Virchows Archiv (1994) 425:211–215

CASE REPORT

Masayuki Shintaku · Yuri Baba · Toshiro Fujiwara

Intra-abdominal desmoplastic small cell tumour in a patient with Peutz-Jeghers syndrome

Received: 10 March 1994 / Accepted: 9 June 1994

Abstract A surgical case of intra-abdominal desmoplastic small cell tumour with divergent differentiation (IDSCT) in a patient with Peutz-Jeghers syndrome (PJS) is reported. The patient was a 23-year-old woman who underwent surgery for a tumour in the left paraovarian region. Widespread peritoneal metastases were noted. Histopathological examination revealed solid cell nests composed of medium-sized cells demarcated by desmoplastic stroma. Gland-like spaces were found within many cell nests. Tumour cells were positive for cytokeratin and smooth muscle actin, but negative for desmin. Both ovaries contained minute foci of a sex cord tumour with annular tubules. This is the first documentation of the association of IDSCT with PJS. Since patients with PJS have an increased risk of cancer in various organs, the occurrence of IDSCT in the present patient might not be fortuitous.

Key words Desmoplastic small cell tumour
Peutz-Jeghers syndrome

Introduction

Intra-abdominal desmoplastic small cell tumour with divergent differentiation (IDSCT) is a very rare neoplasm which was first described by Gerald and Rosai [6]. It predominantly affects young men and presents with a large intra-abdominal tumour with massive peritoneal metastases and the absence of an apparent primary site. Light microscopically the tumour shows solid cell nests which are composed of undifferentiated small round cells and are surrounded by a desmoplastic stroma. On immunohistochemical examination, tumour cell simultaneously express epithelial, mesenchymal, and, less frequently, neuroepithelial phenotypes, and their histogenesis remains controversial [7, 8, 14, 18].

We report here the clinicopathological findings of a young woman with Peutz-Jeghers syndrome (PJS) who had an IDSCT. The association of this type of neoplasm and PJS has, to our knowledge, not been documented in the literature.

M. Shintaku (✉)
Department of Pathology, Osaka Red Cross Hospital,
5–53 Fudegasaki, Tennoji, Osaka 543, Japan

Y. Baba · T. Fujiwara
Department of Obstetrics and Gynaecology,
Osaka Red Cross Hospital, Osaka, Japan

Case report

The patient was a 23-year-old woman, who presented with severe lower abdominal pain of sudden onset. She had been amenorrhoeic for the past 2 months. Ultrasonographic examination revealed a large mass in the pelvic cavity, and emergency laparotomy was performed. A fist-sized tumour was found in the left paraovarian region just behind the broad ligament. The tumour was clearly separated from the left ovary, but involved the left fimbria. It was twisted together with the left oviduct and had fallen into the cul-de-sac. There was no adhesion between the tumour and the surrounding tissue and serosanguinous ascites of about 200 ml was noted. In addition, widespread tumour metastases were found on the uterine, rectal and omental surfaces. Both ovaries were slightly enlarged.

The main tumour was removed with the ovaries, uterus and omentum, and the implanted nodules were resected as far as possible. The ovaries showed typical microscopic appearances of minute, multiple foci of sex cord tumour with annular tubules (Fig. 1). The endometrium showed no hyperplastic changes, and "adenoma malignum" of the uterine cervix was not found. The patient underwent four courses of post-operative combination chemotherapy (mainly consisting of cis-platinum), and has been free from recurrence for about 1 year post-operatively.

The patient had melanin pigmentation of the lips, buccal mucosa, and fingers, and the post-operative roentgenographic and endoscopic examination revealed multiple hamartomatous polyps in the stomach, small intestine, and large intestine. Some of these polyps were resected endoscopically, and they showed characteristic histopathological features of hamartomatous polyps. Her family history was non-contributory except that her paternal grandfather had died of rectal cancer.

