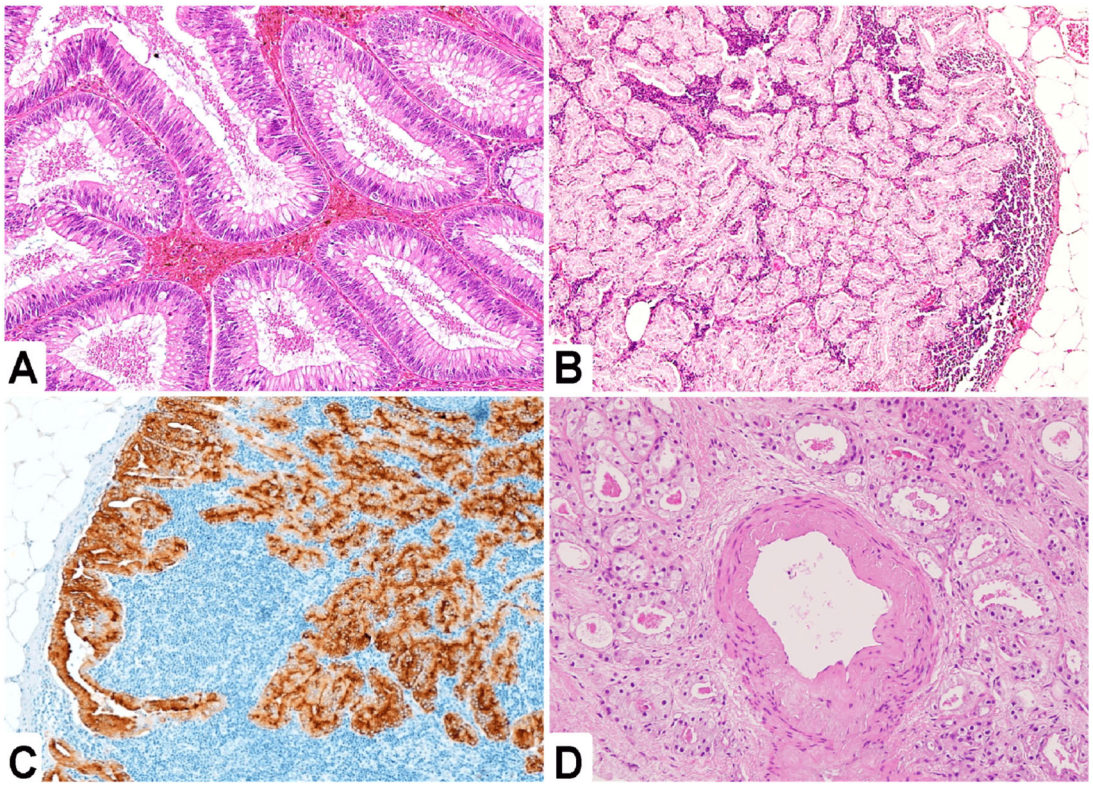

Figure 1 – ***Microscopic findings of the first case: (A) Tubular adenomatous polyp with low grade dysplasia and (B) lymph node metastasis from a prostatic adenocarcinoma, diagnosed in the rectal resection specimen; (C) Positive reaction for PSA within the metastatic deposits in the perirectal lymph node; (D) Subsequently confirmed prostatic carcinoma on core-needle biopsy. HE staining: (A and D) ×200; (B) ×100. Anti-PSA antibody immunomarking: (C) ×100. HE: Hematoxylin–Eosin; PSA: Prostate specific antigen.***

