Histopathological pattern of testicular diseases in western Saudi Arabia

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ABSTRACT

الأهداف: دراسة الخصائص الهيستوباثولوجية لأمراض الخصية في المدينة المنورة.

الطريقة: أجريت هذه الدراسة في قسم علم الأمراض بأحد المستشفيات المرجعية بالمدينة المنورة خلال الفترة من يناير 2006م إلى ديسمبر 2017م، حيث تم مراجعة السجلات والتقارير الطبية لجميع المرضى الذين تم أخذ عينات الخصية لديهم. تم إدخال البيانات وتحليلها باستخدام برنامجي أكسيل و SPSS.

النتائج: من بين 199 عينة للخصية وردت، تم أخذ 108 (54.3%) لأغراض التشخيص، في حين أن 91 (45.7%) كانت لأغراض علاجية. وكان العقم عند الذكور هو المؤشر الوحيد في مجموعة أمراض الخصية التشخيصية، وهو ما يمثل 108 (54.3%) مع متوسط العمر 28±7.9 سنة. من ناحية أخرى، كانت الأمراض الحميدة للخصية هي أكثر المؤشرات شيوعاً في مجموعة خزعات الخصية العلاجية وشكلت 76 حالة (38.2%)، تليها أورام الخصية تمثل 15 حالة (7.5%) كان احتشاء النزفية الناتج من التواء الخصية هو النمط النسيجي الأكثر شيوعاً في مجموعة أمراض الخصية الحميدة، وشكل 46 (23.2%) من الحالات مع متوسط العمر 32.1±8.1 سنة. شكل ورم الخلايا الجرثومية غير الداخمية المختلطة 7 (3.5%) من حالات أورام الخصية، تلاه ورم السيمينوما الذي شكل 5 (2.5%) من الحالات بمتوسط أعمار 33.7±8.1 سنة، 35.6±9.1 سنة على التوالي.

الخاتمة: توافقت نتائج هذه الدراسة مع الدراسات العالمية والمحلية.

Objectives: To determine the histopathological pattern of testicular diseases among Saudi patients in Madinah, Saudi Arabia.

Methods: This retrospective histopathology-based study was conducted in a tertiary care hospital in Madinah, Saudi Arabia, from January 2006 to December 2017. The data collected were entered into MS-Excel and analyzed using the Statistical Packages for Social Sciences Version 19.

Results: Of the 199 testicular specimens received, 108 (54.3%) of the biopsies were taken for diagnostic test, while 91 (45.7%) were for therapeutic test. The male infertility was the only indication in the diagnostic group, accounting for 108 (54.3%) with a mean age of 28±7.9 years. Benign conditions of the testes were the most common indication in the therapeutic group accounting for 76 cases (38.2%), followed by 15 cases (7.5%) of testicular tumors. Hemorrhagic infarction from testicular torsion was the most common histologic patterns in benign testicular conditions group, accounting for 46 (23.2%) of the cases with a mean age of patients 32.1±8.1 years. Mixed non-seminomatous germ cell tumor was the most common primary tumor in 7 (3.5%) cases, followed by seminoma occurring in 5 (2.5%) cases. Mean ages for these patients were 33.7±8.1 years for primary tumor and 35.6±9.1 years for seminoma.

Conclusions: The pattern of testicular diseases on the basis of histopathology experience in the Madinah region appears to conform to world literature and KSA.

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Testicular biopsy and histopathological examination are very important approaches to arrive at definitive diagnosis of many diseases, including a crucial role in male primary infertility.[1] Recently testicular biopsies have been used for testicular sperm extraction in patients of primary infertility.[2] Moreover histological examinations of surgical specimens namely, orchiectomies are also equally essential in testicular tumor pathology as well

as for exclusion of premalignant conditions. Torsions, cryptorchidism, inflammations, and testicular tumors all belong to the broad category of differential diagnosis of chronic orchialgia and constitute a significant proportion of urology clinical practice.[3] The prevalence and incidence of testicular tumors are not particularly high around the globe. During the year 2016, there were only less than 9,000 new cases of testicular cancer in the whole United States.[4] It is specifically rare in Africa[5,6] and Middle Eastern Asia.[7,8] Recently, a number of histological studies for disease patterns have been published in the peer-reviewed scientific literature from Madinah region of Kingdom of Saudi Arabia (KSA) addressing major human body systems such as breast,[9,10] gastrointestinal tract,[11-14] and urinary tract;[15,16] as well as thyroid[17] and lymph nodes.[18]

The objective of our study is to observe the pattern of testicular disease, as experienced in the histopathology department of a tertiary care hospital of Madinah; and privileged to have a large patient catchment area of the western region of KSA.

