QUIZ

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PRIMARY CARCINOID TUMOUR IN HORSESHOE KIDNEY

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Primary renal carcinoid tumours are extremely rare. To date, approximately 60 cases have been reported, mostly as case reports with only few series noted. The pathogenesis of this tumour is uncertain because neuroendocrine cells are not found in normal adult renal parenchyma. We report a case of primary renal carcinoid occurring in a horseshoe kidney in a 66-year-old patient. A clinical, histological and immunohistochemical picture of this tumour is presented.

Key words: carcinoid tumour, renal tumour, horseshoe kidney.

Introduction

Carcinoids are neuroendocrine tumours mostly found in the gastrointestinal tract (73.7%) and respiratory tract (25.1%) [1]. Other localizations [2] like ovary, testis, cervix, biliary duct, breast or gallbladder are rare. Primary renal carcinoids are even less common. To date, approximately 60 cases have been reported. As neuroendocrine cells are not found in normal adult renal parenchyma, the histogenesis remains uncertain. Nevertheless, neuroendocrine cells may be found during renal embryogenesis [2] and some other primary renal tumours were found to show neuroendocrine features [3]. On gross examination, renal carcinoids present as single, well demarcated, solid, yellow or grey coloured tumours. These tumours usually spread locally, metastases are rare but their frequency increases with the increasing tumour size. The most common are metastases to lymph nodes and liver.

Material and methods

Clinical data were retrieved from the archive files of the hospital in Tarnów. The original tumour samples that had been fixed in the formaldehyde solution, routinely processed and embedded in paraffin and stained with haematoxylin and eosin were reviewed. Immunohistochemistry was performed using a standard protocol. For antigen retrieval, heating in citrate buffer (pH 6.0) was used. The following primary antibodies were used: NSE (clone BBS/NC/ VI-H14, dilution 1 : 100), chromogranin (polyclonal, dilution 1 : 500), synaptophysin (polyclonal, dilution 1 : 500), CK-7 (clone OV- TL12/30, dilution 1 : 50), CK-HMW (clone 34βE12, dilution 1 : 50), Ki-67 (clone MIB1, dilution 1 : 50). All primary antibodies were manufactured by DAKO (Dako, Denmark). EnVision (Dako, Denmark) detection system was used.

Case report

A 66-year-old man in good general conditions was admitted with a suspicion of rectal cancer. Colonoscopy did not show any changes in the colon, but on lab tests the patient showed anaemia and thrombocythemia. Results of other laboratory studies were within normal limits. No signs of the carcinoid syndrome were reported. Chest radiography did not reveal any abnormalities. Abdominal ultrasonography and computer tomography scans revealed a horseshoe kidney with a 14 × 6-cm well-circumscribed heterogeneous mass. The tumour was located in the lower pole of the left kidney and in isthmus, near the aortic area. In the left renal vein, a solid mass of 9 cm in length was seen; this was interpreted as tumour infiltration. Bilateral urinary retention was seen, more pronounced on the left side. No lymphadenopathy was seen. Based on an intraoperatory frozen section, the diagnosis of epithelial malignancy was given. The patient underwent radical nephrectomy with lymphadenectomy. Haemodialyses were

started on the next day after the surgery. The postoperatory period was uneventful.

Grossly, the resected horseshoe kidney with fused lower poles measured 17 × 8 × 4.5 cm, and contained a solid yellow-coloured tumour mass located in the lower left and central part of the kidney. The tumour weighed 660 g and measured 8 × 6 × 4 cm. It infiltrated the left renal pelvis, left renal vein, fibrous capsule and surrounding perinephric fat. Microscopically, the tumour showed trabecular growth pattern (Fig. 1). Tumour cells showed moderate polymorphism, narrow rim of eosinophilic cytoplasm surrounded round nuclei with granular ("salt and pepper") chromatin (Fig. 2). The mitotic index was 10/50 HPF. No necrosis or calcifications were seen. Periaortic lymph nodes showed deposits with similar histology. Immunohistochemically, the tumour cells were positive for synaptophysin (Fig. 3), chromogranin and neuron-specific enolase (NSE), while stains for CK-7 and CH-HMW were negative. 5% of tumour cells were positive for Ki-67.

Basing on these findings, the diagnosis of renal carcinoid was formulated.

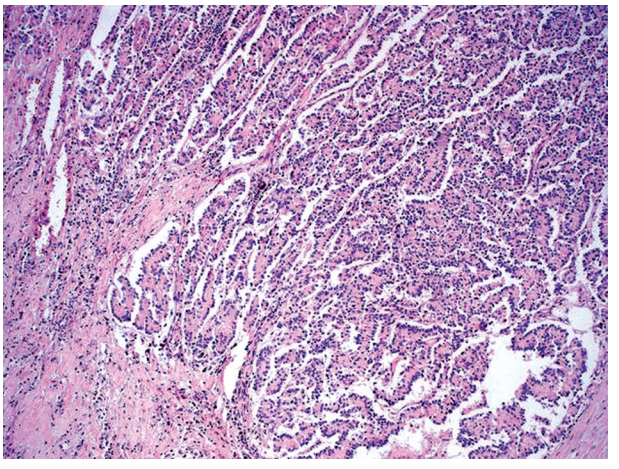

Fig. 1. Trabecular pattern of growth typical of carcinoid tumour (haematoxylin-eosin, magnification 100×)

