Persistent Müllerian duct syndrome (PMDS) is a disorder of male sexual development in which there is failure of regression of the Müllerian ducts in an otherwise normally differentiated 46 XY male[1]. Over 100 cases have been reported in the literature to date[2]. PMDS results from defective synthesis or action of anti-Müllerian hormone (AMH), which is produced by Sertoli cells in the testes and is responsible for the regression of the Müllerian ducts in the male fetus at 8-10 weeks' gestation[3]. Clinically patients have normal male external genitalia but also a cervix, uterus and fallopian tubes.

PMDS may be associated with unilateral or bilateral cryptorchidism, and the syndrome is usually not suspected until surgery for this. Herein the authors report a 9 year old boy with PMDS who was found to have bilateral synchronous testicular germ cell neoplasia on histology following elective orchiectomy and excision of Müllerian remnants. He is the sixth case of bilateral synchronous testicular malignancy in PMDS.

Case report

A 9 year old phenotypically normal male of Asian origin presented with a history of bilaterally undescended testes. Physical examination revealed a normally developed phal-
band of tissue traversed between them but its significance was not initially appreciated, and a first stage Fowler-Stevens orchidopexy was performed. At second stage surgery, the intra-abdominal structures were further examined. There was a thin vas associated with each testis, but it became clear that the band of tissue between them was likely to represent fallopian tubes which were associated with a midline rudimentary uterine structure deep in the pelvis. The testes were biopsied and no further procedure was carried out at the time as discussion with the family was necessary.

The patient's karyotype was 46 XY, and hormonal levels were in the normal range for age. Results from biopsy of the testes showed atrophic testicular tissue bilaterally with hypoplastic seminiferous tubules lined only by Sertoli cells. There was no evidence of ovarian tissue in the specimens. Occasional spermatogonia were seen in tissue from the left testis only. An endocrinological review was obtained, and in view of the atrophic nature of the testes (and high likelihood of sterility) coupled with the risk of testicular malignancy, bilateral orchiectomy and excision of the Müllerian structures was recommended. With the family's agreement, the patient underwent this surgery electively six months later.

Macroscopically, the appearance of the testes and associated Müllerian structures was unchanged from previous. The resected specimens are shown in Figure 1 (a & b). On histology, however, the resected testes were found to have clusters of tubules containing germ cells with large, vesicular nuclei and prominent nucleoli, with scattered mitotic figures (Figure 2). These features were consistent with bilateral synchronous intra-tubular germ cell neoplasia. The tumour cells were positive for CD117 and placental-like alkaline phosphatase (PLAP), which are expressed in germ cell malignancies; the rudimentary uterus was positive for CD10, expressed by normal endometrial stroma. There was no evidence of invasive tumor, and the resection was complete. Analysis of the Müllerian remnants confirmed the presence of fallopian tubes (Figure 3) and a uterus. The patient has made an uneventful recovery from surgery and is under outpatient follow-up.

Discussion

In early gestation, both the precursors for the Wolffian and Müllerian ducts are present in the fetus regardless of the karyotype[1]. In the male, Sertoli cell-produced AMH induces regression of the Müllerian ducts. In the absence of AMH, these differentiate into the uterus, fallopian tubes and upper vagina. PMDS is thought to be caused by deficient AMH activity or an abnormality in the AMH receptors[2].

The continued expression of AMH in the postnatal period in males suggests it may also have a role in the regulation of gonadal function and testicular descent[1]. In our patient, both testes were intra-abdominal, and the atrophic changes on initial biopsy could have been attributed to prolonged exposure to above optimal temperatures. However, in their review of eight patients with PMDS, Brook et al. (1973)[4] reported three patients with bilaterally hypoplastic testes, despite one testis being normally descended.

PMDS may present as cryptorchidism, with or without inguinal hernia, and transverse testicular ectopia. X-linked or autosomal recessive patterns of inheritance for this condition have been proposed[3]. However, the human AMH gene maps on chromosome 19 p13.3[5] which favours an autosomal mode of inheritance[6]. Patients with PMDS and a mutation in this region of chromosome 19 have been described[1,7].

There is debate regarding the management of PMDS. Recent papers have advocated laparoscopic orchidopexy with or without excision of Müllerian derivatives[2,7,8]. However, patients with PMDS are usually infertile[6]. To date, there have been only a few reported cases of fertility, and absolute proof of paternity was not established[4,6]. The quoted figure for the risk of testicular malignancy in patients with PMDS is 15%, which is similar to that of malignancy in an abdominal testis in cryptorchid men[6].
Our patient, aged nine years, was found to have bilateral testicular germ cell neoplasia on histology following elective orchiectomy. In this case, the testes were known to be atrophic on the basis of previous biopsy. Decisions regarding the management of the testes in much younger patients with PMDS may be more difficult if the testicles appear normal macroscopically and biopsy shows the presence of normal testicular tissue. It is of concern that there are five other relatively recent reports of synchronous bilateral malignant testicular neoplasms in patients with PMDS in the literature[9-13]. Malignant change in the Müllerian remnants has been reported in two patients to date[14, 15].

Conclusion

Herein the authors present a case of bilateral testicular neoplasia in a young patient with PMDS. This is the sixth case of synchronous malignant change in the testes of a patient with PMDS, which should be considered when making treatment decisions for this group of patients.

REFERENCES

5. Rey R. Anti-Müllerian hormone in disorders of sex determination and differentiation. Arq Bras Endocrinol Metab 2005; 49(1); 26-36.

Figure 3. Fallopian tube (FT) with adjacent testicular tissue (T) in PMDS