Pathological findings

The excised paraovarian tumour, which measured about 10×7×7 cm and weighed 270 grams, was hard in consis-

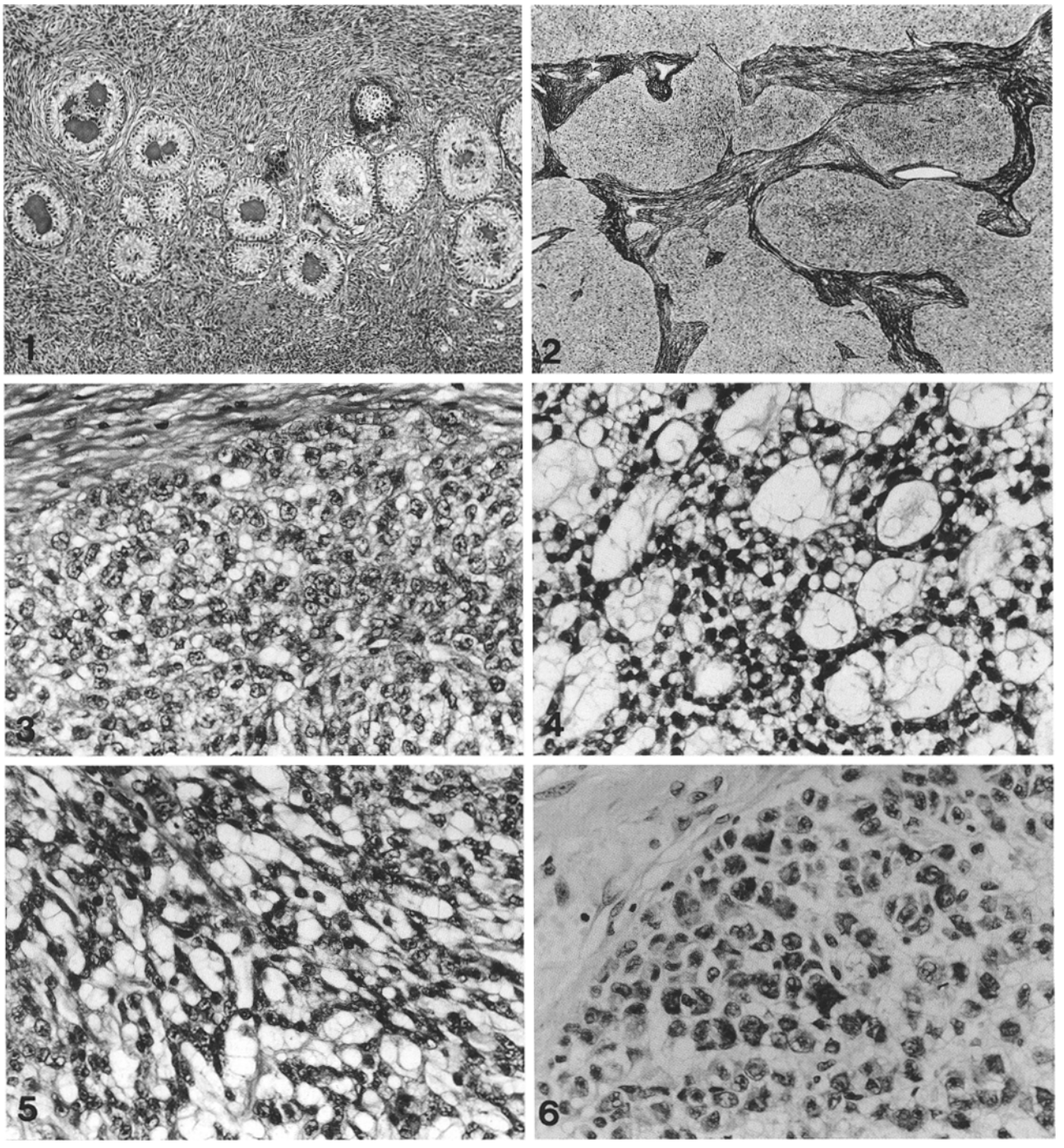

Fig. 1 Microscopic foci of sex cord tumour with annular tubules of the ovary. Haematoxylin and eosin, ×25