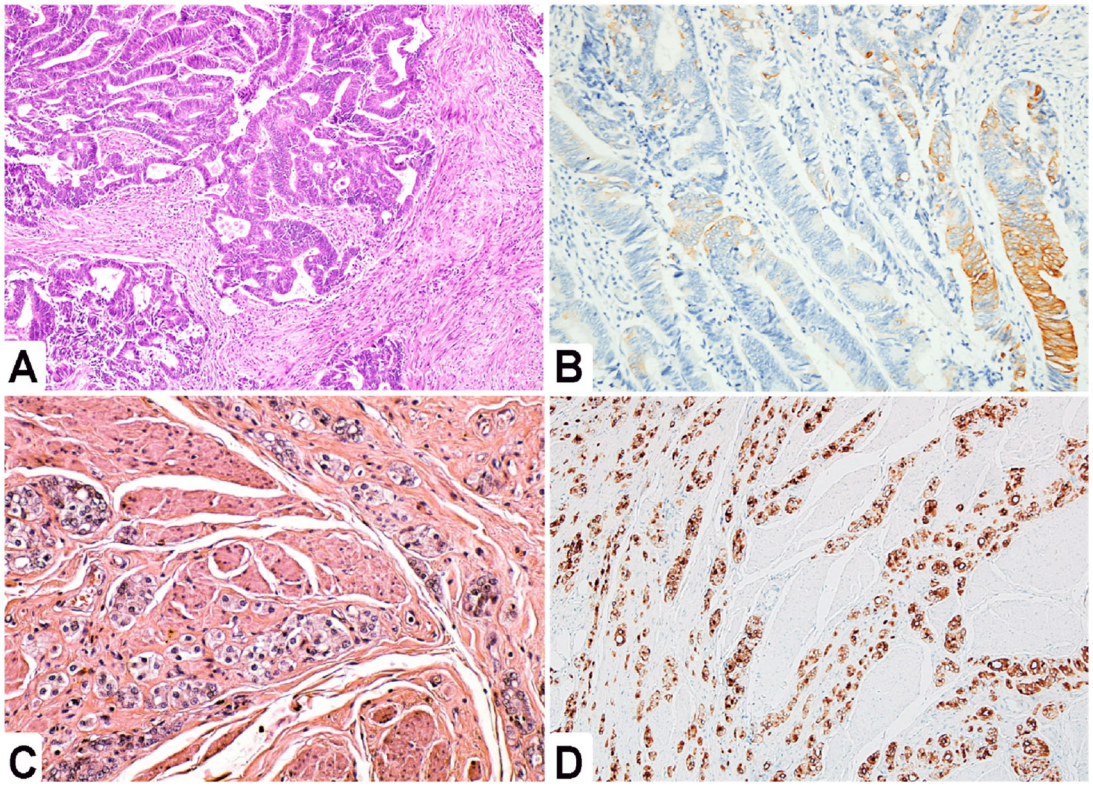

Figure 2 – ***Histopathological features of the second case: (A) Moderately differentiated intestinal adenocarcinoma of the rectum in the resection specimen; (B) Tumor cells showed focal positive reaction for CK20; (C) Simultaneously, the intestinal wall was invaded by a prostatic adenocarcinoma composed of poorly formed/fused glands and individual infiltrative cells, with (D) positive reaction for PSA. HE staining: (A) ×100; (C) ×200. Anti-CK20 antibody immunomarking: (B) ×200. Anti-PSA antibody immunomarking: (D) ×100. CK20: Cytokeratin 20; HE: Hematoxylin–Eosin; PSA: Prostate specific antigen.***

A CT of the thorax, abdomen and pelvis, performed in another clinic, described secondary pleural determinations, multiple lymphadenopathies: mediastinal, in the pulmonary hilum, retrocrural, retroperitoneal, interaortocaval, paracaval, paraaortic and adjacent to the left renal hilum, of maximum dimension of 2.7 cm, intrapelvic lymphadenopathies, with a maximum diameter of 2.56 cm, secondary peritoneal determinations in the form of peritoneal micronodules between the loops of the small intestine, plated at the distal 1/3 of the sigmoid colon and the rectum that had a thickened wall, reduced ascites, and edema in the subcutaneous cellular tissue of the abdominopelvic walls and the proximal 1/3 of the thigh, multiple osteosclerotic bone lesions in the ribs, sternum, shoulder blades, thoracic spine, lumbar spine, pelvis and proximal 1/3 of the femoral bones. The prostate had the following dimensions: 2.89/2.94/3.47 cm, with a prominent posterior contour in the right lobe and seminal vesicles with heterogeneous iodophilia. Suspecting a malignant proliferation of the digestive tract, gastroscopy and colonoscopy were performed that ruled out such a tumor. The re-evaluation of the abdominal and pelvic CT images in our hospital excluded the presence of the described peritoneal metastases and the thickening of the recto-sigmoid wall, changes attributed to the obstructive edema.

