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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Pure squamous cell carcinoma of primary pancreatic origin

Bojana Mišković[1], Milica Mitrović-Jovanović[2,3], Boris Tadić[3,4], Dušan Šaponjski[2,3], Đorđe Knežević[3,4]

[1]University Clinical Center of Serbia, Center for Radiology, Emergency Radiology Department, Belgrade, Serbia;
[2]University Clinical Center of Serbia, Center for Radiology, Radiology Department of the First Surgery Clinic, Belgrade, Serbia;
[3]University of Belgrade, Faculty of Medicine, Belgrade, Serbia;
[4]University Clinical Center of Serbia, First Surgery Clinic, Department of Hepatobiliary Surgery, Belgrade, Serbia

SUMMARY
Introduction Primary, "pure" squamous cell carcinoma (SCC) is an exceptionally rare pancreatic malignancy that has been described in sporadic case reports. The appearance of this rare entity created a diagnostic dilemma for us, therefore, in this case report, we are focused on the radiological detection and characterization, pathogenesis, and therapeutic options of pure pancreatic SCC.
Case outline In an 80-year-old female patient, a partially necrotic mass in the tail of the pancreas was detected by computed tomography, which is the rarest localization of this tumor. On the performed imaging, the tumor showed predominantly malignant features with a surprising definitive histopathological diagnosis in the direction of pure SCC. Distal pancreatectomy with splenectomy was performed because of the infiltration of lienal vascular structures.
Conclusion Due to the very aggressive form of this tumor and poor prognosis, early detection, risk factors control, genetic burden, and optimization of surgical and therapeutic management can improve the quality of life and prolong the overall survival period.
Keywords: squamous cell carcinoma; computed tomography; distal pancreatectomy

INTRODUCTION

Primary squamous cell carcinoma (SCC) of the pancreas is a supremely rare entity and the main reason for this is the lack of squamous cells in the pancreas [1, 2]. Pathophysiology is not entirely clear, but there is suspicion of inflammatory-based squamous metaplasia of the ductal columnar cells [3]. There are not many published articles describing the pure SCC of the tail of the pancreas. Consequently, there is no clinical management protocol for this type of pancreatic carcinoma and the survival rate is poor, because of its highly aggressive behavior [2]. In 2020, Qin et al. [4] presented the results of their population-based study that showed for SCC a median overall survival of only three months. Classic risk factors for ductal adenocarcinoma (ADC) like smoking and chronic pancreatitis, do not show association with SCC [5]. Adenosquamous carcinoma (ASC) is another rare entity (with mixed elements of ADC) and squamous carcinoma), but yet more common than pure squamous carcinoma as in our case. ASC is the main differential diagnosis for SCC, but there is also metastatic SCC from other sites in the body and pancreatoblastoma [2, 6].

CASE REPORT

An 80-year-old woman was admitted to the Clinic for Digestive Surgery of the University Clinical Center of Serbia because of epigastric pain and nausea that lasted for a year and a half. Laboratory analyses showed elevated C-reactive protein (11.9 mg/L), as well as elevated tumor markers CA 19-9 (201 kU/L) and carcinoembryonic antigen (CEA) (12.4 μg/L), but the pancreatic amylase (39 U/L) and lipase (52 U/L) were in a normal range. A computed tomography (CT) was performed in our hospital and revealed a necrotic lesion in the pancreatic tail with postcontrast enhanced borders, with a maximum diameter of 52 × 43 mm. The surrounding adipose tissue was of higher density primarily due to the infiltrative growth of the tumor. The contact of the described tumor lesion with the stomach wall and the spleen capsule was clearly visualized (Figures 1 and 2). The splenic vein was thrombosed (Figure 1). Considering the values of CA 19-9 and CEA, the conclusion of the performed diagnosis was a centrally necrotic lesion of the tail of the pancreas with predominantly malignant CT characteristics. An esophagogastroduodenoscopy was performed and even though the extramural compression on the minor gastric curve was

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Correspondence to:
Bojana MIŠKOVIĆ
Južni bulevar 130
11000 Belgarde
Serbia
bomis310@gmail.com

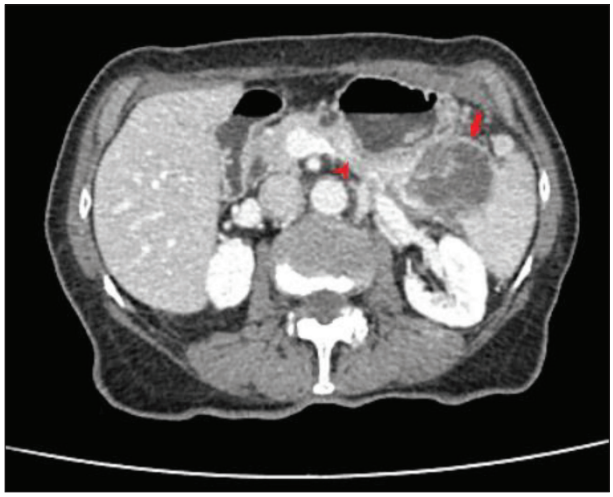

Figure 1. Axial contrast-enhanced computed tomography scan (125 ml iodine contrast, 1 mm slice thickness); the necrotic lesion with post-contrast enhanced borders (arrow) which is in the contact with the gastric body and spleen capsule; thrombosed splenic vein (arrowhead)

