

Case Report

Primary rectal seminoma with the presence of disorder of sex development characteristics: a case report

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Received June 6, 2017; Accepted August 9, 2017; Epub September 1, 2017; Published September 15, 2017

Abstract: Background: Although the occurrence of primary extragonadal seminoma is rare, there are reported clinical cases of seminoma occurring in mediastinum, lung, retroperitoneal, central nervous system, and even in the small intestine. However, there is lack of report of rectal seminoma. Here we report a case of rectal seminoma in a 53 years old Chinese patient. Case description: This 53-year-old male patient presented with bulging anus and abnormality in the shape of his stool. Physical examination revealed that the patient's external genital organs have abnormal development, presenting characters of disorder of sex development, which was absence of testis in scrotum. Computed tomography (CT) scan of abdomen and pelvic cavity found that there was a tumor of irregular shape in the lower rectum. In addition, there was no other tumor found in the other parts of the body. Results from immunohistochemistry showed that placental alkaline phosphatase (PLAP) and CD117 were positive. Based on the examination results described above, this clinical case was diagnosed as seminoma. Conclusion: Due to the rareness of rectal seminoma in patients of disorder of sex development, diagnosis should be made with extra cautious by taking into account of clinical symptoms, images of tomography scan, pathology test and immunohistochemical analysis. When seminoma occurs in extragonadal, it needs to be examined with extra care to exclude the possibility of other types of tumor. Further research is required to evaluate whether there is any association between disorder of sex development and extragonadal seminoma.

Keywords: Seminoma, rectum, disorder of sex development, immunohistochemistry

Introduction

The most common tumors occurring in testis is seminoma. It mostly happens in middle aged and elder people, and usually occurs unilaterally. Depending on its originating location, seminoma is divided into two types: one type occurs in the gonad including testicle and prostate gland [7] while the other type arise in extragonadal region including mediastinum [1], lung [2], retroperitoneal [3], central nervous system [4] and small intestine [5, 6]. Its occurrence may be associated with gonad ectopic during embryo development, which could lead to the inability of germ cells to grow in the normal locations. Subsequently, the condition could be worsening upon subject to local temperature, disordered blood transportation and endocrine disorder [8]. The specific cause is still not clear. The incidence varies among races and geographic locations. In American male population, seminoma is five times more frequent in

white men as compared with African American men [9].

The occurrence of disorder of sex development is very rare while patient with disorder of sex development and co-occurrence of extragonadal seminoma is even rarer. It is reported that 46 XY gonad dysgenesis may be due to the impairment of Sertoli cell-Leydig cell interaction and the occurrence of seminoma in such patients is possibly associated with the mutation of desert hedgehog (DHH) gene [10]. However, the specific cause is still not clear.

This case report presents the clinical pathology and immunohistochemical features of a patient with the characters of disorder of sex development and primary rectal seminoma. Through examination of various biomarkers, we have confirmed the histology type of the seminoma. Following the confirmation of the histology diagnosis, we have examined the patient's scrotum,

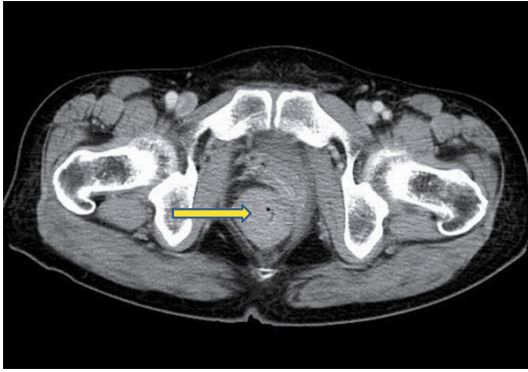


Figure 1. CT scan revealed that the wall was thickened in the lower portion of the rectum, stenosis was found in the lesion area and a mass of irregular shaped mass was adjacent to the anus.

prostate gland, bladder, retroperitoneal, central nervous system and pelvic cavity, and found no tumorous lesions. Though the patient has external genitals of both sexes, his physical appearance is male with the presence of prostate gland and sex chromosome as 46 XY. However, there is no testis in his scrotum. Based on these observations, we assume that the tumor originated from rectum. Such findings indicate that gonad tissues can infiltrate into rectum and lead to the occurrence of rectum seminoma.