The magnetic resonance imaging (MRI) investigation confirmed this interpretation, indicating the need for a urological evaluation. The DRE detected a moderately enlarged prostate with clear boundaries, smooth surface, flattening of median sulcus, firm consistency, no clear signs of malignancy, but based on the heterogeneous appearance of the prostate on MRI and the osteosclerotic nature of the bone metastases, it was decided to determine the serum PSA level that had a value of 324 ng/mL. CNB of the prostate was performed, and a poorly differentiated adenocarcinoma (Figure 3, A and B) was identified, represented by solid sheets, cords and trabeculae of cells, rare cribriform and abortive glands, monotonous tumor cells, with hyperchromatic nuclei, prominent nucleoli, and aspects of perineural invasion. The IHC investigations showed an extensive positivity for PSA (Figure 3C), NKX3.1 (Figure 3D), and PSMA and focal positivity for Syn and CgA, establishing the diagnosis of prostatic adenocarcinoma with focal neuroendocrine differentiation, with a Gleason score of 9 (grade group 5). The ALP measured in a dynamic mode showed an initial value of 335 U/L and then 935 U/L before starting the treatment. After seven months of treatment with Docetaxel, Goserelin and more recently Zometa, the patient's condition improved significantly, with a weight gained of 9 kg, a decreased PSA value to 1.7 ng/mL, increased Hb of 13 g/dL, and an ALP level of 116 U/L.

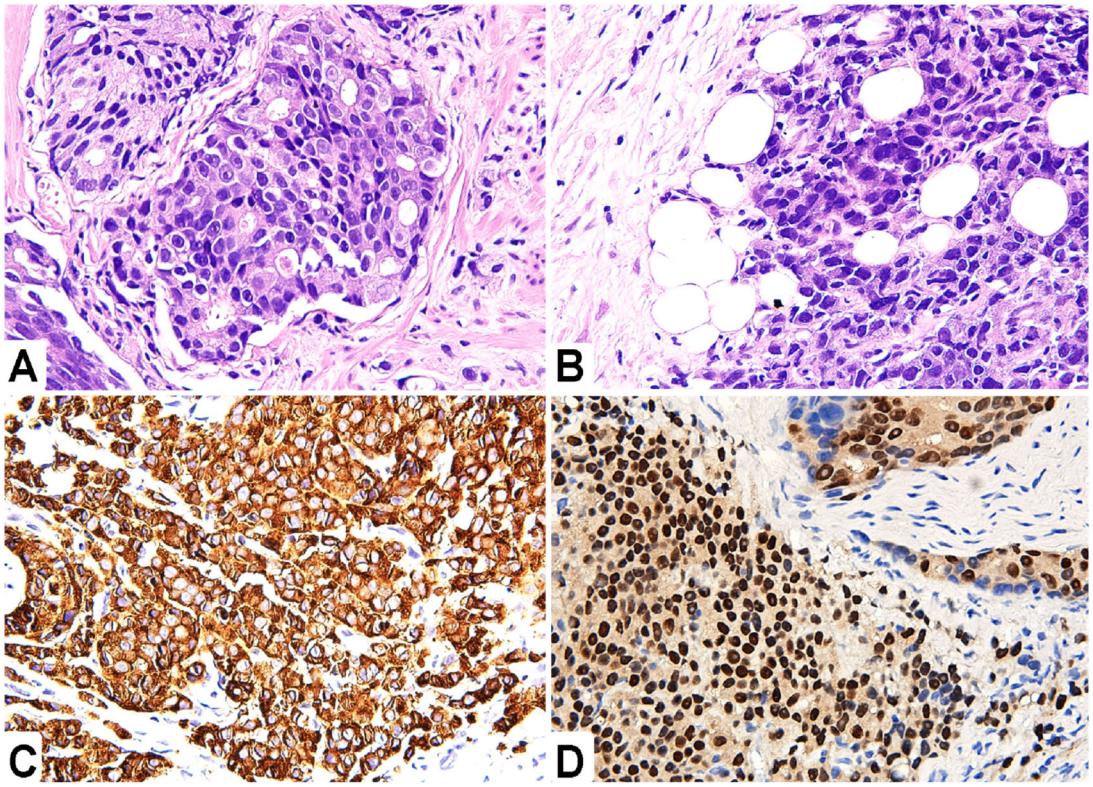

Figure 3 – ***Microscopic features of the third case: (A) Histopathological aspects of prostate acinar adenocarcinoma (Gleason score 9 = 5+4, grade group 5) with (B) extraprostatic extension; (C) Tumor cells with positive reaction for PSA and (D) nuclear staining for NKX3.1. HE staining: (A and B) ×400. Anti-PSA antibody immunomarking: (C) ×400. Anti-NKX3.1 antibody immunomarking: (D) ×400. HE: Hematoxylin–Eosin; PSA: Prostate specific antigen.***