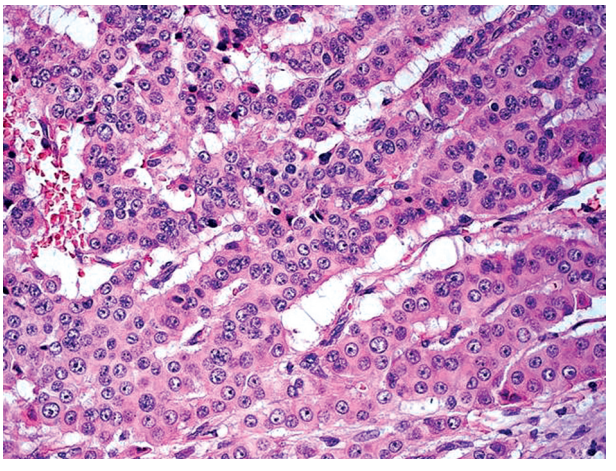

Fig. 2. On higher magnification, carcinoid cells are polygonal with eosinophilic cytoplasm, round, rather monomorphic nuclei with a granular ("salt and pepper") chromatin pattern (haematoxylin-eosin, magnification 400×)

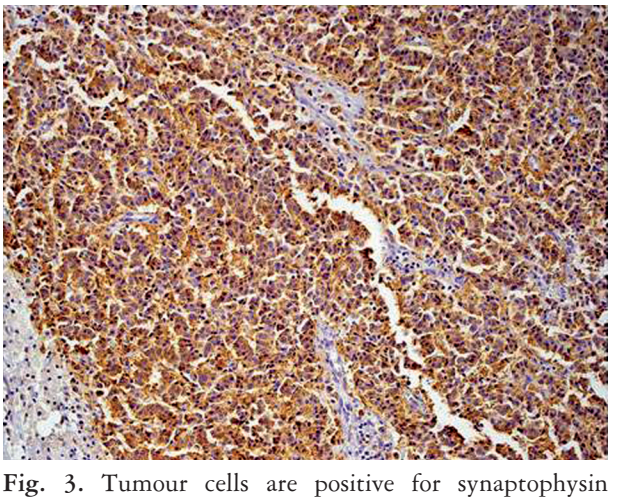

Fig. 3. Tumour cells are positive for synaptophysin (immunohistochemistry, magnification 100×)

Discussion

Primary renal carcinoids are extremely rare. To date, approximately 60 cases have been reported. It is distinctly more frequent in the horseshoe kidney. The relationship with congenital renal defects is however not entirely specific, as other tumour types were also shown to be more frequent in such cases [4, 5]. Nearly 25% of all carcinoid tumours occur in the horseshoe kidney [6]. Krishman *et al.* [7] calculated the relative risk (RR) to be 62, and Motta [8] – 120. The histogenesis is uncertain since to our knowledge, neuroendocrine cells are not found in normal adult renal parenchyma. On the other hand, they occur in the kidney during embryogenesis [6, 9]. There are several hypotheses about the histogenesis of renal carcinoids. They might originate from neuroendocrine cells found in metaplastic, chronically inflamed pyelocaliceal urothelium. Alternatively, they might derive from misplaced pancreatic, intestinal or pulmonary or neural crest-derived neuroendocrine cells. Interestingly, carcinoids may coexist with congenital renal defects; this feature is shared however with other renal tumours. Multipotential stem cells could give rise to a carcinoid through activation of genes responsible for the neuroendocrine phenotype. Some seemingly primary renal carcinoids could constitute metastatic focus from an undiscovered primary. Distinction of primary and metastatic renal carcinoids may be of practical importance but this may not be achieved by histological examination alone [2].

Renal carcinoid tumours occur predominantly in the fifth and sixth decades of life, but some cases

were reported at the age of 12 years and over the age of 70 years. Generally, there is no gender predilection, but carcinoids located in the horseshoe kidney are more frequent in males (M : F ratio is 1.5 : 1). The most common clinical symptoms include abdominal or flank pain, haematuria, fever, weight loss, and thus do not differ from other renal tumours. In 28% of cases, a palpable mass is seen. The carcinoid syndrome is present in 15% of the cases only. Approximately 25% of patients are asymptomatic [2]. On imaging studies (CT, MRI, US), renal carcinoids do not differ from other renal tumours. Renal cell carcinoma is thus a common preoperative diagnosis.

Grossly, carcinoids are usually single, yellowish to tan to grey tumours. The reported sizes range from 2 to 17 cm (average 6.4 cm). The lesion is usually solid, but occasionally may be associated with a cystic component. Although renal carcinoid is usually well demarcated, in several cases, extrarenal spread with fat tissue infiltration may be seen and 10% show vascular invasion. Histologically, the growth pattern is the same as in other locations: trabecular or ribbon-like arrangement or solid nests with peripheral palisading. Stroma is highly vascularized. Cells are rather monomorphic with granular eosinophilic cytoplasm and blurred cytoplasmic borders. Nuclei are round to oval, characteristically uniform in size and shape, with coarse chromatin. The nucleoli are small. Single mitotic figures may be seen. Calcification, haemorrhage or necrosis are uncommon. The diagnosis is confirmed by immunohistochemistry, with positive reactions for common neuroendocrine markers such as chromogranin, enolase or synaptophysin [2].

Metastases occur in about half of all cases; their typical locations are lymph nodes (92%), liver (34.5%), bone (9%), lung (2%), spleen (1.8%), gastrointestinal tract (1.8%) and kidney (1.8%). This metastatic pattern is obviously different from most renal tumours [4]. The size of the primary tumour is reported to correlate with the incidence of metastases [10], which can occur as late as 7 years after treatment [2]. The only treatment modality is partial or radical nephrectomy, accompanied by lymph node dissection. Chemotherapy is used only in the case of liver metastases [2, 10]. Because of the tumour rarity, there is little data on prognosis or prognostic factor [11]. The main prognostic factor might be the tumour size, and patients below the age of 40 years, with a horseshoe kidney, with a tumour less than 4 cm and in which the rate of mitoses is less than 1/10 HPF fare better [2].

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