Case presentation

A 53 year old patient was admitted to hospital for examination due to the bulging feeling of his anus and his shapeless stool. The patient presented as male phenotype with the following characters: thin beard, small prominentia, laryngea, male breast appearance at both side of the breast duct, scarce pubic hair, penile atrophy, incomplete development of urethra within the penis, absence of testis in both scrotum, presence of female genital in the posterior of the scrotum, urethra localized above the labia minora, incomplete development of vagina, no experience of period, and anus localized in the central without any malformation. Ultrasound scan showed there was presence of prostate gland and there was no obvious uterus and ovary structure. CT scan revealed that the wall was thickened in the lower portion of the rectum, there was stenosis in the lesion area and irregular shaped mass was adjacent to the anus (**Figure 1**). Therefore, the case was diagnosed as rectum cancer. During the surgical resection of the rectum, there is no adherence

found between the rectum and its surrounding tissues and organs and a nodular mass is found 5 cm from the anus in the lower portion of the rectum. In addition, there is no tumor found in other locations. The patient was given four weeks of radiotherapy and chemotherapy following the operation. Follow up at 5 month after the therapy found that the patient was in good health and presented no significant clinical symptoms.

Material and methods

Sample collected during surgical resection was fixed by formalin solution. Following fixation, the resected tumorous tissues were dehydrated, cleared and infiltrated with liquid paraffin. After the removal of the water, the tissue was then embedded in paraffin. Section was carried out after the sample was cooled down. The histological section is heated and stained with traditional hematoxylin and eosin stain for histology diagnosis.

The section was heated in the oven at 65°C for 2 hours, prior to the application of xylene for deparaffinization. After deparaffinization, the section was incubated in 3% H₂O₂ for 10 min. The section was then washed with distilled water and incubated in PBS for 5 min. Subsequently, the section was placed in a pressure cooker filled with sodium citrate buffer for antigen unmasking under high pressure and high temperature. The slide was taken out after the pressure was stabilized for 2.5 minute. Once the slide cools down to 35°C or below, the slide was incubated twice in distilled water for 1 minute each before being washing with PBS twice. The slide was placed in the chamber and primary antibody was added. The slide was incubated in the chamber for 1 hour with primary antibody P-CK, EMA, CK18, CK20, P63, CK5/6, CD3, CD20, CD56, EBV, GRB, HMB45, Ki-67, S-100, Mart-1, CgA, Syn, CD34, PLAP and CD117 (all the antibodies were purchased from Fuzhou Maixin Biotech. Co., Ltd.) The slide was washed with PBS for three times. After addition of biotin marked secondary antibody, the slide was incubated at 37°C in the chamber for 8 minutes. The slide was then washed with tap water for 1 minute before being stained with hemotoxylin for visualization of the nuclei. Afterwards, the slide was dehydrate and mounted. In this study, rabbit serum was used as negative control while tissue prepared recently,

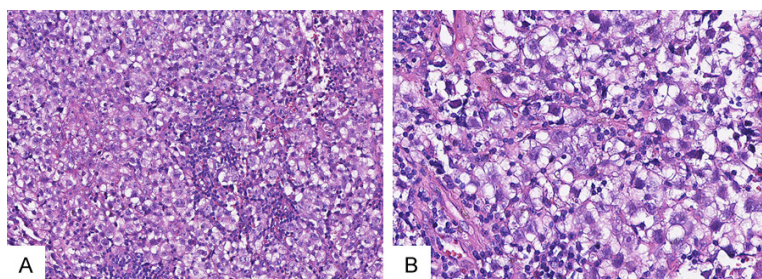


Figure 2. Microscopic examination revealed that all the cells were uniform with clear cell membrane, abundant clear cytoplasm and centrally located large nucleus. The nucleoli were obvious with a diversity of shapes and irregular contours. Tumor cells were arranged in nests of different size outlined by fibrous bands. In the background, there were lymphocytes and infiltration by histiocytes. Lymphocytes were distributed around the tumor cells. There was accumulation of lesions. A: HE 200 \times ; B: HE 400 \times .