Discussions

We identified three cases of PC with an atypical form of presentation, which initially suggested or mimicked a digestive pathology. The first case, in which PC was diagnosed in a 57-year-old patient, is different from most cases in the literature reporting the diagnosis of PC after the examination of LN, extracted during low anterior resection or abdominoperineal resections for RC [13, 14], through the absence of an invasive rectal tumor. In this

case, RC was suspected based on the symptoms, the presence of polyps at the colonoscopy examination and on the intraoperative findings. Given the relatively young age, less common for a PC and the concomitant presence of intestinal polyps, which certainly contributed to the digestive symptoms of the patient, the case is illustrative for the diagnosis difficulties of simultaneous rectal and prostate tumors, here represented by intestinal polyps and PC. There may be lymphatic drainage connecting the pararectal regions to the internal and external iliac regions [15] and a lymphatic connection could exist between the hypogastric lymphatic drainage and the mesorectal one [16] which would explain the presence of PC metastases in the perirectal LN. Extended surgery for the presumed RC could have been avoided in this case if the preoperative investigation had included PC screening by DRE and determination of serum PSA levels that had a value higher than that accepted as the normal maximum value in the patient age group – 2.5 ng/mL in the study of Anderson *et al.* [17]. The value of 5.8 ng/mL of serum PSA is still surprising for a PC with LN metastases, the direct relationship between serum PSA value and PC extension being well known, only a small proportion of patients (about 5%) with PSA levels of 4.0–10.0 ng/mL having either seminal vesicle or LN involvement [18]. However, if the rectal resection had not been performed, PC would have remained undiagnosed in a relatively young patient, because Romania offers no implemented screening for PC detection, screening that address men above 50–55 years, according to most of the guidelines developed by the entities recommending the screening for PC [19]. The involvement of the rectum through PC can produce digestive symptoms such as constipation, alternating constipation and diarrhea, rectal bleeding [20], narrow stool, abdominal or rectal pain, the urgency of defecation, incontinence [21], all of can be wrongly attributed to a colonic tumor. Similarly, the rectal invasion by the PC, with ulceration of the mucosa, may lead to errors in the interpretation of preoperative biopsies in patients where the digestive symptoms caused by PC raise the suspicion of RC. In this case, the diagnosis of LN metastasis from PC was facilitated by the good differentiation of the prostate tumor (Gleason score 7/grade group 2), but in most cases, the rectal invading PC is poorly differentiated, with a Gleason score between 8 and 10, thus discriminating between the two types of carcinomas can be difficult [22]. Although, theoretically, the two categories of tumors could be distinguished based on the histological aspects evaluated on Hematoxylin–Eosin (HE)-stained slides, namely: the columnar appearance of tumor cells, mucus secretion or signet ring features with mucin content of the tumor cells, the presence of dirty necrosis, desmoplastic stroma, dense inflammatory infiltrate in the intestinal adenocarcinomas *vs.* small glands, a cuboidal appearance of cells, prominent eosinophilic nucleoli, a generally reduced mitotic activity in prostate adenocarcinomas. However, some of these separate criteria overlap sometimes, so that the differentiation remains, in some cases, the prerogative of IHC methods: positive reaction for PSA, prostate-specific acid phosphatase (PSAP), PSMA, prostein, NKX3.1 and erythroblast transformation specific (ETS)-regulated gene (ERG) in prostate adenocarcinomas [22–25], and CK20, carcinoembryonic antigen (CEA), caudal-type homeobox 2 (CDX2), nuclear β-catenin, villin or special AT-rich sequence-binding protein 2 (SATB2) in rectal adenocarcinomas [26–28]. The confusion between prostatic and colorectal adenocarcinoma is more likely to occur in particular forms of PC, such as ductal adenocarcinomas and mucinous prostate adenocarcinomas or prostate adenocarcinomas with a focal mucinous contingent. Prostate ductal adenocarcinomas may be confused with intestinal adenocarcinomas due to a complex glandular or sometimes papillary architecture, obvious mitotic activity, to which comedonecrosis and sometimes mucin-secreting or goblet cells reported in particular subtypes of ductal adenocarcinoma may be added [29–31]. Prostatic mucinous carcinoma or carcinoma with vacuoles/"signet ring"-like cells (formerly called "signet ring" cell carcinoma) can be misinterpreted as intestinal adenocarcinomas due to the extracellular mucin in the first case or intracellular vacuoles that give the cell a "signet ring" appearance in the latter, but in both cases, the tumor cells are positive for prostatic specific markers and in the case of PC with vacuoles, the vacuoles do not contain mucin [23, 32]. The colonization of normal prostate ducts by intestinal adenocarcinoma has been documented very recently [33], thus representing an extremely difficult situation to differentiate from intraductal carcinoma of the prostate or ductal adenocarcinoma of the prostate, the only diagnostic method that can confirm this diagnosis is IHC.

