Calcifying Nested Stromal-Epithelial Tumour of the Liver: case report and review of literature

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Abstract

Calcifying nested stromal-epithelial tumour (CNSET) of the liver is a rare tumour, recently included in the WHO Classification of Digestive system Tumours 2019. Its hallmark is the nested proliferation of epithelial and spindle cells with surrounding desmoplastic stroma, calcifications and ossifications. Less than 40 cases have been reported, whereas none has been reported in Middle Eastern descendants. We report the first case of CNSET in a 22-year-old Egyptian lady with detailed histological and clinical data.

Keywords: CNSET, Mesenchymal tumours, Liver

Background

Calcifying nested stromal-epithelial tumour (CNSET) is a rare, low grade hepatic neoplasm that was recently included in the WHO Classification of Digestive system Tumours 2019 [1]. It was first described by Ishak et al in 2001 [2]. CSET is considered a non-hepatobiliary tumour [3] of an uncertain lineage, and is characterized by a distinctive nested architecture of epithelioid and spindle cells, surrounded by cellular myofibroblastic stroma, and calcification [1].

Less than 40 cases have been reported with detailed clinical and pathologic data [7]. None has been reported in Middle Eastern descendants. We report the first case of CNSET in a 22-year-old Egyptian lady with detailed histological and clinical data. To the best of our knowledge, this is the 39th reported case of CNSET.

Case presentation

A 22-year-old young lady presented to our hospital with right hypochondrial pain for one month. Post contrast tri-phasic CT showed a right hepatic focal lesion, 6.5x9 cm, with calcification, no significant contrast enhancement, and no extra-capsular extension or infiltration of extra-hepatic structures. No intra-hepatic or venous channel dilatation. Tumour markers (CEA, CA15.3, CA125 and AFP) were normal. Exploration and surgical resection was done.

On gross examination, a non-cirrhotic hepatic segment

12x10x7 cm, weighing 270 grams, showed a non-capsulated fairly defined, lobulated rubbery, solid, homogeneous, tan whitish mass 10x8.5x5.5 cm, with central hard bony area 3x3 cm (Figure 1). Microscopic examination (Figure 2) showed nests of spindle and epithelioid cells, surrounded by a cellular stroma entrapping proliferating bile ducts. Tumour cells were blastema-like to large epithelioid with ovoid nuclei, and low mitotic activity (1-3/ 10 HPFs). Areas of osseous metaplasia were seen. Neither tumour necrosis nor vascular invasion was seen. Immunostaining (Figure 3) revealed positive reaction for synaptophysin, INI-1, Beta catenin (nuclear and cytoplasmic), CK (epithelioid cells), vimentin, WT-1 and PR, but negative for AFP, HepPar-1, CD99, GFAP, SMA (stains the surrounding stroma) and chromogranin A. CK7 was negative in tumour cells, but stained the proliferating bile ducts. Ki67 labeling index was low (<5%). The patient did not receive any adjuvant treatment and is under follow-up for 15 months and is disease free.

Discussion and conclusion

Calcifying nested stromal-epithelial tumour is a rare low grade hepatic neoplasm that predominates in females, with a male to female ratio of 1:2.5. It is more common in children and young adults, with an age range between 2 and 34 years [8,9].

Despite most of reported CNSET cases are sporadic [1], yet some cases were reported to be associated with cortisol-related syndrome and rarely, Beckwith-Wiedemann syndrome (BWS) [4].

The majority of cases have been discovered incidentally, with occasional cases presented with abdominal pain or mass [5]. Liver function tests, serum a-fetoprotein [AFP] and carcinoembryonic antigen [CEA] are typically within normal ranges [6]. CNET is a tumour of uncertain histogenesis [7]. An epithelial

origin with mesenchymal differentiation has been proposed [10], however another study stated that expression of WT-1 suggests a mesenchymal to epithelial phenotype [11].

Hepatoblastomas (HB) is an important differential diagnosis for CNET [12]. Distinguishing features include high AFP serum

Figure 1. Gross pathology assessment revealed a well-demarcated, unencapsulated, homogeneous white, solid mass in a background of normal-appearing liver.

Figure 2. Photomicrographs of H&E stained sections revealed well-circumscribed tumour with a sharp interface with adjacent liver, arranged in nests surrounded by prominent fibrous septa (A) (x40). Some nests harbor ossification (B) (x40). The fibrous septa contain bile ductular proliferation (C) (x100). Tumour cells formed of epithelioid cells exhibited rounded nuclei (C x100 and D x400) and spindle cells exhibited oval nuclei (E x100 and Fx400).

Figure 3. Photomicrographs of immunostained sections revealed tumour cells showed positive nuclear reaction for WT-1 (A) (x400), β-Catenin (B) (x400), PR (focally) (C) (x400), INI-1 (D) (x400) and a low proliferative index of Ki67 (E) (x40). Tumour cells showed cytoplasmic staining for CK (stronger intensity in bile ductules) (F) (x400), vimentin (stained stromal cells also) (G) (x40) and synaptophysin (H) (x100). Tumour cells are negative for SMA (stains the surrounding stromal cells) (I) (x40), HepPar-1 (stains the adjacent normal liver tissue) (J) (x100), CK7 (stains the bile ductules) (K) (x40), AFP, CD99, GFAP and chromogranin A (L) (x100).

levels in more than 90% of HB cases, positive immunostaining for AFP and HepPar-1 [13]. Small cell undifferentiated (SCUD) HB is, as CNET, negative for AFP and HepPar-1 [14], however the increased proliferation index and the lost INI-1 expression may aid in the differential with CNET [7].

Other differential diagnoses include biphasic synovial sarcoma (SS) and Desmoplastic small round cell tumour (DSRCT) [7]. Identifying the characteristic translocations of SS is helpful in distinguishing both tumours. *WT1-EWS* translocation, typically found in DSRCT, is lacking in CNET cases [15].

Surgical resection is the currently adopted treatment modality for CNET with proved to be curative in more than half of the reported cases [16]. The role of chemotherapy protocols used soft tissue sarcoma or HB is unclear whether of value in preventing tumour recurrence, additionally, neoadjuvant chemotherapy does not affect tumour size or necrosis in radiological findings or subsequent surgical specimens [17].

Competing interests

The authors declare that they have no competing interests.

Authors' contributions

Authors' contributions	NM	BA	AE
Research concept and design	✓	--	--
Collection and/or assembly of data	✓	✓	--
Data analysis and interpretation	✓	--	--
Writing the article	✓	--	✓
Critical revision of the article	--	--	✓
Final approval of article	✓	✓	✓
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