

Missing Clinical Work Up Leading to Misdiagnosis of a Case of Germ Cell Tumour

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Abstract

Background: The large majority of primary testicular tumours originate from germ cells. Cryptorchidism remains the most common risk factor for testicular germ cell tumors. Approximately 10% of the cases are associated with past (corrected) or present cryptorchidism. Seminoma is the most frequent GCT and frequently occurs in undescended testes (5% to 8%).

Case report: A 30-year male attended surgery OPD with a mass in the right lumbar region. CT scan revealed a small intestinal mass which was also verified by the surgeons intraoperatively. On histopathological examination of the resected specimen a diagnosis of neuroendocrine tumour (Carcinoid) was offered. The patient came to us requesting immunohistochemistry for confirmation but it showed CK and chromogranin negativity. Further marker study showed the tumour to be positive for CD117. Revised histomorphology along with immunohistochemistry favoured the diagnosis of extragonadal germ cell tumour (seminoma). Surgeons later confirmed the soft tissue mass to be that of undescended testis, thereby leading to a final diagnosis of seminoma.

Conclusion: Cryptorchid patients have approximately a fourfold elevated risk of testicular germ cell tumors. The histopathological diagnosis at times is sufficient when proper background information is available to the pathologist. In the absence of such information, the use of adjunct studies helps us to arrive at a correct diagnosis.

Keywords: Germ cell tumour; Cryptorchidism; Immunohistochemistry

Introduction

Testicular neoplasms constitute approximately 1% of all cancers in men. The large majority of primary testicular tumours originate from germ cells (94% to 96%). Cryptorchidism (undescended testis) remains the most common risk factor for testicular germ cell tumors. In many series, approximately 10% of the cases are associated with past (corrected) or present cryptorchidism [1,2].

Seminoma is the most frequent GCT and frequently occurs in undescended testes (5% to 8%). "Pure seminoma" represents approximately 50% of all testicular germ cell tumors and occurs at an average age of 40 years [3], which is 5 to 10 years older than patients with non-seminomatous germ cell tumors. We present a case of seminoma testis which was misdiagnosed as a neuroendocrine tumor due to wrong clinical background provided by the clinicians. The correct identification of these tumors is necessary since the treatment for seminoma is different from that of a neuroendocrine tumor. Seminoma testis is a highly radiosensitive tumor and treatments include radical orchidectomy, radiation therapy and chemotherapy according to the stage of the disease. On the other hand, neuroendocrine tumors would be treated by surgical removal of the tumor with medical treatment.

Case History

A 30-year male had attended surgery out patient department with a complain of pain abdomen for 6 months. Clinician on examination found a mass in the right lumbar region. CT scan revealed a non-enhancing, hypo attenuated SOL measuring 80 mm × 60 mm with in the right lateral aspect of the abdominal cavity, origin possibly in the walls of the small bowel jejunum. Exploratory laparotomy was done, that also revealed an extraluminal duodenal growth, which was excised and sent for histopathology.

Gross examination of the resected specimen was reported as

greyish white tissue measuring 7 cm × 6 cm with lobulated appearance with soft, solid areas and foci of haemorrhage and necrosis on cut section. Microscopical examination of the sections from the tissue showed uniform cells with vesicular chromatin, prominent nucleoli arranged in sheets, intervened by fibrous trabeculae with associated lymphocytic infiltration and extensive areas of necrosis. The histological

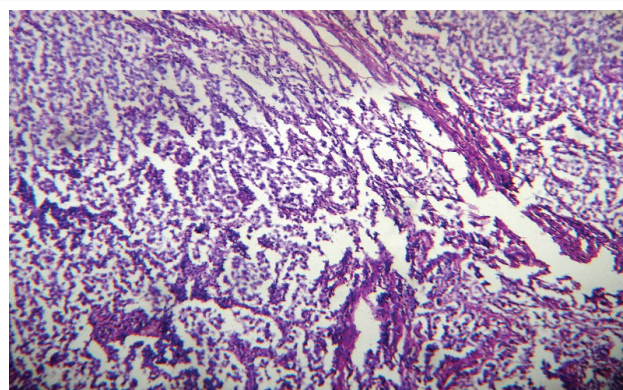


Figure 1: Showing low power view (10X).