Fig. 2 The tumour consists of irregular-shaped solid cell nests sharply demarcated by desmoplastic stroma. Reticulin, ×10

Fig. 3 The tumour cells are medium-sized and have vesicular nuclei and eosinophilic or clear cytoplasm. Haematoxylin and eosin, ×100

Fig. 4 Gland-like spaces containing palely basophilic fluid are observed in many cell nests. Haematoxylin and eosin, ×100

Fig. 5 Lace-like arrangement of cellular cords is occasionally found. Haematoxylin and eosin, ×100

Fig. 6 Some of tumour cells are stained positively with monoclonal antibody KL-1. Immunoperoxidase, ×100

tency and showed a whitish bosselated surface. The cut surface was entirely solid and varied from pale yellow to whitish grey. Irregular small foci of necrosis and haemorrhage were noted.

Histologically the tumour consisted of medium-sized polygonal cells which formed irregular-shaped solid cell nests sharply demarcated by desmoplastic stroma (Fig. 2). Cells within these cell nests were closely packed together with little intervening reticulin fibres. Tumour cells at the periphery of the nests showed a tendency toward palisading. Their nuclei were moderately pleomorphic and of vesicular appearance with coarsely clumped

Table 1 Antibodies used for immunohistochemistry (*CEA* carcinoembryonic antigen, *EMA* epithelial membrane antigen, *NSE* neuron-specific enolase)

Marker	Source	Monoclonal/ polyclonal	Dilution	Result
Cytokeratins:				
KL-1	MOC	monoclonal	1:25	+
PKK-1	Lab System	monoclonal	1:100	−
MA 902	Enzo Biochem	monoclonal	1:7000	−
MA 903	Enzo Biochem	monoclonal	1:7000	−
EMA	DAKO	monoclonal	1:100	−
CEA	DAKO	polyclonal	1:100	−
CA 125	Centocor	monoclonal	1:100	−
α-smooth muscle actin	Lipshaw	monoclonal	1:100	+
Desmin	Lipshaw	monoclonal	1:75	−
Vimentin	DAKO	monoclonal	1:100	−
S-100	DAKO	polyclonal	1:100	+
NSE	DAKO	polyclonal	1:100	+
Neurofilament	DAKO	monoclonal	1:100	−
Synaptophysin	Boehringer-Mannheim	monoclonal	1:10	−

