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CASE REPORT

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Squamous cell carcinoma and lipomatous pseudohypertrophy of the pancreas

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Abstract A 68-year-old woman who had been treated for non-insulin-dependent diabetes mellitus for the past 20 years was admitted to hospital because of abdominal pain and weight loss. Radiological investigation revealed a tumour in the body of the pancreas and numerous intraductal calcifications in both the tail and the head of the pancreas. Left-sided pancreatectomy was performed to remove the tumour. The resection specimen showed fatty enlargement of the parenchyma and numerous intraductal calcifications in the tissue adjacent to the tumour, which was 7 cm in diameter and was found to be a primary squamous cell carcinoma with a spindle cell component. There was also lipomatous pseudohypertrophy.

Key words Pancreatic neoplasm · Squamous cell carcinoma · Sarcomatoid carcinoma · Lipomatous pseudohypertrophy

Introduction

Pure squamous cell carcinoma is a rare malignant epithelial tumour of the exocrine pancreas, accounting for 0.5–3.5% of ductal cell carcinomas [3, 5]. Although its histogenesis is poorly understood, it has been suggested that it may be a variant of adenosquamous carcinoma in which the squamous component has overrun the glandular elements [17].

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We report a case of squamous cell carcinoma of the pancreas with a spindle cell component in association with lipomatous pseudohypertrophy and numerous intraductal calculi in the rest of the gland. Lipomatous pseudohypertrophy is an unusual benign entity, which has, in exceptional cases, been associated with malignancy [2]. The associated tumours in the cases reported were adenocarcinoma [14] or leiomyosarcoma [16] of the pancreas, but to our knowledge, fatty replacement of the whole pancreatic gland co-existing with squamous cell carcinoma has not been described. Such an association seems to be merely fortuitous.

Clinical history

A 68-year-old woman (1.71 m, 86 kg) was examined because of a 1-year history of left upper abdominal pain and weight loss (6 kg in the last 4 months). The pain had gradually worsened over time and radiated into the back, without nausea, vomiting, diarrhoea, or jaundice. There was no history of alcohol consumption, acute or chronic pancreatitis or hereditary pancreatic disease. For 20 years, she had been receiving gliclazide (160 mg per day) for treatment of non-insulin-dependent diabetes mellitus. This treatment had effectively controlled her blood glucose level. There was no evidence of pancreatic exocrine insufficiency. The physical examination was normal except for a tender left upper abdomen. Carcinoembryonic antigen and CA 19.9 levels in the serum were normal. Endosonography and computed tomography scan revealed numerous amorphous intraductal calcifications in the pancreas, some obliterating the main and accessory ducts. They also showed a mass with a diameter of 40 mm in the body of the pancreas, with no involvement of splenic vessels. Intraductal stones were also present in the head of the pancreas, suggesting that they had preceded the development of the neoplasm. A pancreatic needle biopsy of this mass revealed a squamous cell carcinoma. The preoperative work-up excluded a pancreatic metastasis of an extrapancreatic squamous cell carcinoma. Oesogastroscopy, chest CT scan, and pelvic, rectal, ear, nose and throat examinations were normal. A distal pancreatectomy and a cholecystectomy were performed. During the operation neither ascites nor metastasis was found, but the nontumour part of the pancreatic gland appeared to be replaced by fat. Eight months after the surgical resection, the patient is alive without any signs of recurrence or metastasis.