Methods. This retrospective study included histopathological reports of all patients with testicular diseases who had undergone testicular biopsies (92 cases) and surgical orchiectomies (107 cases) between January 2006 and December 2017 at the King Fahad Hospital, Madinah, Saudi Arabia. Diagnosis of testicular tumors was made only in the orchidectomy specimens, on clinical grounds and radiological examinations, which was performed in the urology outpatient clinic. The specimens were preserved in 10% buffered formalin as fixative and read by a consultant pathologist after routine slide staining with hematoxylin and eosin stain. The data collected from the records of the histopathology department included age of the patients, indication for the biopsy and the final histology report were analyzed using the Statistical Package for Social Sciences software version 19 (SPSS Inc, Chicago, IL, USA). The only exclusion criteria was non-Saudi (expatriate) patients, who underwent the testicular biopsies or orchidectomy procedures.

For prior related research, services of general search engines namely Google search and MSN Bing search engine were utilized; as well as specific medical search engine Pubmed/Medline, Science Direct, Scopus and Google scholar were used. The present study was a retrospective research involving the histopathology record and did not touch the patients personal information or implicate upon the management, thus was according to the principles of Helsinki Declaration.

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Results. One hundred and ninety-nine patients with testicular biopsies were received at the Department of Pathology, King Fahad Hospital, Madinah, Saudi Arabia from January 2006 to December 2017. Their age ranged from 5 to 96 years with a mean age of 29.4±7.2 years. One hundred and forty-four patients had unilateral and 55 patients had bilateral testicular biopsies.

Table 1 shows the frequency and percentages of common indications for testicular biopsy and summary of breakdown. Male infertility was the most common indication accounting for more than half of patients.

The mean age of patients with male infertility group was 28 ±7.9 years (range 13-50); and the most

Table 1 - Common indications for testicular biopsy.

Indication	Histopathologic diagnosis	n	(%)
Diagnostic	Male infertility	108	(54.3)
Therapeutic	Benign testicular diseases	76	(38.2)
	testicular tumors	15	(7.5)
Total		**199**	**(100)**

Table 2 - Histological diagnoses, frequencies, percentages and mean ages of all testicular specimens (n=199).

Histopathologic diagnosis	n	(%)	Mean age (years)
Male infertility (n=108)			
Hypospermatogenesis	45	(22.7)	26.3
Sertoli cell only syndrome	32	(16.1)	31.3
Complete spermatogenic arrest	17	(8.5)	29.6
Testicular atrophy	9	(4.5)	14.8
Tubular hyalinization	5	(2.5)	35.6
Benign testicular diseases (n=76)			
Testicular torsion	46	(23.2)	32.1
Inflammatory conditions	17	(8.5)	27.6
Cryptorchidism	13	(6.5)	19.0
Testicular tumors (n=15)			
Primary tumors			
Mixed nsgct	7	(3.5)	33.7
Seminoma	5	(2.5)	35.6
Mature cystic teratoma	1	(0.5)	31.0
Adenomatoid tumor of the epididymis	1	(0.5)	16.0
Secondary tumors			
Diffuse large b-cell nhl	1	(0.5)	21.0
Total	**199**	**(100)**	

common histologic pattern in this group was hypo spermatogenesis (**Table 2**).The mean age of patients with benign testicular conditions was 31.5±7.8 years (range 5-96 years). Hemorrhagic infarction from testicular torsion was the most common histologic pattern in this group (**Table 2**).

The age of patients with testicular tumors ranged from 16 to 70 years with a mean age of 38.2±9.5 years. Primary tumors of the testes accounted for 93.3% of testicular tumors and the most common primary malignant tumor of the testis was mixed non-semi nomatous germ cell tumor (**Table 2**).

Discussion. Testicular biopsy has been conventionally used as an important procedure in the diagnosis and management of infertility. Radiologically guided testicular biopsy is a less invasive method of obtaining specimen for histological diagnosis;[19] however, open biopsies or orchidectomies have also been performed, frequently in difficult cases, inflammatory conditions and testicular tumors, accounting for substantial workload on the histopathologist. Recently, robotic assisted surgery has also been introduced in andrological surgical practices.[20] Excisional surgery of the testis is also therapeutically indicated for benign conditions of the testis such as infarctions of testicular torsion, testicular atrophy in cryptorchidism, or in chronic epididymo orchitis irresponsive to traditional treatments.[5]

During the study period, we reported 108 cases of primary infertility; the mean age of patients who underwent testicular biopsies for male infertility was 28 ±7.9 years (range 13-50). A study on testicular biopsies from Zaria, Nigeria in their 472 cases, reported a mean age of 31 years,[21] whereas a group from Lagos Nigeria reported a mean age of 30 years.[22] A group of Pakistani scientists in their study on evaluation of azoospermia and testicular biopsies reported a mean age of 28 years.[23] From within the KSA, a study from the city of Jeddah reported a mean age of 24.5 years.[24] Most of the studies cited in the discussion appear to observe a mean age above 30 years including this present study, suggesting a possibility that the female partners have to go through detailed investigations before the male partner is submitted to the invasive procedure of testicular biopsies. However, in one study from Jeddah, KSA that observed a younger mean age of less than 25 years, this difference as well as many other observed differences in their study as compared with other studies have not been well understood.[24] On the basis of age range, we also noted testicular biopsy for infertility, carried out at a very young age of 13; most likely due to typographic error or other errors of recording, beyond our control.