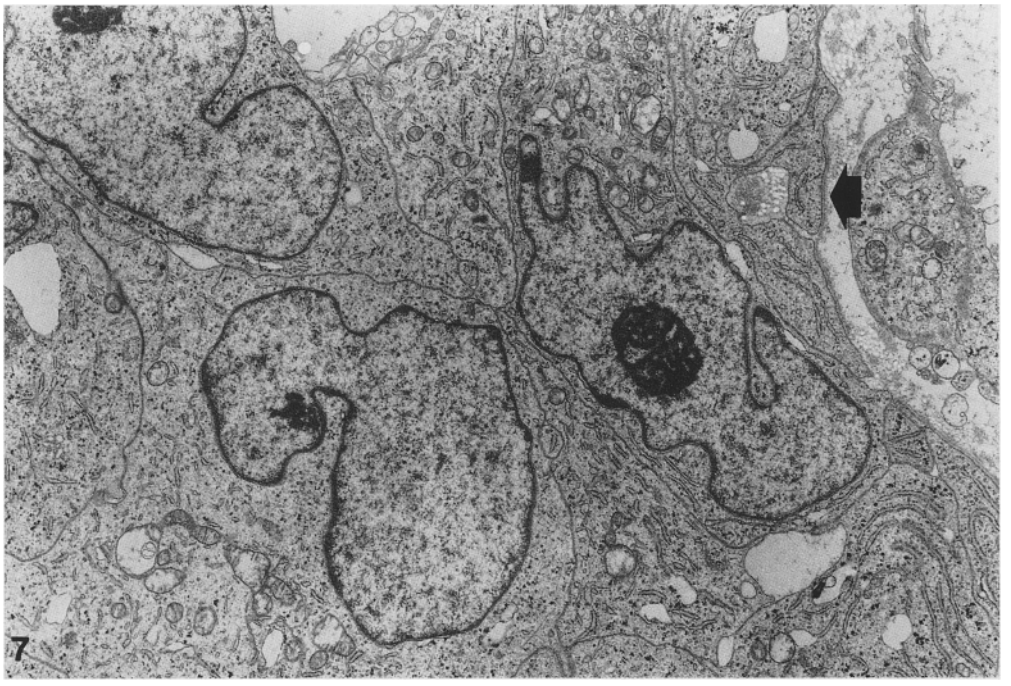

Fig. 7 Tumour cells are closely apposed, and a small lumen-like space lined by microvilli is seen (top of the Figure). A thin basal lamina is also observed (*arrow*). ×5400

chromatin and small eosinophilic nucleoli. Mitotic figures were frequently observed. There was no nuclear grooving. Cytoplasm was relatively abundant, and was eosinophilic or optically clear (Fig. 3). There were no intracytoplasmic hyaline inclusions. Many tumour cells contained glycogen in moderate amounts, but no intracytoplasmic lipids were demonstrated on frozen sections. Gland-like small round spaces, which contained palely basophilic and Alcian blue-positive fluid and rarely showed cystic dilatation, were found within many cell nests (Fig. 4), and a lace-like or reticular arrangement of tumour cells was noted (Fig. 5). The fluid in the spaces was periodic acid-Schiff-negative and did not contain basal lamina-like material. In small areas of the tumour, the cells became spindle-shaped and formed loose, intersecting cellular fascicles.

The stroma between the cell nests contained variable amounts of collagen fibres and a small number of inflammatory cells, and in some areas it divided the cell nests into small cell clusters or thin cellular strands. There was extensive and confluent coagulative necrosis.

The tumour had invaded the tubal wall deeply, and tubal epithelium was tightly stretched over the surface. Transition between the tumour cells and tubal epithelium was not observed. Disseminated nodules on the peritoneal surface showed histopathological features similar to those of the main mass.

Immunohistochemical examination was done on paraffin sections of the tumour, using the standard labelled streptoavidin-biotin method after the blocking of endogenous peroxidase by hydrogen peroxide. The antibodies

used in this study and their sources and dilutions are presented in Table 1 with the results of immunostaining.

Some tumour cells showed diffuse cytoplasmic immunoreactivity with KL-1 (monoclonal antibody recognizing a 56 kDa cytokeratin) (Fig. 6). Tumour cells also showed diffuse but weak positivity for S-100 protein and neuron-specific enolase. Focal immunoreactivity for α-smooth muscle actin was seen, the staining pattern of which was mostly fibrillar along the plasmalemma. None of the cells reacted with antibodies against desmin, vimentin, epithelial membrane antigen, carcinoembryonic antigen, CA 125, neurofilament, and synaptophysin, and with monoclonal antibodies for various subclasses of cytokeratin, that is, PKK-1, MA 902, and MA 903.

The nuclei of the tumour cells were irregular with prominent indentations, coarsely clumped chromatin and distinct nucleoli (Fig. 7). The contour of the cytoplasmic surface appeared generally smooth, and tumour cells were closely apposed with very little intervening extracellular material. A small number of filopodia-like cytoplasmic processes were found. Small intercellular lumen-like spaces lined by microvilli-like projections were occasionally found. Although the intercellular junctional apparatus was poorly developed in general, at the luminal margins adjacent cells were connected by well-developed junctional apparatus. The cytoplasmic surface facing the wide intercellular space was rimmed by basal lamina. Intracytoplasmic organelles were moderately developed and composed of many free ribosomes, stacked rough endoplasmic reticulum, mitochondria and Golgi apparatus. There were no neurosecretory granules. Some cells contained a moderate number of glycogen granules. Intracytoplasmic filamentous material was generally scanty, and a dense accumulation of intermediate filaments was not detected.