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diagnosis of neuroendocrine tumour (Carcinoid) of small bowel was given (Figures 1-3).

The patient came to us for immunohistochemistry to confirm the diagnosis. However, CK and Chromogranin were found negative. Revised histopathology and suspicion of extra gonadal seminoma was high so larger panels of immunomarkers were subjected. CD117, Vimetin and CD45 (in the lymphocytic population) all were positive in appropriate tumour morphology. CD117 was strongly positive (Figure 4a-4d) in tumour cells whereas CD45 was positive in lymphocytic infiltrates in interlobular stroma. So a diagnosis of extragonadal germ cell tumour was confirmed (seminoma). Surgeons later confirmed that the patient had undescended testes and the soft tissue mass to be that of

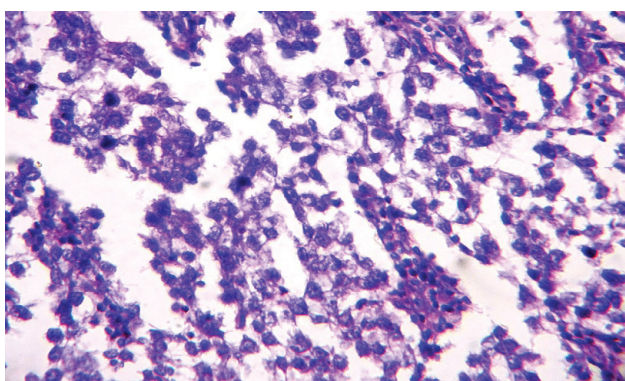


Figure 2: Showing sheets of uniform cells along with intervening fibrous septa and lymphocytic infiltration (40X).

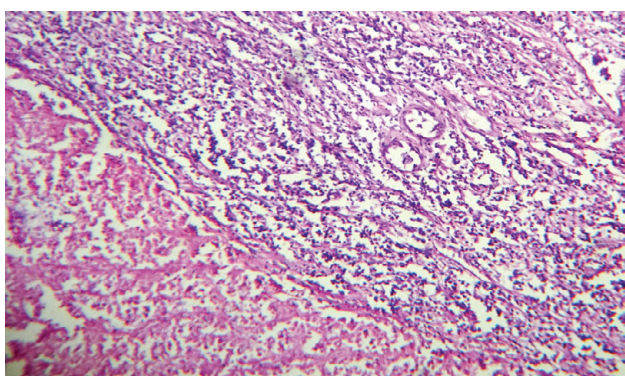


Figure 3: Showing neoplastic cells along with areas of necrosis (40X).

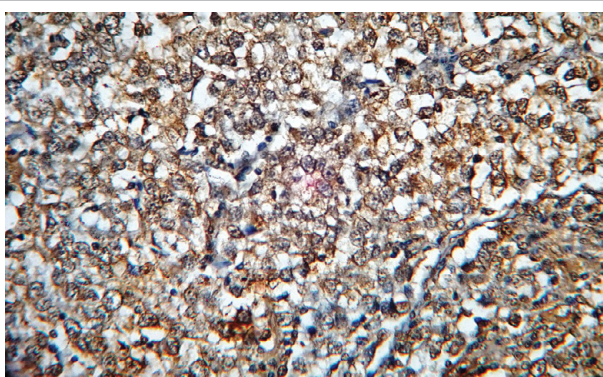


Figure 4a: Showing positive staining for CD 117 (40X).

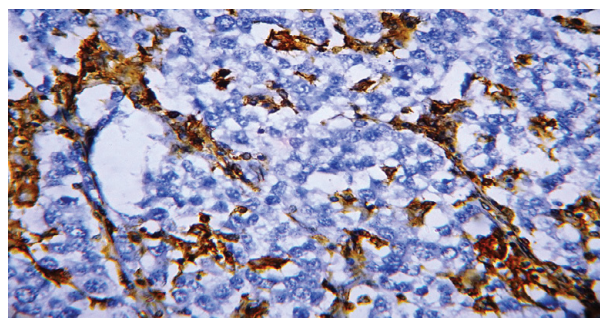


Figure 4b: Showing positive staining for CD 45(40X).

