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A rare testicular tumor with elevated alkaline phosphatase

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ABSTRACT

Background: The majority of Leydig cell tumors (LCTs) are found in males, usually when they have 5–10 years of age. Children typically present with precocious puberty due to excessive testosterone secreted by the tumor, one-third of female patients present a recent history of progressive masculinization. Alkaline phosphatase is normally at low levels.
Case Presentation: A 30-year-old male referred to the hospital with a complaint of fever, chills, nausea and weight loss, and history of diabetes mellitus type 1. In the physical examination of testis, no abnormal findings were revealed. Scrotal ultrasonography demonstrated a small (7.5 ×4.8 mm) mass which seemed to be very vascular and suggestive of neoplastic lesion. Echogenicity of the head of the right epididymis was heterogeneous and the small cyst of about 4.5 mm was present on it. Left testis had normal size and no space occupying lesion in it. The hormonal test revealed high levels of alkaline phosphatase, ferritin, FSH and LH, normal level of testosterone, LDH, β-HCG and α-feto-protein. Immunohistochemistry results revealed negative CD30, alpha-fetoprotein and CK results, but calretinin, vimentin and S-100 were positive in tumor cells.
Conclusions: LCTs are rare testicular tumors arising from male gonadal interstitium and very rare in adulthood. Because this tumor consists of immature embryonic tissues it can be accompanied by an elevation in alkaline phosphatase level.

Case Report

Implication for health policy/practice/research/medical education:
Leydig cell tumors (LCTs) comprise 1%-3% of all testicular neoplasms. High elevated alkaline phosphatase may be a possible finding in LCT.

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1. Background

Leydig cell tumor is a rare germ cell tumor that originates from gonadal stroma, accounting for about 15 to 3% of testicular neoplasms in adults and about 4% in pediatric patients who have not yet reached maturity (1). Leydig cells are named after Franz Leydig. They are interstitial cells located between the seminiferous tubules. They are involved in the development of secondary male characteristics and maintenance of spermatogenesis as they produce testosterone when stimulated by LH (2). Adult males aging between 20- and 60-years are rarely affected. However, in adults about 7-10 cases are diagnosed with malignant form per 100 cases (2,3). Early detection and management of these tumors is necessary to preserve the reproductive capacity with long-term follow-up for recurrence or metastasis. Contrary to the results of previous studies that found malignancy to be recognizable based on the presence of lymphatic invasion, prominent cellular pleomorphism, and abnormal myotic forms, it is suggested that the most trusted criteria to

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detect malignancy would be metastasis (4). These tumors not only mainly secrete testosterone but also have the ability to release estrogen. Studies that have been conducted over the past years have shown an increase in the incidence of this type of tumor. This may be due to the developments on the knowledge on this tumor and increasing facility in the use of ultrasonography. Despite the suspicions about endocrine origins for this tumor, its etiology is still not well-known. It may be due to symptoms such as endocrine disorders, libido depression, erectile dysfunction, gynecomastia, testicular tenderness, swelling and infertility. Rare cases reported its association with precocious puberty, cryptorchidism and Klinefelter syndrome although cryptorchidism is not considered as a risk factor (5). Radical orchiectomy has been used as one of the most important surgical procedures for the treatment of this disease, and testis sparing surgery is being considered as an alternative modality, according to its resistance to conventional chemotherapy and radiotherapy (6). Presently, we discuss a case of the Leydig cell tumor (LCT) that had a remarkable serum level of alkaline phosphatase.

2. Case Presentation

The patient is a 30-year-old male who referred to the hospital with a complaint of fever and chills (Considering the duration of fever and chills in the course of several weeks) and the presence of nausea, 4 kg of weight loss in 3 weeks, and a history of diabetes mellitus type 1 since he was 20 years old. Scrotal ultrasonography demonstrated a 7.5×4.8 mm well-demarcated sub-capsular low-echo space occupying lesion in the upper pole of the right testis, which seemed to be very vascular and suggestive of neoplastic lesion. Echogenicity of the head of the right epididymis was heterogeneous and the small cyst of about 4.5 mm was present on it. Also bilateral mildly tortoise veins dorsal to right testis and the surrounding left spermatic cord with a diameter up to 2.3 mm compatible with low grade varicocele was seen. The hormonal test revealed high levels of alkaline phosphatase, ferritin, FSH and LH. Other findings such as β-HCG-, ALT, AST, LDH, ESR, CRP, RF, CBC and urine analysis were normal. Immunohistochemistry included negative CD30, α--fetoprotein (AFP) and CK results. However, calretinin and vimentin and S-100 were positive in tumor cells. For further examination and for the purpose of conducting the pathologic result, a test specimen with dimensions of 6.5×3.5×3.5 cm and weighing 55 g was prepared. In this section, a mass of 7 mm diameter was seen on the upper testicular pole with a homogeneous orange cross section and a relatively specific range, without necrosis or bleeding. Findings of the microscopic investigations showed fragments of tissue including testis with epididymis and cords. The testicular parenchyma represented a neoplasm, composed of proliferated cells, having round vesicular nuclei with nucleoli nest and abundant granular cytoplasm, at times clear and vascularized. They were closely packed with intervening congested vessels and forming a circumscribed nodule (Figure 1). LCT was diagnosed according to immunohistochemistry and pathological findings. Tunica albuginea capsule, epididymis and cord were unremarkable and dilation moderate with maturity arrest and non-tumoral seminiferous tubules were