Discussion

PJS is an autosomal dominant disorder characterized by hamartomatous polyposis of the gastrointestinal tract and mucocutaneous pigmentation. This syndrome is associated with a higher incidence of various neoplasms in the gastrointestinal tract [1, 9] as well as in other organs [1, 5, 16] compared with that in the general population. The present case is the first report of a unique association of this syndrome with IDSCT, a very rare neoplasm which was recently established as a clinicopathological entity [6, 7, 8, 14, 18].

The present patient also had multiple microscopic foci of sex cord tumour with annular tubules in both ovaries. Patients with PJS have this type of ovarian neoplasm very frequently [15, 19], and less frequently, "adenoma malignum" of the uterine cervix [12, 19]. Other kinds of ovarian neoplasms have also been documented in association with this syndrome [5, 12, 20].

Although clinicopathological features of the tumour in the present patient were as a whole compatible with those of IDSCT, the paraovarian location of the tumour and somewhat atypical histological appearances including the gland-like spaces and lace-like arrangement of cellular cords, still caused considerable diagnostic difficulty. Granulosa cell tumour (supposedly arising from a supernumerary or accessory ovary [3]) was considered as an alternative. In the present case, however, there were no typical Call-Exner bodies, the gland-like spaces did not contain basal lamina material, and there was no nuclear grooving. Moreover, the tumour cells were immunohistochemically negative for vimentin, which is usually expressed in granulosa cell tumours [2]. Similar gland-like structures and lace-like arrangement of cellular cords have been described in some cases of IDSCT [7, 8, 13, 14, 17, 21].

Small cell carcinoma of the ovary with hypercalcaemia [4] was also considered in the differential diagnosis. In the present case, however, the tumour was clearly separated from the ovary and the patient did not have hypercalcaemia. Pathological appearances including immunohistochemistry and ultrastructure of the present tumour were also different from those of small cell carcinoma of the ovary.

The immunohistochemical profiles of tumour cells in IDSCT are characteristically divergent and vary somewhat in reports from different authors. Most investigators agree that this neoplasm expresses cytokeratin and desmin simultaneously [6, 7, 8, 13, 14, 18, 21]. In the present case, some tumour cells stained positively for cytokeratin (KL-1), but were negative for desmin. Negativity for desmin might be correlated with an absence of a paranuclear accumulation of intermediate filaments on ultrastructural examination in the present case. Negativity for desmin has also been noted in a few cases of IDSCT [7, 17]. Some tumour cells in the present case were reactive for another immunohistochemical marker of muscular differentiation, that is, α-smooth muscle actin. Smooth muscle actin has been detected in some cases [14, 21]. Some of the immunohistochemical findings of the present case, especially the negativity for desmin, vimentin, and epithelial membrane antigen, are apparently not compatible with the results of other authors on IDSCT. However, the most characteristic immunohistochemical feature of IDSCT consists in the "polyphenotypic" nature of the neoplastic cells, and this basic nature seems to be expressed also in our case in the form of simultaneous positivity for cytokeratin (KL-1), α-smooth muscle actin, neuron-specific enolase, and S-100 protein.

The histogenesis of IDSCT has not been elucidated and undifferentiated mesothelial cells (mesothelioblast) or submesothelial mesenchymal cells have been suggested as the cell of origin by some authors [7, 10]. The relationship between IDSCT and small cell variant of malignant mesothelioma [11] remains to be clarified.

The clinical course of IDSCT is highly aggressive, and its prognosis is generally poor [7]. Although it affects young men predominantly, it should also be considered in the differential diagnosis in young female patients with a malignant neoplasm in the abdominal cavi-

ty, especially when major visceral involvement is not apparent.

Acknowledgements We are grateful to Dr. Robert H. Young (Massachusetts General Hospital, Boston) for kindly reviewing the pathological material of the present case and providing us with invaluable comments.