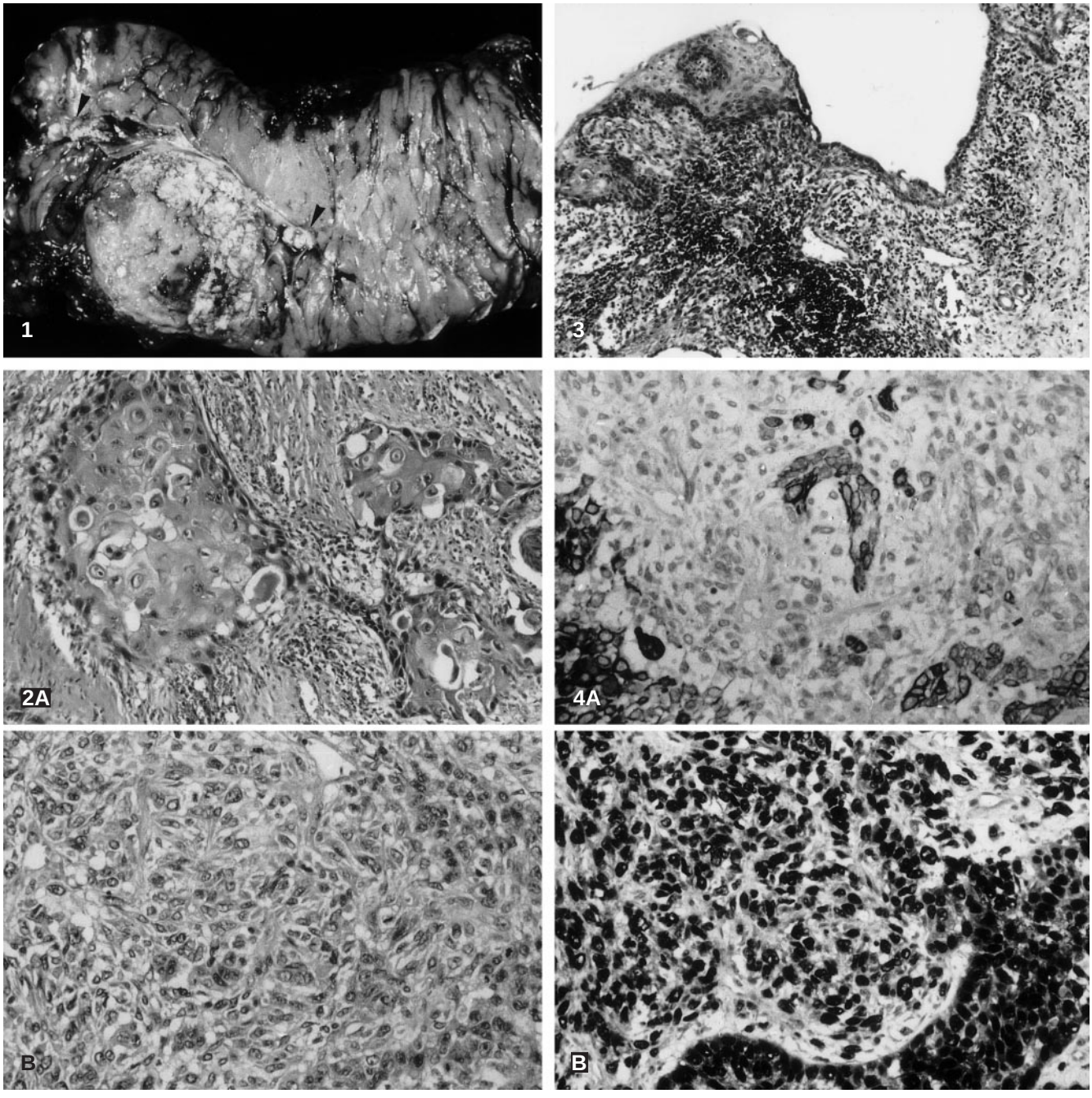

Fig. 1 Gross appearance of the tumour. A whitish mass, 7 cm in diameter, can be seen in the inferior part of the body of the pancreas. Note the calcifications in the duct of Wirsung (*arrowheads*) and the fatty replacement of the gland

Fig. 2 A, B Microscopic appearance of the tumour. **A** Irregular nest of malignant epithelial cells showing a pavement-like growth pattern and keratinization. **B** Area of interlacing bundles of malignant spindle cells

Fig. 3 Immature squamous metaplasia of the epithelium lining a large pancreatic duct

Fig. 4 A, B Immunohistochemical staining of the tumour. **A** Cytokeratin (KL1) is strongly expressed in the cytoplasm of carcinomatous squamous cells; it is expressed focally in the malignant spindle cells. **B** Nuclear p53 expression is strongly detected in both carcinomatous squamous cells and spindle cells

Materials and methods

The surgical specimens were fixed with 10% formaldehyde and embedded in paraffin. Sections (3 μm thick) were stained with haematoxylin & eosin, alcian blue and periodic acid–Schiff with and without prior diastase digestion. Immunohistochemical analysis was performed using an indirect immunoperoxidase technique with DAB revelation and the following primary antibodies: anti-cytokeratin cocktail (KL1, Immunotech, 1:100 dilution), anti-p53 protein (DO-7, Dako, 1:100 dilution), anti-vimentin (Dako, 1:50 dilution), anti-desmin (Dako, 1:50 dilution) and anti-smooth muscle actin (Dako, 1:25 dilution).

Macroscopically (Fig. 1), the body and tail of the pancreas weighed 570 g and measured 21×7×5 cm. They showed extreme liposis and contained multiple intraductal calcifications, with a large one obliterating the duct of Wirsung. The body of the pan-

creas was occupied by a whitish tumour with a diameter of 70 mm, which was compressing the duct of Wirsung without invading it. The whole tumour was sampled and embedded in 25 paraffin blocks.

Histologically, the tumour was composed of a moderately differentiated squamous cell carcinoma with nests of cells showing a pavement-like growth pattern and keratinization in the form of horn pearls (Fig. 2A). There was neither gland formation nor mucin secretion. Areas of neoplastic spindle cells were identified that gave the tumour a sarcomatoid appearance (Fig. 2B). These cells were moderately pleomorphic and fusiform and merged with the squamous cell carcinoma component. The nontumour pancreatic tissue was completely replaced by mature fat separated by thin fibrous septa. This resulted in the disappearance of the exocrine tissue and to a lesser extent of the islets of Langerhans. Foci of immature squamous metaplasia were observed in the epithelial lining of the large pancreatic ducts (Fig. 3), but we were not able to demonstrate an obvious transition between this squamous metaplasia and the squamous carcinoma. The pancreas at the line of resection was free of tumour and replaced by fat, with a few persisting islets of Langerhans and rare pancreatic acini. The large squamous cell carcinoma component stained strongly with the anti-cytokeratin antibody (KL1) and was negative for vimentin, desmin and smooth muscle actin. The spindle cell component stained focally for cytokeratin (Fig. 4A) and was strongly positive for vimentin, but negative for desmin and smooth muscle actin. Anti-p53 antibody showed strong nuclear staining in both carcinoma components (Fig. 4B), but no evidence of positivity in the ductal squamous metaplasia.