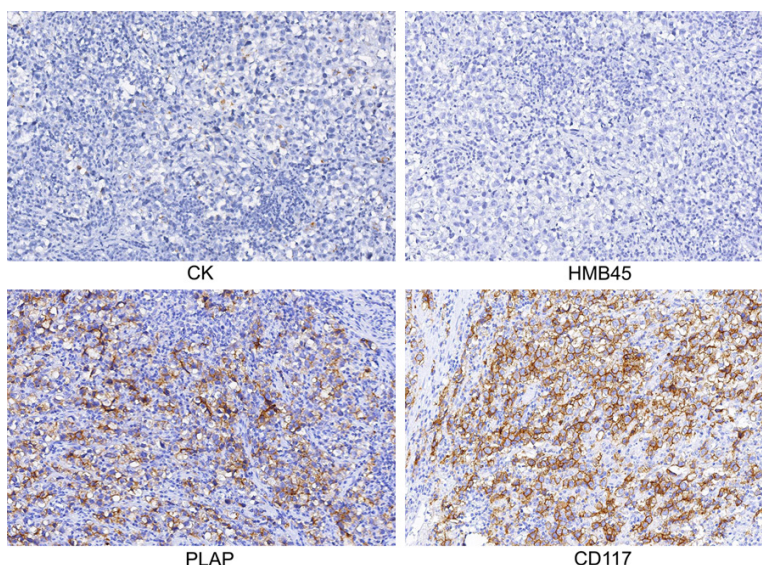


Figure 3. Immunohistochemistry results demonstrated that the tumor was negative for P-CK, HMB45, EMA, CK18, CK20, P63, CK5/6, CD3, CD20, CD56, EBV, GRB, S-100, Mart-1, CgA, Syn, CD34; but positive for placental alkaline phosphatase (PLAP) and CD117.

which showed positive for same primary antibody as used for the samples prepared for this study, was used as positive control.

Results

Gross examination revealed that there was nodular mass 5 cm away from the anus, projecting from the mucus membrane of the rectum to its cavity. The mass was 7 cm \times 5.5 cm \times 3 cm in size, solid, with anabrosis on the surface, and contained areas of necrosis. Its cross section is of grey color. The rectum serous membrane was smooth.

Microscopic examination revealed that the cancer cells were located in the submucosal and muscular with invasive growth. All the cells are uniform with clear cell membrane, abundant clear cytoplasm and centrally located large nucleus. The nucleolus was obvious with a diversity of shapes and irregular contours. Tumor cells were arranged in nests of different size outlined by fibrous bands. In the background, there were lymphocyte and infiltration by histiocytes. Lymphocytes distributed around the tumor cells. There was accumulation of lesions (**Figure 2A** and **2B**). Immunohistochemistry results demonstrated that the tumor was negative for P-CK, EMA, CK18, CK20, P63, CK5/6, CD3, CD20, CD56, EBV, GRB, HMB45, S-100, Mart-1, CgA, Syn, CD34, 70% positive for Ki-67 and positive for PLAP and CD117 (**Figure 3**).

Discussion

The most common place for the occurrence of seminoma is in testis. Extragonadal seminoma is usually seen at mediastidium, lung, retroperitoneal and central nervous system. In this case report, there was no tumor found in tissues around rectum and other area following careful examination. Therefore we conclude that the tumor originate from the rectum. Combining the tumor's growth type, cell's morphology and immunohistochemical characters, we made the diagnosis as malignant primary rectum seminoma.

We performed differential diagnosis as described below: 1. (Poorly differentiated carcinoma) Primary epithelial tumors are very common in rectum. When the differential level is low, the distribution pattern of the tumor cells is as a sheet and the nucleus have diverse mor-

phologies. In this case, due to the structure of the mass presented and the type of growth of the tumor, misdiagnosis could be made. However, as the immunohistochemistry results demonstrated that the tumor was P-CK, EMA, CK18, CK20, P63 and CK5/6 negative, the possibility of being primary epithelia tumor was excluded. 2. Malignant melanoma: Nucleus is stained with darker color; nucleus membrane is irregular; an eosinophilic nucleolus of large size and irregular shape can be found in the nucleus. In this clinical case, there was abundant transparent cytoplasm and large centrally localized nucleolus that was not eosinophilic. There was no lesion of skin pigmentation observed over the whole body of the patient. In addition, immunohistochemical results demonstrated that the tumor tissues were HMB45, S-100 and Mart-1 negative. Therefore the possibility of being malignant melanoma was excluded. 3. Neuroendocrine tumor: low level of cytoplasm, unclear cell boundaries, the chromatin has the fine stipple pattern and the nucleolus is not obvious. As in this clinical case the tumor tissue is negative against the neuroendocrine markers including CD56, CgA and Syn. Therefore, the possibility of being neuroendocrine tumor is excluded. 4. Lymphoma: The size of lymphoma cell is relatively large and has significant abnormal morphology with rich chromatin stained as blue. The normal lymph node and tissues are destroyed and filled with tumor cells. In this case, there was no observation of lymph node enlargement in the patient and there was no history of lymph related diseases for the patient. In addition, the immunohistochemical results demonstrated that the tumor tissues were negative against the lymphoma biomarkers including CD3, CD20, EBV and GRB. Therefore, the possibility of being lymphoma was excluded. 5. Metastatic seminoma: The patient was presented with disorder of sex development which was characterized with the absence of testis in the scrotum. Ultrasound scan prior to surgical operation and examination carried out during the surgical operation found no testis in the abdomen and inguinal region. CT scan of the abdomen did not find the presence of testis. Therefore the possibility of having undescended testis was excluded. There was no lesion observed in prostate gland, lung, mediastinum, head, retroperitoneal, and central nervous system, indicating that the tumor was not due to metastasis. Though the

patient's external genitalia presented with the characters of both sex, the sex chromosome was 46 XY. Together with the finding that there is no testis found in the scrotum and no tumor found in the surrounding of rectum and other body parts, we made the diagnosis as malignant rectum primary seminoma.