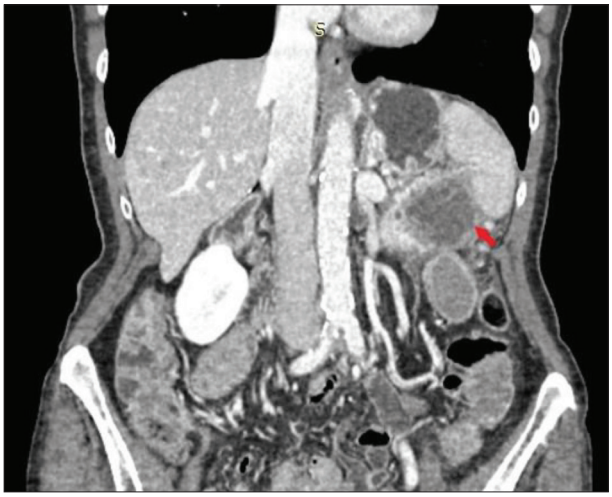

Figure 2. Coronal contrast-enhanced computed tomography scan (125 ml iodine contrast, 1 mm slice thickness); the same necrotic lesion (arrow) which is in this image in contact with the spleen capsule

seen, the mucosa had a normal appearance, without clear signs of infiltration. After preparation, the patient underwent surgery, and distal pancreatectomy and splenectomy were performed. The pathohistological finding was the primary *squamocellulare* invasive carcinoma of the pancreatic tail with a histological aspect of "pure" squamous differentiation of pancreatic carcinoma, showing frequent foci of pseudoglandular arrangement of squamous cells (Figure 3). The patient was discharged from the hospital after 16 days with the decision to receive systemic chemotherapy (5-fluorouracil) in the regional oncological center.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments and comparable ethical standards. Written consent to publish all shown material was obtained from the patient.

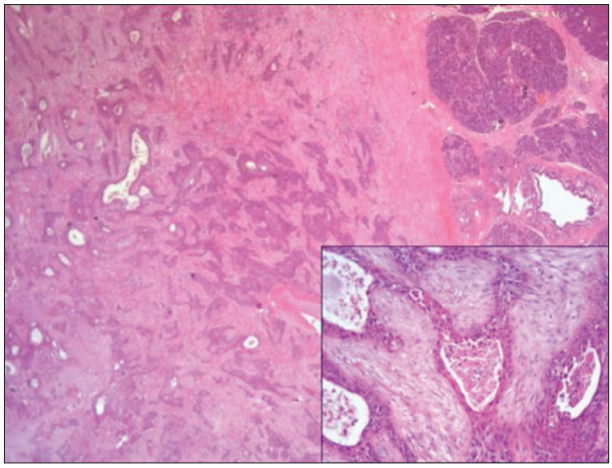

Figure 3. Histological aspect of "pure" squamous differentiation of pancreatic carcinoma, showing frequent foci of pseudoglandular arrangement of squamous cells (inlet picture) suggesting precancerous squamous metaplasia of pancreatic ducts

DISCUSSION

Primary pure SCC of the pancreas is a very rare tumor with an incidence from 0.5% to 2% of all exocrine pancreatic neoplasms [1, 7]. In a survey conducted in Japan back in 1992, researchers investigated 1300 cases of pancreatic cancer through autopsies. Among these cases, only 0.7% were identified as SCC [8]. When comparing pancreatic ADC to pancreatic SCC, the latter is linked with poorer differentiation, displaying a more aggressive nature and leading to worse overall outcomes [9]. Currently, there are no studies available regarding the molecular profile of pancreatic squamous carcinoma. Additionally, there are no retrospective or prospective studies that have identified the optimal therapy for these tumors. Unlike pancreatic ADC, risk factors like smoking and chronic pancreatitis do not seem to be associated with pancreatic SCC.