In the present study, we found hypospermatogenesis to be the most common pattern of histology accounting for 22.7% cases. Ahmed and Bello from Zaria, Nigeria in their 472 cases, also found hypospermatogenesis to be the most frequent histology accounting for 35.2% of their cases.[21] Whereas a scientists from Lagos, Nigeria, found a testicular atrophy in 30 (58.8%) as the most common diagnosis.[22] In the same year, Parikh et al from India reported Sertoli cell only syndrome (SCOS) to be the most common abnormal histopathological finding accounting for 18.75% of their cases.[25] Similar was the observation by a group from Pakistan, who observed SCOS in 30.2% of their cases.[23] There is only one recent study on the histological patterns of testicular biopsies from KSA, in which Abdulla and Bondagji from Jeddah, also found hypospermatogenesis to be most frequent, accounting for 29% of their cases.[24] Although different observations have been reported from recent studies from a number of geographical regions, hypospermatogenesis appears to be the most common diagnosis reported by most of them and our observations are in concordance with other studies including the study from KSA.

In our experience, hemorrhagic infarction from testicular torsion accounted for about a quarter of all cases (46 out of 199 cases). Although these figure appear to be high, our study is only a hospital-based pathology data and is obviously biased by the local practices of the urology surgeons. However, this condition is quite rare and figures of as low as 1.1 per 100,000 have been reported recently from Korea.[26] The cause or the precipitating factor of torsion is usually not detectable, in majority of cases; however, in rare instances trauma has been reported to be the underlying factor.[27]

We also found complete hemorrhagic infarction in all our patients of torsion of testis. Recently from Central KSA, a case of torsion of testis in an elderly 63 year old patient, was found to have a seminoma as the underlying cause.[28] Torsion of testis is predominantly a disease of young age, with highest incidence reported in adolescent age group.[26] The mean age of our torsion was 32.1±8.1 years (range 15-91 years). Case reports of testicular torsion in extremes of ages have been reported in the medical literature at the age of 67 years age from UK.[29] One of our patient was 91 year old, but we do not have any clinical history, investigations or follow-up to present and publish it as a case report in the medical literature. Cryptorchidism considered as the most

common anomaly of genitourinary tract accounting for 3% cases in full term boys.[30] In our experience too, cryptorchidism accounted for about 10% of total cases (22 out of 199 cases). This is a condition of newborns and infants, and a delay in surgery can lead to infertility and high risk of testicular cancers. At most centres, the target for surgery is within one year.[31] In the present study, patients of cryptorchidism had a mean age of 19±4.7 years (range 15-39 years). The possible explanation of this gross difference in the age at presentation and performance of surgery can be explained by lack of education and possible problems with access to treatment. Interestingly, none of the cases revealed any premalignant or malignant lesion on histological examination of the orchidectomy specimens. These aspects of our observation need to be followed up in well-designed prospective clinicopathological studies.

In our experience, there were 12 cases of malignant primary testicular tumors, accounting for only about 6% of our testicular histopathology workload. Although these figures are quite low, nonetheless are in conformation with world literature, which report its rarity especially in Asian populations;[6] as well as from the KSA.[7,8] Scientists from London, analyzing the global incidence of testicular cancer have reported its incidence rate to be highest in New Zealand and lowest in India.[32] Researcher from Denmark found testicular cancer to be a rare disease, with approximately 300 cases per year in their whole country, although it was the most common cancer in men aged 20 to 40 years.[33] Similarly, Assi et al[6] from Lebanon report a mean age of 32 years in their testicular tumor patients. The finding of these studies are also endorsed locally by the Saudi Cancer registry (published in September 2017) which reported testicular cancer as a rare tumor, with only 98 new testicular cancers reported in 2014.[34] The age of our patients with testicular tumors ranged from 16 to 70 years with a mean age of 38.2±9.5 years. Although the number of testicular cancer patients are low; our observation are in conformation with figures reported from the global, regional, and national studies.

The limitations of the study were the possible errors of data recording (such as age), which were not within our control, as it was a retrospective study. Moreover, due to very low number of testicular malignancies, in-depth discussion on malignancies and any meaningful epidemiological conclusion could not be made.

In conclusion, our observation of testicular histopathology pattern appears to be similar to the reported world literature as well as from the KSA. Minor differences in age range appear to be due to limitations of retrospective study such as improper recording of data or possibly lack of education in the rural population, leading to late presentation to the hospitals.

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