The second case, in which PC was simultaneously diagnosed with RC in a 71-year-old patient, falls into the category of double-synchronous primary malignancies. Synchronous, rectal/rectosigmoid and prostate tumors are not so rare, in approximately 1/6 of men over 50 years of age diagnosed with RC, preoperative screening detects synchronous PC [34]. Due to the proximity of the two organs, the invasion of a malignant prostate tumor in the rectum or *vice versa*, a neoplasm of the rectum in the prostate, is possible, although the prostate capsule and Denonvilliers' fascia are barriers that initially oppose this invasion [26]. Literature data show that the rectal/rectosigmoid involvement through PC is more frequent than the involvement of the prostate by RC [21, 26]. The involvement of the rectum through PC can be achieved by direct invasion or by metastasis [13], leading to the following models of damage: anterior rectal mass with or without ulceration in 52% of the cases, an annular stricture in 45%, and separate metastasis in 3% [21]. Given the concomitant presence of PC and RC, the patient's digestive symptoms are comprehensible, and it cannot be estimated to what extent PC also contributed to it, although usually the digestive symptoms dominate the clinical picture [35]. Also, the simultaneity of the two tumors made it impossible for the DRE to document the two tumors, as the difficulties in identifying synchronous rectal and prostate tumors in DRE are known, both for those with limited experience and for experienced medical practitioners, given the low sensitivity of the method [36]. In the context of the same simultaneity, identifying the involvement of the rectum by PC, in the form of infiltration of intestinal external layer and specifying the prostatic origin of LN metastasis was facilitated by the experience of the pathologist who noticed the different HP appearance of the two tumors,

contributing to the documentation of the two distinct tumor categories, thus the avoidance of RC upstaging and/or PC downstaging, with important therapeutic consequences. Given that the highest incidence for PC is seen in elderly men (>65 years of age) [37], and that the patient was 71 years old, as in the first case, a determination of the serum PSA level would have raised the suspicion of a PC, which could have been confirmed by transrectal CNB, a maneuver impossible to perform after rectal amputation [36, 38]. Subsequently, it is worth noting the suggestion to investigate all patients with RC, by DRE, determining the serum level of PSA and MRI [38], to detect a synchronous PC, a scenario that, if true, requires an adapted therapeutic strategy, which must address both tumors and to be individualized considering the age of the patients, the stage of the tumors, the presence of comorbidities and, last but not least, the patient's choice. In cases where RC and PC are synchronous, failure to recognize diagnostic clues on usual staining and the absence of IHC investigations may lead to the misinterpretation of PC metastases in perirectal LN as determined by RC, an aspect also reported by Murray *et al.*, who showed that in 40% of synchronous prostate and rectal tumor cases, PC metastases from perirectal LN were misinterpreted as RC metastases [13].