Due to its rarity, sporadic case reports of this exceptionally unusual tumor have been published. The appearance of this rare entity created a diagnostic dilemma for us and required a review of the available literature, therefore, in this case report we are focused on the radiological detection and characterization, pathogenesis, and therapeutic options of pure pancreatic SCC [10]. Exocrine pancreatic lesions such as SCC and ADC arise from the ductal tissue. A form of ASC has also been described. The origin of this tumor is based on squamous metaplasia of ductules along with other pathogenic factors that contribute to malignant alteration [10, 11]. Some of the theories explaining malignant differentiation to SCC mention the neo-transformation of multipotent stem cells as well as aberrant or ectopic squamous cells. Differentiation of ADC into SCC is also possible, as well as a mixed tumor form [12]. There is a frequent association of this malignancy with chronic pancreatitis, which is considered a risk factor. There is not much data on gene mutations associated with SCC, but there are indications of a hereditary influence as well as the detection of *BRCA-2* mutation in a few published cases [10].

In their study, Ford et al. [5] showed that the majority of patients are diagnosed with the condition in their eighth decade of life, and they found no discernible difference in diagnosis based on gender. The leading symptoms include anorexia, pain in the epigastrium and back, and diabetes, depending on the localization in the pancreas, icterus, gastric outlet obstruction, and rarely may occur upper gastrointestinal bleeding [13, 14].

Radiological characterization is very challenging. CT plays a very important role in the evaluation of patients with pancreatic pathology. Likewise, in our case, the CT examination showed a dominantly necrotic lesion with expansive and extra-pancreatic growth. The main differential diagnosis is pancreatic ADC or ASC, in contrast to which SCC shows more pronounced neovascularization, which contributes to CT detection of intralesional postcontrast viable zones [12]. In our case, the peripheral area of the tumor was hyperdense with irregular borders along with a higher density of perilesional fat tissue. The tumor involved the tail of the pancreas, which is the rarest localization when it comes to pure SCC. Vascular invasion is common, as in our patient, where the tumor process infiltrated the lienal vein, so together with the distal pancreatectomy, a splenectomy was performed. The role of positron emission tomography/CT is in the evaluation of the secondary dissemination of the disease as well as in the detection of the possible primary origin of SCC. Unfortunately, at the time of the discovery of this disease, the tumor is often in a locally advanced stage. CT and endoscopic ultrasound-guided needle biopsy or laparoscopic biopsy are procedures that are very important in obtaining an adequate sample of the tumor tissue for further histological and immunohistochemical processing [10]. Palliative chemotherapy and radiotherapy are the only treatment options in unresectable patients. Surgical resection is possible in less than one third of the patients, and bearing in mind the greater aggressiveness of this type of tumor, the prognosis is worse [15]. As Ntanasis-Stathopoulos et al. concluded, survival is significantly longer in patients after surgical resection [13, 16].

Thanks to the progress in prevention in recent years, early detection, and treatment of pancreatic cancer, an improvement in overall survival after resection is observed. Although a very rare and aggressive form of malignant pancreatic process, due to the improvement and optimization of the surgical techniques and neoadjuvant chemoradiotherapy, as well as advances in imaging modalities, we can hope for better results when it comes to the prognosis of the disease [13].

Conflict of interest: None declared.

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„Чисти“ сквамоцелуларни карцином примарно панкреасног порекла

Бојана Мишковић[1], Милица Митровић-Јовановић[2,3], Борис Тадић[3,4], Душан Шапоњски[2,3], Ђорђе Кнежевић[3,4]

[1]Универзитетски клинички центар Србије, Центар за радиологију, Одељење ургентне радиологије, Београд, Србија;
[2]Универзитетски клинички центар Србије, Центар за радиологију, Одељење радиологије Прве хируршке клинике, Београд, Србија;
[3]Универзитет у Београду, Медицински факултет, Београд, Србија;
[4]Универзитетски клинички центар Србије, Прва хируршка клиника, Одељење хепатобилијарне хирургије, Београд, Србија

САЖЕТАК

Увод Примарни, „чисти“ сквамоцелуларни карцином је изузетно редак малигнитет панкреаса, који је описан у спорадичним приказима болесника. Појава овог ретког ентитета створила је дијагностичку дилему за нас, те смо у овом приказу болесника фокусирани на радиолошко откривање и карактеризацију, патогенезу и терапијске опције „чистог“ сквамоцелуларног карцинома панкреаса.

Приказ болесника Код болеснице старе 80 година компјутеризованом томографијом је откривена делимично некротична маса у репу панкреаса, што је најређа локализација овог тумора. На урађеном прегледу, тумор је показао предоминантно малигне карактеристике, са изненађујућом дефинитивном хистопатолошком дијагнозом у правцу „чистог“ сквамоцелуларног карцинома. Урађена је дистална панкреатектомија са спленектомијом, због инфилтрације лијеналних васкуларних структура.

Закључак С обзиром на то да је овај тумор веома агресиван и има лошу прогнозу, рано откривање, контрола фактора ризика, генетског оптерећења и оптимизација хируршког и терапијског лечења могу побољшати квалитет живота и продужити укупан период преживљавања.

Кључне речи: сквамоцелуларни карцином; компјутеризована томографија; дистална панкреатектомија