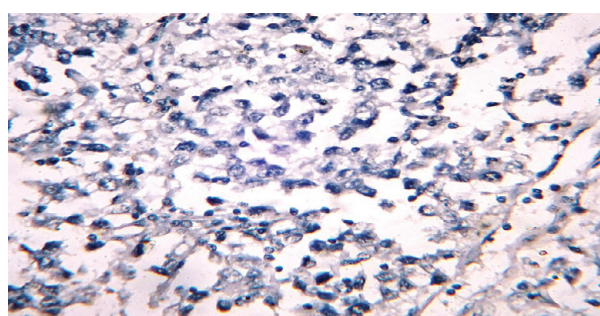


Figure 4c: Showing negative staining for cytokeratin (40X).

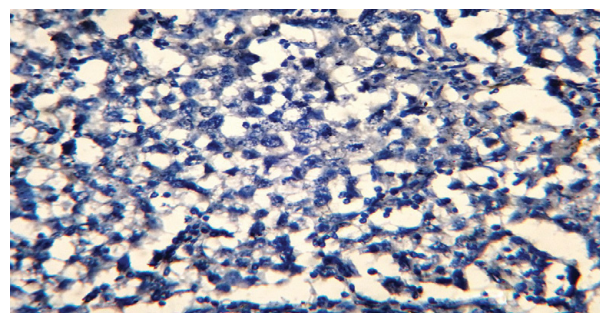


Figure 4d: Showing negative staining for chromogranin (40X).

undescended testis. A final revised diagnosis of classical seminoma was made (Table 1 shows the IHC profile of the tumor).

Discussion

The incidence germ cell tumour is about 3-5 folds increased in men with a history of cryptorchidism [4]. In those with unilateral cryptorchidism, both the undescended testicle and the normal, contralateral testicle have increased risk of testicular cancer [5]. The incidence of testicular cancer is possibly increased in men with hypospadias and in men with inguinal hernia, but the evidence is less strong than for cryptorchidism [6]. Atrophy adds to the risk of germ cell tumours in maldescent [7] and the normal, contralateral testicle has an increased risk of testicular cancer. The presence of atrophy in maldescent testes is a major factor in germ cell neoplasia [5].

Seminoma is the most common testicular neoplasm and as mentioned above, frequently occurs in undescended testis; 85% to 90% of seminomas are of the "typical" or classic type, and the remainder consist of rare variants such as anaplastic seminoma and seminoma with syncytiotrophoblastic giant cells [8].

IHC marker	Results
Cytokeratin	Negative
Chromogranin	Negative
c-Kit	Strongly positive
Vimentin	Positive
CD45	Positive in background lymphocytes

Table 1: Showing IHC characteristics of the tumor.

Solid patterns of embryonal carcinoma may be confused with seminoma. In poorly fixed specimens, cytoplasmic autolysis occurs, obscuring the cell borders and causing apparent nuclear overlapping, thus creating confusion with solid patterns of embryonal carcinoma. Solid patterns of yolk sac tumor may also resemble seminoma, but these are usually associated with more characteristic yolk sac tumor patterns. Otherwise, in most well-fixed seminomas, diagnosis is not that difficult, provided the proper site or history of undescended testis is mentioned in the clinical note.

The pathologist plays a key role in the management of patients with testicular tumours by accurately classifying the tumour, by providing the appropriate pathologic stage, and by identifying prognostic parameters. Therefore, evaluation of a testicular tumour must include a careful gross examination to document tumour size, to determine whether the tumour extends into the spermatic cord and tunica, to note the presence of variations in gross appearance including necrosis and haemorrhage, and to direct adequate sampling for microscopic examination. Microscopic examination must identify the histologic type i.e. germ cell or non-germ cell tumor, seminoma or non-seminomatous (NSGCT) or mixed germ cell tumors (MGCT), including the different components and their relative percentages, determine the involvement of the spermatic cord and tunica albuginea, and confirm the presence or absence of vascular or lymphatic invasion.

In our case, radiological study suggested the mass to be originating from the small bowel wall. Surgeons also in their intraoperative findings mentioned it to be a case of extraluminal duodenal mass. Nowhere it was mentioned the possibility of the tissue mass to be that of undescended testis or nor the history of cryptorchidism was being provided. This possibly led to failure to recognise the tumour correctly on gross examination.