It was very difficult to make the diagnosis of seminoma before surgical operation as the patient presented with no clinical symptoms. When the tumor grows to a certain extent, oppressing the surrounding organs and blocking the bowel defecation, the patient was admitted to the hospital for hospitalization. Based on the tumor's growth site and type and general examination, it is difficult for us to consider seminoma in the early stage of diagnosis of. The specific cause of gonadal ectopic is still unclear. Patients with gonadal ectopic at the same time with the characteristics of disorder of sex development are relatively rare. The probability of having germ cell tumor associated with gonad ectopic is relatively high. However, whether disorder of sex development has any influence on the formation of germ cell tumors is still unclear. In addition, the gonadal ectopic rectum is extremely rare. From the study of this case, we learnt that when the patient presented with characteristics of disorder of sex development and no gonads found in normal parts, clinical symptoms and imaging results should be both taken into account to assist the search of ectopic glands throughout the body. During its development, gonad can stay in any part of the body, and when its growth is affected, it may develop into a germ cell tumor, which should raise our attention. Accurate diagnosis will provide reliable basis for clinical treatment.

Acknowledgements

We are very grateful to Dr Qi Ke (Pathology department, Mianyang city's central hospital, Mianyang, Sichuan, China) for his support in clinical case consultation and discussion. We would also like to acknowledge the assistance provided by Dr Yuanyu Zhao (Sichuan science city hospital, Mianyang, Sichuan, China) in literature review. In addition, we would like to thank Dr. Yutao Zhang (Zigong No.1 People's Hospital, Zigong, Sichuan, China) for his advice in the editing of this manuscript.

Disclosure of conflict of interest

None.

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References

- [1] Pugliese C, Michetti G, Villa R, Bamberg M, Alesina R, Cottini M, Pezzica E, Motta T. Primary mediastinal seminoma. *Monaldi Arch Chest Dis* 1994; 49: 475-9.
- [2] Zhu S, Li Y, Liu G, Han X, Gong L, Yao L, Lan M, Zhang W. Primary lung seminoma in a 76-year-old man: a case report. *Int J Clin Exp Pathol* 2010; 3: 730-5.
- [3] Bokemeyer C, Droz JP, Horwich A, Gerl A, Fossa SD, Beyer J, Pont J, Schmoll HJ, Kanz L, Einhorn L, Nichols CR, Hartmann JT. Extragonadal seminoma: an international multicenter analysis of prognostic factors and long term treatment outcome. *Cancer* 2001; 91: 1394-401.
- [4] Hsu YJ, Pai L, Chen YC, Ho CL, Kao WY, Chao TY. Extragonadal germ cell tumors in Taiwan: an analysis of treatment results of 59 patients. *Cancer* 2002; 95: 766-74.
- [5] Balogun-Ojuri B, Lee YM, Save V, Ibrahim A, Warren AY, Fearnhead NS. A rare case of primary seminoma of the small bowel with lymph node involvement. *J Gastrointest Cancer* 2011; 42: 183-5.
- [6] Brown RS, Yassin J, Colville DH, Harland SJ, Payne HA. First report of an isolated jejunal seminoma: presentation with melaena and iron deficiency anaemia. *Clin Oncol (R Coll Radiol)* 2001; 13: 455-7.
- [7] Kimura F, Watanabe S, Shimizu S, Nakajima F, Hayakawa M, Nakamura H. Primary seminoma of the prostate and embryonal cell carcinoma of the left testis in one patient: a case report. *Nippon Hinyokika Gakkai Zasshi* 1995; 86: 1497-500.
- [8] Woodward PJ. Case 70: seminoma in an undescended testis. *Radiology* 2004; 231: 388-92.
- [9] McGlynn KA, Devesa SS, Sigurdson AJ, Brown LM, Tsao L, Tarone RE. Trends in the incidence of testicular germ cell tumors in the United States. *Cancer* 2003; 97: 63-70.
- [10] Werner R, Merz H, Birnbaum W, Marshall L, Schröder T, Reiz B, Kavran JM, Bäumer T, Capetian P, Hiort O. 46, XY gonadal dysgenesis due to a homozygous mutation in desert hedgehog (DHH) identified by exome sequencing. *J Clin Endocrinol Metab* 2015; 100: E1022-9.