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LETTER TO THE EDITOR

Mixed germ cell sex cord-stromal tumours of the testis

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Dear Editor,

We have recently published a series of seven cases of mixed germ cell sex cord-stromal tumours (MGSCT) of the testis and ovary comparing their morphological, immunohistochemical and molecular genetic findings [1]. MGSCT of the ovary and testes varied considerably in all these aspects. Germ cells in ovarian MGSCT stained positively with the antibodies to NSE, PLAP, and OCT4 with the exception of one case, which reacted positively for the c-kit protein antibody. The immunoprofile of the germ cells in ovarian MGSCT was identical to that of ovarian dysgerminomas and testicular classical seminomas. In addition, germ cells in one of the ovarian cases showed amplification of 12p, which is a typical feature of ovarian dysgerminomas and testicular classical seminomas [1].

Germ cells in testicular MGSCT were similar in morphology, immunoprofile and molecular genetic findings to those of spermatocytic seminomas. Immunohistochemically, they tested negative with all the above-enumerated antibodies and, in addition, they lacked on molecular biological analysis amplification of 12p [1]. However, there is not a single antibody positively distinguishing germ cells in spermatocytic seminoma from non-neoplastic testicular germ cells in contemporary pathology that we are aware of and that we could have used in our study. It may be one of the reasons why Drs. Ulbright and Young questioned the neoplastic nature of the germ cells in the testicular MGSCT [3, 4]. They reviewed nine testicular sex cord-stromal tumours containing germ cells, which closely mimicked MGSCT but differed from the latter, in that the germ cells were entrapped and non-neoplastic rather than neoplastic [3]. They thought that these tumours closely resembled MGSCT, but represented sex cord stromal tumours with entrapped germ cells, which they considered non-neoplastic. The evidence they presented to support their view was that the germ cells were distributed peripherally, were associated with entrapped seminiferous tubules or occurred in clusters with vaguely tubular shape consistent with preexisting seminiferous tubules [3]. Although some of these cases may have represented sex cord-stromal tumours with entrapped germ cells, in some of them, germ cells seemed not to have any relation to pre-existent seminiferous tubules and were scattered haphazardly forming a true predominant part of the lesion, whilst in other parts of the sex cord, the elements predominated. In one of those cases, inhibin stain showed an association of the germ cells with non-neoplastic Sertoli cells. The germ cells in Drs. Ulbright and Young's cases lacked large, vesicular nuclei with prominent nucleoli, closely resembling type A spermatogonia; the authors thus concluded that true testicular MGSCT most probably does not exist and these neoplasms represent sex cord-stromal tumours with entrapped, non-neoplastic germ cells [3]. A similar view was reiterated by the authors in a letter to the editor in relation to our paper [4].

In our paper, however, we have mentioned a very important morphological finding that proves the neoplastic nature of the germ cells in testicular MGSCT and militates against their reactive nature, namely, the presence of

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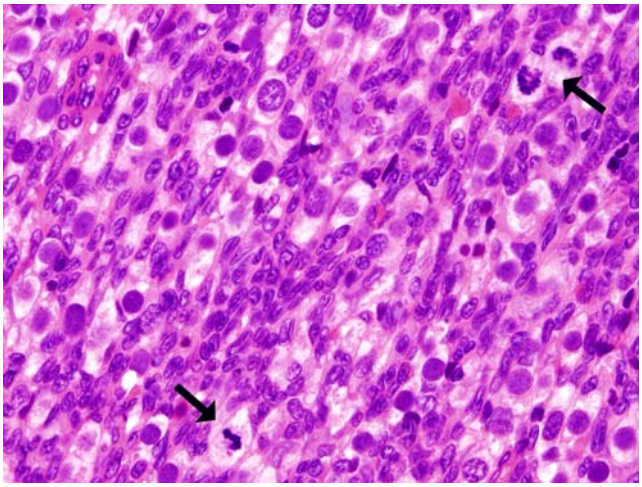

Fig. 1 Testicular MGSCT. Germ cells growing on the background of sex cord-stromal cells. There are three atypical mitoses in the germ cells at low magnification (*arrows*)

atypical, sometimes even bizarre mitotic figures in the germ cell component. We showed one atypical mitosis in Figure 4 of our original paper [1]; however, owing to the photographic reduction of the size, the details are not well apparent. Because this feature was very prominent in case 1 in our series [1] and from this case we were able to process the whole accessed surgical tumour tissues, we decided to cut through all blocks and review the slides again. The newly cut slides demonstrated places where we encountered several atypical mitoses within the germ cells (Fig. 1) (up to five atypical mitoses per one low-power field). When viewed on high magnification, these areas show clearly

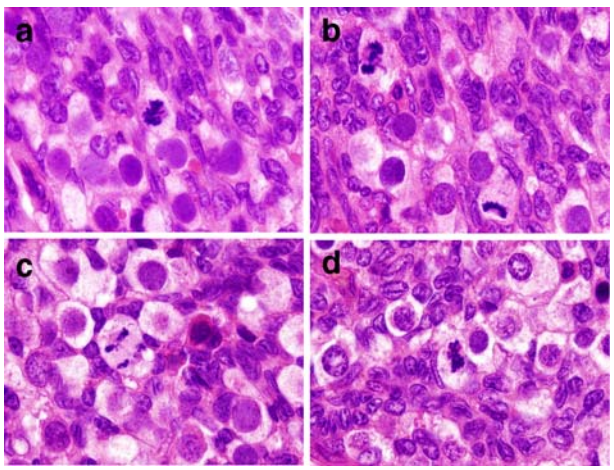

Fig. 2 **a**–**d** Testicular MGSCT. Atypical mitoses in germ cells at high magnification

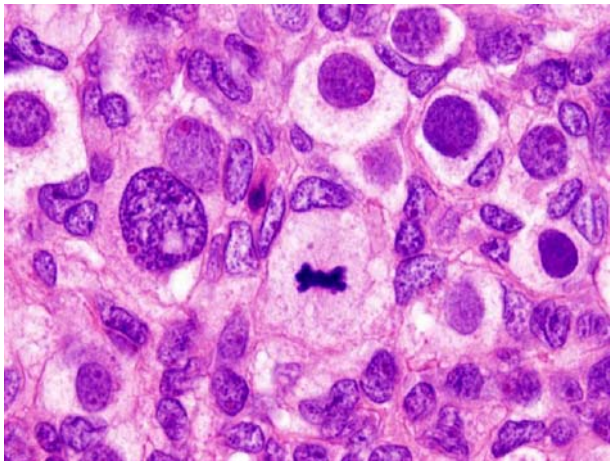

Fig. 3 Testicular MGSCT. Distinct variation in size of the germ cells

the atypical nature of the mitoses in the germ cells that leaves no doubt these germ cells are not only neoplastic, but malignant as well (Fig. 2). In addition, MIB1 antibody in these areas stained up to half of the germ cell component. We also found a distinct variation in size of the germ cells in this case, which would be quite unusual for the non-neoplastic germ cells (Fig. 3.). It is important to note that this morphological variation is quite similar to the germ cells of spermatocytic seminomas. In addition, we have not found a single focus in the entire neoplasm in which the germ cells resembled entrapped cells within testicular tubules or within a sex cord stromal tumour.

In our opinion, all the above-enumerated features point to the neoplastic, rather than reactive, nature of the germ cells in testicular MGSCT and to the existence of testicular MGSCT as an entity. Talerman and Roth recently expressed a similar opinion in their paper dealing with MGSCT [2].

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