The reporting pathologist diagnosed it keeping in mind a small intestinal mass. Testicular mass was missed completely on radiology, clinical and gross examination. A possible diagnosis of neuroendocrine tumour (carcinoid) was given with an advice to perform immunohistochemistry for CK and Chromogranin for confirmation.

Immunostaining for PLAP is diffusely positive in 85% to 100% seminomatous cells with a membranous or perinuclear dot pattern. C-Kit (CD117) has a similar established incidence and distribution. Vimentin can be positive, but epithelial membrane antigen (EMA), AFP, and CD30 are negative in most seminomas. Cytokeratin is usually negative but may be focally positive in up to 40% of the tumor.

Both CK and Chromogranin came out to be negative in our case. CD45 came to be positive only in the lymphocytic population scattered in between the tumour cells. After that out of curiosity, we performed CD117 and vimentin. Both showed positivity, but CD117 showed strong and diffusely positive reaction.

Revised histomorphology along with immunohistochemistry favoured the diagnosis of extragonadal germ cell tumour, resembling seminoma. We conveyed our findings to the operating surgeons and

later on they confirmed the tissue mass sent for histopathology to be that of undescended testis, which they missed during their initial clinical examination.

Our final conclusive diagnosis was seminoma occurring in an undescended testis and an advice was given for clinical and radiological evaluation of the remaining testicle as many a times the normal, contralateral testicle had an increased risk of testicular cancer as mentioned above.

Histopathological picture can be confusing if not interpreted in the proper clinical context. Therefore, every part of the patient-doctor interaction is crucial to a proper diagnosis, right from clinical history and examination to the inputs from radiologist, gross examination and finally the microscopy and special techniques like immunohistochemistry. Especially when there is failure at any of these steps, immunohistochemical examination of the sections can redirect the pathologist towards the correct diagnosis.

Conclusion

Though histopathology is the gold standard for most of the tumours, especially for those of the germ cell origin but can be confusing at times if proper history is not provided or a wrong site is mentioned. The histopathological diagnosis often necessitates the use of adjunct studies that allow for differentiation among neoplasms. A treatment protocol for a certain tumour like seminoma can be completely different from that of a neuroendocrine neoplasm or a poorly differentiated carcinoma. So, clinicians should always be careful while sending the specimens for histopathology because facility for immunohistochemical study is not available in all the laboratories. A suspicion regarding the histological picture with ancillary techniques led us to ultimately diagnose the case correctly. We would like to emphasize the point that minor clinical details, which many a time our clinicians forget to mention, can save both patient's harassment and pathologists' valuable time and avoid a wrong diagnosis.

References

- Halme A, Kellokumpu-Lehtinen P, Lehtonen T, Teppo L (1989) Morphology of testicular germ cell tumours in treated and untreated cryptorchidism. *Br J Urol* 64: 78-83.
- Pike MC, Chilvers C, Peckham MJ (1986) Effects of age at orchidopexy on risk of testicular cancer. *Lancet* 1: 1246-1248.
- Fischer CG, Waechter W, Kraus S, Perez EF, Weidner W, et al. (1998) Urologic tumors in the Federal Republic of Germany: data on 56,013 cases from hospital cancer registries. *Cancer* 82: 775-783.
- United Kingdom Testicular Cancer Study Group (1994) Aetiology of testicular cancer: association with congenital abnormalities, age at puberty, infertility, and exercise. United Kingdom Testicular Cancer Study Group. *BMJ* 308: 1393-1399.
- Moller H, Prener A, Skakkebaek NE (1996) Testicular cancer, cryptorchidism, inguinal hernia, testicular atrophy, and genital malformations: Case-control studies in Denmark. *Cancer Causes Control* 7: 264-274.
- Prener A, Engholm G, Jensen OM (1996) Genital anomalies and risk for testicular cancer in Danish men. *Epidemiology* 7: 14-19.
- Harland SJ, Cook PA, Fossa SD, Horwich A, Mead GM, et al. (1998) Intratubular germ cell neoplasia of the contralateral testis in testicular cancer: Defining a high risk group. *J Urol* 160: 1353-1357.
- Ulbricht TM (1993) Germ cell neoplasms of the testis. *Am J Surg Pathol* 17: 1075-1091.