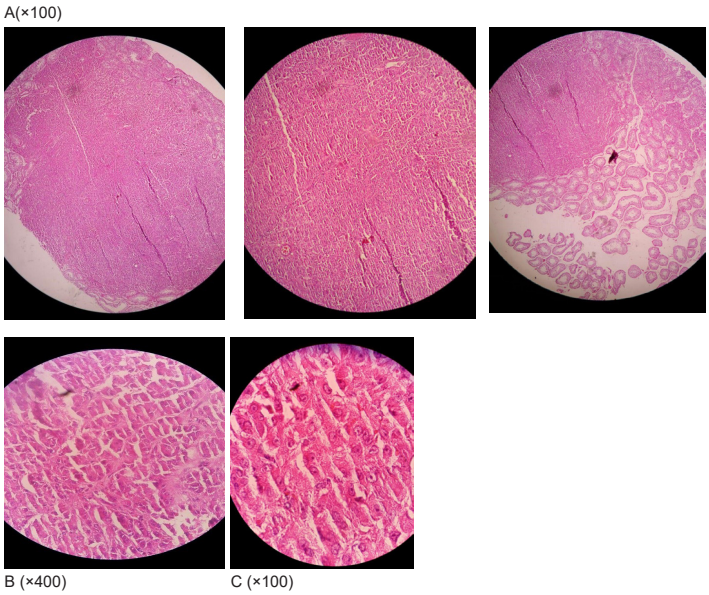

Figure 1. Abundant eosinophilic cytoplasm with vesicular nucleus and prominent nucleoli.

seen. Considering the possibility of malignancy, further evaluations were conducted to reveal additional abnormal findings. Abdominopelvic and chest CT scanning, bone scan and MRCP were normal.

3. Discussion

It is rare for LCT to be diagnosed with a malignancy. If not malignant, it is reported to have a remarkable prognosis while survival in the malignant form of LCT is reported to have a mean age of 2 years (2). Metastasis is a key criterion for the diagnosis which its common sites are liver, lungs and bone respectively (7). Laboratory findings are usually nonspecific but serum testosterone levels might be elevated in some cases. Scrotal ultrasonography may be used to confirm the diagnosis and would reveal a hyperechoic mass with an obvious border rather than the surrounding tissues (8). MRI with contrast might distinguish LCTs with marked enhancement on the contrary to other testicular tumors (9). Computed tomography would be helping to reveal available distant metastasis of the tumor if malignancy is suspected (1). Macroscopic and microscopic histology alongside with immunohistochemical marker studies are valuable in order to identify LCT (10). Surgery plays an important role in the treatment, while chemotherapy and radiotherapy have little effect on management of the tumor since it does not respond well to such treatments (11), It was primarily conducted using radical inguinal orchiectomy and testis-sparing surgery was further introduced. Alkaline phosphatase is a glycoprotein with the capability of hydrolyzing phosphate monoesters. Intestinal, placental, germ cell and bone alkaline phosphatase are its known four subtypes. Cancerous cells can overexpress the gene coding this enzyme and therefore elevated the level of alkaline phosphatase might be detected (12). Germ cell alkaline phosphatase is normally at low levels (13). Although it has been reported that alkaline phosphatase could act as an informative and useful tool of diagnosing of germ cell tumor (14), other studies which focused on LCT laboratory findings revealed no significant amount of alkaline phosphatase in their studies. It should be noted that alkaline phosphatase levels might increase if metastasis occurs. The fact that such levels are due to overexpression of alkaline phosphatase genes in germ cells or lysis of metastatic cells is questionable. Determining the isoenzyme types of alkaline phosphatase in such cases would help to distinguish the cause of the elevated alkaline phosphatase, if it is related to the tumor itself or another source is exerting the enzyme into the serum. Further studies with greater sample size would be necessary.

4. Conclusions

LCTs (LCTs) are rare testicular tumors originating from male gonadal interstitium.

Alkaline phosphatase levels might be increased due to the presence testicular leydig tumor.

Authors' contribution

MRKF and RN managed the patient and prepared the manuscript. SMKN, MB and MD finalized the paper. All authors read and signed the final manuscript.

Conflicts of interest

There were no points of conflicts.

Ethical considerations

Ethical issues (including plagiarism, data fabrication, double publication) have been completely observed by the authors. The patient has given his informed consent regarding publication of this case report.

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