In the third case, the relatively young age of the patient (59 years), unusual for a PC, cumulated with weight loss, constipation, asthenia, and the initial description of the abdominal and pelvis CT with low level ascites, peritoneal micronodules and the thickening of the sigmoid colon and rectum walls, all contributed to the suspicion of a metastatic tumor originating in the digestive tract, which was ruled out after thorough endoscopic examinations. The involvement of the peritoneum, described in the pelvic and abdominal CT investigation, is common in gastric, colorectal, pancreatic, and gynecological carcinomas [39], and is very rarely reported in PC, with rare case reports and small series of cases, in which PC, usually with a Gleason score higher than 7 and in advanced stages, sometimes including castrated resistant tumors, that involve the peritoneum, with or without ascites [40–43]. However, there are reported cases of localized prostate tumors, surgically removed with minimally invasive technics (laparoscopic/robotic), which evolved with peritoneal metastases, the peritoneum representing the only metastatic location of PC. One of the hypotheses that try to explain this phenomenon is the iatrogenic theory, with peritoneal seeding during laparoscopic ± robotic radical prostatectomy [40, 42]. Peritoneal metastases reported in the evolution of PC, can be single [42] or multiple [41, 43, 44], of various sizes, ranging from a few millimeters to a few centimeters in diameter, involving the peritoneum, omentum or mesentery, the single ones and/or the ones that appear after laparoscopic interventions being located just proximal to the prostatectomy exit port above the umbilicus [42]. Involvement of the peritoneum in the absence of other localizations of PC metastases raises problems regarding the method of peritoneal seeding, the hematogenous path being excluded by the authors of a study [42], based on the absence of circulating tumor cells in repeated determinations. Apart from iatrogenic dissemination [42], the possibility of peritoneum involvement at the level of positive margins [42] or other yet unexplained mechanisms, remains under discussion. From the perspective of the presumed peritoneal involvement, the case is illustrative for the difficulties of the imagistic diagnosis of peritoneal metastases, with the possible errors of interpretation determined by the obstructive edema. With the exclusion of the digestive origin of the tumor, the presence of extensive osteosclerotic bone metastases and imaging aspects of the prostate and seminal vesicles raised the suspicion of a PC, although the DRE findings were not in favor of such a diagnosis in a relatively young patient (59 years), without a family history of PC, physically active, who had no previous serum PSA determination. It should be noted that although osteoblastic/osteosclerotic bone metastases are usually encountered in PC, digestive cancers mostly causing osteolytic metastases, there are reports of esophageal, colonic [45] and gastric [46] tumors that produce osteosclerotic or mixed metastases (osteolytic and osteosclerotic) [47]. Lastly, another case peculiarity is that the patient also presented metastatic pleural involvement, which is extremely rare in PC, as shown by Vinjamoori *et al.* who found that of the rare cases of PC with lung metastases, only 1% were found to have pleural involvement or effusions [48].

Conclusions

Clinicians, urologists, radiologists, pathologists, and oncologists need to become familiar with unusual forms of PC presentations that are not so uncommon. PC should always be considered in the differential diagnosis of a rectal tumor, and patients should be screened by DRE and serum PSA level, even if they are less than 60 years of age. IHC investigations are essential for the diagnosis in such cases and should include prostatic line markers. The integrated interpretation within interdisciplinary teams, of the clinical manifestations, imagistic and serological changes, in a patient suspected of a malignant tumor, would shorten the diagnosis time, and would contribute to the reduction of clinical, imaging, and pathological diagnostic errors.

Conflict of interests

The authors declare that they have no conflict of interests.

Two of the three cases were briefly presented at the 30th European Congress of Pathology, Bilbao, Spain [E-PS-24-036: Dema A, Taban S, Anderco D, Georgescu G, Lazureanu C, Bardan R, Cumpanas A, Dema S. Atypical presentation of prostate carcinoma. Virchows Arch, 2018, 473(Suppl 1):S334. https://doi.org/10.1007/s00428-018-2422-1; https://link.springer.com/content/pdf/10.1007/s00428-018-2422-1.pdf], but in the present paper the two cases are more detailed, with additional data on the history and evolution of the disease.

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Corresponding author
Alis Liliana Carmen Dema, Professor, MD, PhD, Discipline of Morphopathology, Department of Microscopic Morphology, Victor Babeş University of Medicine and Pharmacy, 2 Eftimie Murgu Street, 300041 Timişoara, Romania; Phone +40722–771 966, e-mail: dema.alis@umft.ro

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