References

1. Burdick D, Prior JT (1982) Peutz-Jeghers syndrome. A clinicopathologic study of a large family with a 27-year follow-up. Cancer 50:2139–2146
2. Chadha S, Kwast TH van der (1989) Immunohistochemistry of ovarian granulosa cell tumours. The value of tissue specific proteins and tumour markers. Virchows Arch [A] 414:439–445
3. Cruikshank SH, Drie DM van (1982) Supernumerary ovaries. Update and review. Obstet Gynecol 60:126–129
4. Dickersin GR, Kline IW, Scully RE (1982) Small cell carcinoma of the ovary with hypercalcemia. A report of eleven cases. Cancer 49:188–197
5. Dozois RR, Kempers RD, Dahlin DC, Bartholomew LG (1970) Ovarian tumors associated with the Peutz-Jeghers syndrome. Ann Surg 172:233–238
6. Gerald WL, Rosai J (1989) Desmoplastic small cell tumor with divergent differentiation. Pediatr Pathol 9:177–183
7. Gerald WL, Miller HK, Battifora H, Miettinen M, Silva EG, Rosai J (1991) Intra-abdominal desmoplastic small round-cell tumor. Report of 19 cases of a distinctive type of high-grade polyphenotypic malignancy affecting young individuals. Am J Surg Pathol 15:499–513
8. Gonzalez-Crussi F, Crawford SE, Sun CCJ (1990) Intraabdominal desmoplastic small-cell tumors with divergent differentiation. Observations on three cases of childhood. Am J Surg Pathol 14:633–642
9. Hsu SD, Zaharopoulos P, May JT, Costanzi JJ (1979) Peutz-Jeghers syndrome with intestinal carcinoma. Report of the association in one family. Cancer 44:1527–1532
10. Layfield LJ, Lenarsky C (1991) Desmoplastic small cell tumors of the peritoneum coexpressing mesenchymal and epithelial markers. Am J Clin Pathol 96:536–543
11. McCaughey WTE, Kannerstein M, Churg J (1985) Tumors and pseudotumors of the serous membranes. Atlas of tumor pathology, 2nd series, fascicle 20. Armed Forces Institute of Pathology, Washington D.C.
12. McGowan L, Young RH, Scully RE (1980) Peutz-Jeghers syndrome with "adenoma malignum" of the cervix. A report of two cases. Gynecol Oncol 10:125–133
13. Ordóñez NG, Zirkin R, Bloom RE (1989) Malignant small-cell epithelial tumor of the peritoneum coexpressing mesenchymal-type intermediate filaments. Am J Surg Pathol 13:413–421
14. Ordóñez NG, El-Naggar AK, Ro JY, SilvaEG, MacKay B (1993) Intra-abdominal desmoplastic small cell tumor. A light microscopic, immunocytochemical, ultrastructural, and flow cytometric study. Hum Pathol 24:850–865
15. Scully RE (1970) Sex cord tumor with annular tubules. A distinctive ovarian tumor of the Peutz-Jeghers syndrome. Cancer 25:1107–1121
16. Trau H, Schewach-Millet M, Fisher BK, Tsur H (1982) Peutz-Jeghers syndrome and bilateral breast carcinoma. Cancer 50:788–792
17. Variend S, Gerrard M, Norris PD, Goepel JR (1991) Intra-abdominal neuroectodermal tumour of childhood with divergent differentiation. Histopathology 18:45–51
18. Wills EJ (1993) Peritoneal desmoplastic small round cell tumours with divergent differentiation. A review. Ultrastruct Pathol 17:295–306
19. Young RH, Welch WR, Dickersin R, Scully RE (1982) Ovarian sex cord tumor with annular tubules. Review of 74 cases including 27 with Peutz-Jeghers syndrome and four with adenoma malignum of the cervix. Cancer 50:1384–1402
20. Young RH, Dickersin GR, Scully RE (1983) A distinctive ovarian sex cord-stromal tumor causing sexual precocity in the Peutz-Jeghers syndrome. Am J Surg Pathol 7:233–243
21. Young RH, Eichhorn JH, Dickersin GR, Scully RE (1992) Ovarian involvement by the intra-abdominal desmoplastic small round cell tumor with divergent differentiation. A report of three cases. Hum Pathol 23:454–464