A diagnosis of squamous cell carcinoma of the body of the pancreas with a spindle cell component coexisting with pancreatic lipomatous pseudohypertrophy and numerous intraductal calculi was made.

The gallbladder did not contain gallstones and was histologically normal.

Discussion

Lipomatous pseudohypertrophy of the pancreas and intraductal calculi were found in a 68-year-old woman who underwent partial surgical resection of the pancreas for a squamous cell carcinoma.

Partial replacement of the exocrine pancreas with mature fat is one of the most common histological changes observed in the pancreas [11, 18]. It usually correlates significantly with overweight and increasing age [11, 15], without being associated with structural changes in the pancreas. Lipomatous pseudohypertrophy of the pancreas is a rare benign change characterized by an increase in the size and weight of the pancreas. Histologically, there is virtually a complete absence of exocrine parenchyma, which is replaced by normal adipose tissue with preservation of the duct system and the islets of Langerhans [6]. It has been reported in childhood with such rare diseases as Shwachman-Diamond syndrome and Bannayan syndrome [4, 10]. The pathogenesis of replacement of the pancreatic acini by fat is unknown. It might be a degenerative process occurring secondary to various lesions that have resulted in severe atrophy of the gland. Marked pancreatic lipomatosis has been described in adult patients with obstruction of the pancreatic excretory duct caused by impacted calculi, cysts or carcinoma [2, 12]. A distinct entity consisting in idiopathic pancreatic atrophy associated with clinical evidence of exocrine and endocrine pancreatic insufficiency and lipomatous pseudohypertrophy has been reported in middle-aged adults [2]. In our case, we favour the existence of a primary lipomatous pseudohypertrophy with endocrine insufficiency that could have been accentuated by several predisposing factors, including overweight, age, and pancreatic duct impairment. Since in our case both intraductal calcifications and fatty replacement were also present in the head of the pancreas, it seems very unlikely that these changes were due to duct obstruction by the tumour. Moreover, chronic pancreatitis caused by tumour-related duct obstruction does not usually involve such changes as ductal calcification and fatty replacement of the parenchyma [6, 7].

Lipomatous pseudohypertrophy is a benign lesion, but in occasional cases it has been associated with tumours, including adenocarcinoma [14] and leiomyosarcoma [16], in the pancreas. Here, we report a case of pure squamous cell carcinoma developing in conjunction with lipomatous pseudohypertrophy. Apart from metastases of squamous cell carcinoma to the pancreas, pure squamous cell carcinoma of the pancreas is an unusual tumour. Its clinical profile and biological behaviour are similar to those observed in typical ductal adenocarcinoma. The majority of squamous and adenosquamous carcinomas of the pancreas occur in patients over the age of 50 years, with gradually increasing upper abdominal and back pain, anorexia, weight loss, vomiting, nausea and jaundice [3]. They respond poorly to chemotherapy and radiotherapy and are generally associated with short survival [17]. The histogenesis of squamous cell carcinoma of the pancreas is unclear. Moreover, there is some doubt about the existence of pure squamous cell carcinoma, since extensive sampling of tissue from carcinomas with a squamous pattern usually reveals some foci of tumour glands [17].

Two hypotheses can be proposed to explain the origin of squamous cell carcinoma of the pancreas; either it could arise from an adenosquamous carcinoma in which the glandular component has disappeared or it could result from the malignant transformation of squamous metaplasia of pancreatic ductal epithelium. We favour latter hypothesis in this case, because we were not able to find any glandular component and squamous metaplasia of the epithelial lining of the ducts was present. Futhermore, we found a prominent spindle cell component. While carcinoma of the oesophagus with prominent spindle cells has been well described [8], the incidence of pancreatic spindle cell carcinoma is difficult to establish, because it is a very rare tumour and the criteria for its diagnosis are variable and arbitrary [1]. Moreover, the terminology for this entity is not standardized, and terms such as carcinosarcoma, spindle cell carcinoma, and carcinoma with sarcomatoid changes have all been used to describe similar tumours. In addition, small areas of sarcomatoid changes have been noted in ordinary ductal carcinomas or squamous cell carcinomas [1].

The histogenesis of spindle cell carcinoma is uncertain and controversial. Two theories have been put forward, one suggesting a monoclonal origin of the tumour

with metaplastic changes of the carcinomatous component toward mesenchymal differentiation, the other suggesting a biclonal origin with collision of two independent malignant tumours. To clarify the histogenesis of this combined tumour, many immunohistochemical studies have been done, showing that in most cases both carcinomatous and sarcomatous components have the same staining properties [13]. However, such data are inconclusive and need to be confirmed by genetic analysis [9]. The immunohistochemical detection of p53 in the spindle cell component, as observed in our case, suggests that this component is neoplastic and not a reactive response to the carcinomatous component.

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