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Case Report

Intratunical injection of methotrexate for the treatment of seminoma of the testicle

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A bilateral testicular seminoma in a 32 year old man is reported. The patient was unmarried and refused bilateral orchidectomy for its sterile result. He was treated with four courses of methotrexate (MXT) injected in the tunica vaginalis sac. Each course comprised the administration of 50 mg MXT in each tunical sac every 5 days for five consecutive doses followed by 3 weeks rest. No toxicity was encountered. Testicular biopsy 6 months after the start of treatment was negative for malignant cells. A temporary drop of sperm count occurred during treatment. Treatment was performed 6 years ago, and the patient has had no recurrence and is fertile. The treatment was done on an outpatient basis.

Key words: Methotrexate, seminoma, testicle, testicular tumors.

Introduction

In the last few decades, the treatment of malignant testicular tumors has been much improved due to better staging, and radiologic and chemotherapeutic management, as well as surveillance.[1,2] The 5 year survival rates in seminoma are 90–95% in stage I, 80% in stage II and 20–30% in stage III.[3] The treatment of choice in stage I seminoma is radical orchidectomy and retroperitoneal irradiation.[1–3] Chemotherapy is used as salvage therapy for cases that relapse following irradiation. However, there is a staging error varying between 15 and 25% in stage I seminoma.[3,4]

Although the results of treatment of stage I seminoma are satisfactory, the price is orchidectomy. Between 1 and 2% of malignant testicular tumors are bilateral.[5] Seminoma is the most common germ cell tumor in bilateral primary testicular tumors.[5] With bilateral seminoma, bilateral orchidectomy leaves the patient sterile. In this communication we describe a case of a middle-aged man with bilateral testicular seminoma. This patient was treated with chemotherapy administered through the tunica vaginalis sac. The patient is alive 6 years after onset of the disease, with no recurrence, and is fertile.

Case history

A 32-year-old unmarried man had noticed an asymptomatic enlargement of both testicles, with only a sensation of testicular heaviness, 4 weeks prior to presentation. Physical examination in January 1986 revealed hard and slightly enlarged testicles on both sides. The testicles were not tender and the epididymis was normal. A bilateral small-sized hydrocele was detected. Abdominal examination was negative. Liver and kidney function tests as well as α-fetoprotein (AFP), B-human chorionic gonadotropin (hCG) and lactic acid dehydrogenase (LAD) values were normal. Chest and abdominal X-rays revealed no abnormalities. Scrotal sonography showed a highly echogenic solid mass in both testicles. A computed tomography (CT) scan of the abdomen and pelvis and pedal lymphangiography (LAG) were negative. Semen examination, three times weekly-spaced, showed a normal character with a mean sperm count of 82.2 ± 4.2 million ml, with motility of 58 ± 6.6% and abnormal forms of 12.8 ± 1.6%. Bilateral inguinal exploration orchidectomy for a possible testicular tumor was refused by the patient who consented for testicular needle biopsy. The pathologic diagnosis was bilateral classic seminoma. The histologic examination showed sheets of large cells with clear cytoplasm and densely staining nuclei.

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Technique of intratunical injection

The technique has been described elsewhere[6] and will only be mentioned briefly. MXT (100 mg) was dissolved in 5 ml solvent and 2.5 ml was injected in each tunical sac. The patient lay supine, the scrotal compartment grasped at the scrotal neck and the testicle was gently squeezed forward. A 21-gauge needle applied to an empty syringe was inserted through the scrotal skin into the tunica vaginalis cavity. The proper position of the needle was assured by the appearance of tunical fluid on aspiration. The tunical sac was emptied of its fluid and the syringe was exchanged against another syringe containing the dissolved MXT solution which was injected into the tunical sac. The MXT was similarly administered into the contralateral tunical sac.

The intratunical MXT administration was given every 5 days for five consecutive doses. Routine hematological assessment was performed before each injection. The course was repeated at 3 week intervals. MXT levels in the blood were assessed 4 and 24 h after administration. The injections were given on an outpatient basis. The patient completed four courses. He was followed at 3 month intervals for 2 years, then every 6 months until 5 years and then yearly. The follow-up visits included examination of the testicle, abdomen and lymph node areas. Laboratory investigations comprised AFP, hCG, LDH and semen. Abdominal sonography and CT scanning was included at each visit.

The hematologic reserve and tumor marker levels remained almost unchanged throughout the treatment. No toxic manifestations were encountered and the treatment was not interrupted. MXT serum showed low levels compared with intravenous administration[7] (Table 1). Three months after onset of treatment, the highly echogenic solid mass in both testicles disappeared. Testicular biopsy performed 6 months from the start of treatment was negative for tumor cells. During the 6 months of treatment, the semen showed a significant drop in sperm count and motility ($p < 0.05$) and increase of abnormal sperm forms ($p < 0.01$) (Table 2). Three months after cessation of treatment, the semen character returned to the pre-treatment level ($p > 0.05$) (Table 2). At this time the patient got married. It is now 6 years after the onset of treatment, and the patient has had

Table 1. MXT serum level after intratunical (100 mg) administration (it was compared with that of intravenous administration)

Route	MXT serum level (μmol)			
	4 h after injection		24 h after injection	
	range	mean	range	mean
Intratunical (100 mg)	0.9–1.45	1.3 ± 0.1	0–0.32	1.15 ± 0.03
Intravenous (50 mg)	2.0–3.6	2.8 ± 0.6	0.38–0.52	0.46 ± 0.1

Values are given as mean ± SD.

Table 2. Sperm character after 3 months of the onset and 3 months of the end of treatment

	Sperm count ($\times 10^6$/ml)		Motile sperms (%)		Abnormal sperm forms (%)	
	range	mean	range	mean	range	mean
Before treatment	78–96	82.2 ± 4.2	72–86	77.8 ± 6.6	10–18	12.8 ± 1.6
After 3 months of onset of treatment	42–58	51.3 ± 6.8[b]	38–53	44.8 ± 7.8[b]	38–56	48.6 ± 8.9[c]
After 3 months of end of treatment	72–88	80.5 ± 5.8[a]	66–84	80.2 ± 7.1[a]	16–22	15.6 ± 2.1[a]

Values are given as mean ± SD.
[a] $p > 0.05$; [b] $p < 0.05$; [c] $p < 0.01$.

no recurrence of the disease and is fertile. He has two daughters.

Discussion

Although orchidectomy and retroperitoneal irradiation were indicated in the present case, the patient's refusal for fear of sterility posed the present modality of treatment, i.e. intratunical administration. A recent study has demonstrated that intratunical MXT administration achieved a higher MXT level in the testicle and a lower serum level than the parenteral route.[6] This would result in low toxicity with high drug efficacy in testicular lesions. It was proposed that the intratunical route would be ideal for chemotherapy administration in malignant tumors of the testicle.[6]

The present case report demonstrates the efficacy of intratunical MXT administration in the treatment of bilateral testicular seminoma with preservation of the two testicles and their fertile function. No toxic manifestations were encountered. The temporary suppression of semen quality during treatment could be due to the direct cytotoxic effect of MXT at high concentration on the testicular germ cells; however, the semen character was normalized after cessation of treatment. The treatment was given on an outpatient basis.

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