31 The Mesh and the Spermatic Cord

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Introduction

The fibrotic reaction of polypropylene mesh after tension-free (TFR) inguinal herniorrhaphy causing vasal obstruction has been implicated as the reason for infertility in a group of patients presented in a recent paper by Shin and colleagues [1]. The purpose of this presentation is to examine the controversial subject of infertility and inguinal hernia repair and analyze some of the currently available evidence.

Discussion

Can prosthetic material actually cause infertility by virtue of the dense fibroblastic reaction which it is designed to produce? The manuscript referred to above by Shin and colleagues incriminating the polypropylene mesh fibrotic reaction as a cause of infertility would seem to provide evidence of this [1]. Fourteen patients with infertility secondary to obstructive azoospermia (normal sperm in a testicular biopsy yet no sperm in the ejaculate) felt to be related to the fibroplastic involvement of the vas deferens after a heterogeneous group of mesh repairs (conventional, laparoscopic, unilateral, bilateral) are presented. All patients underwent surgical exploration with intra-operative vasography. The vasogram determined the site of the obstruction in the inguinal region and the surgical exploration identified the cause of the obstruction to be the mesh.

But could there be another explanation for these findings? Experienced surgeons who perform re-operative groin explorations after mesh inguinal hernia repairs for reasons other than fertility such as recurrence or postherniorrhaphy groin pain know that the intense fibrotic response described in the manuscript is invariably present. Polypropylene and the other mesh materials used in hernia surgery are supposed to incite a dense fibroplastic tissue response for the purpose of creating a strong mesh-aponeurotic complex to replace weakened native tissue. Eight hundred thousand groin hernia repairs are performed in the US per year, of which approximately 90% are now mesh repairs [2]. Given the fact that inguinal hernias occur at all ages of life and inguinal herniorrhaphies are performed in sizable numbers of patients who are still planning to bear children, why then are we not seeing an epidemic of infertility? Do these 14 patients represent a subset that is exquisitely sensitive to the normal fibroblastic response to mesh? Or was the real cause of the vasal obstruction described in this manuscript the result of a more traditional injury (see list below) followed by scarification to the most convenient structure, which in this case would be the mesh?

Causes of vasal obstruction related to inguinal herniorrhaphy:

- Division
- Ligation
- Clipping
- Stapling

- Electrocauterization
- Devascularization
- Scarification.
- Traction injuries [3]

Infertility caused by inguinal hernia surgery can be related to either the vas deferens or the testicle. The incidence of injury to the vas deferens during inguinal herniorrhaphy has been estimated at 0.3% for adults and between 0.8 to 2.0% for children [4]. Injury to the testicle which eventually leads to atrophy is estimated to occur in about 0.5% for primary hernia repairs but increases tenfold to 5% for recurrent hernia repair [5, 6]. The routine use of prosthetic material for inguinal hernia repair has resulted in a marked decrease in the historical recurrence rate when compared to population-based studies of non-tension-free herniorrhaphies [7]. The irony of this discussion of polypropylene mesh causing infertility is the theoretical effect of decreasing the recurrence rate in the general population from 10–15% seen with Bassini and its variants to less than 5% with the mesh tension-free approach. One should expect a parallel decrease in infertility because of the decreased need for re-operative surgery for recurrence.

We know that the overall incidence of infertility after inguinal herniorrhaphy is higher than the general population. Yavetz et al. looked at 8500 infertile patients and found that 565 or 6.65% gave a history of an inguinal hernia repair [8]. However, this does not shed light on the incidence of the infertility caused by the operation. The issue is clouded by the fact that that many herniorrhaphy patients have no intention of conceiving a child, so fertility status cannot be known; the fertility status of the patient prior to herniorrhaphy is usually not known and the time period between the herniorrhaphy and the diagnosis of infertility introduces the variable of intervening causation. We must look to investigators like Shin and colleagues who conduct specialty infertility clinics to try to extrapolate the incidence. But that literature is dominated by case reports or small series calling into question the quality of the estimates [9]. It is possible that the incidence is so low that the fertility advantages of mesh repair as the result of the avoidance re-operation for recurrence outweighs it.

If one were to assume that polypropylene mesh does indeed cause obstruction of the vas, then one logically must consider the mechanism. Is it caused by an exaggerated fibroblastic response in some patients? If so, why is not the entire structure obliterated? Or does it have only to do with sites where the vas comes in contact with edges of the mesh? It should then occur only at the external and internal rings where the cord rides over these edges. Would the modified Lichtenstein operation in which the tails of the split mesh are simply approximated lateral to the cord at the internal ring put the patient at greater risk than the classic operation in which the inferior surface of the superior tail is sutured to the inferior surface of the inferior tail and the inguinal ligament which creates a shutter valve effect?

Additional Clinical Papers

This is not the first report of abnormality of the vas deferens after mesh inguinal herniorrhaphy. For example, an often-quoted case report by Silich et al. describes a patient who presented 4 years after an inguinal herniorrhaphy with a painful subcutaneous nodule in the repair site [10]. At groin exploration the patient was found to have a spermatic granuloma "imbedded in surrounding fibroareolar tissue and mesh". The authors concluded that cut edges of the mesh where the tails had been wrapped around the cord eroded into the cord, and even provided a diagram depicting this, despite the fact that the original operation was performed at "an ambulatory surgery centre" and no details of that operation were available. One might speculate that an isolated injury to the vas deferens was the more likely explanation, as a spermatic granuloma is by definition an immunological response to extravasated sperm. A direct injury to the vas resulting in a sperm leak might be a more plausible explanation than the gradual erosion by the edge of the mesh. Similarly, a case report published by Seifman et al is often purported to show unequivocal evidence that mesh can cause obstruction of the vas [11]. The 32-year-old patient was diagnosed with secondary infertility (infertility which develops after a successful conception) 1 year after a right inguinal hernia repair with mesh. The patient underwent a groin exploration after he was determined to have obstructive azoospermia on the right based on the absence of viable sperm in a seminal vesical aspirate compared to a right testicle aspirate showing many sperm. An isolated segment of vas was resected that was "incorporated into a scarification process involving the mesh and the vas was totally obstructed" and a reconstruction performed. The patient successfully conceived a child 6 weeks later. It seems pretty clear: the site of blockage was identified precisely, the problem corrected surgically, and the patient was almost immediately able to conceive a child. However, what is commonly omitted when this article is referenced is that the patient also underwent a simultaneous varicocelectomy on the op-

posite side. The authors felt that the short time interval between the varicocelectomy and the conception was too brief to have any effect. It must be left to the reader whether the correction of a known cause of infertility, a varicocele, or a technically challenging reconstruction was responsible for the pregnancy.

There is literature other than case reports useful for the purposes of a discussion concerning infertility that addresses not only vasal obstruction but other potential causes. Aydede and colleagues looked at a group of 60 patients who had undergone TFR herniorrhaphies, 30 of whom were preperitoneal and 30 conventional anterior [12]. The study parameters included spermiograms and testicular perfusion with color Doppler ultrasonography. The spermiograms were identical pre-operatively and postoperatively in both groups. The testicular perfusion studies showed a significant difference between pre-operative and early postoperative values but not late postoperative values in either group. The authors concluded that the results "supported the idea that inguinal mesh application is still a safe procedure in patients with no children or who are undergoing infertility treatment, where testicular function is important."

Color Doppler ultrasonography was used to assess testicular perfusion in another study by Dilek et al. [13]. Twenty-six patients were randomly assigned to undergo a totally extraperitoneal preperitoneal or a standard Lichtenstein TFR hernia repair. The specific blood flow indexes of the spermatic artery studied included end diastolic velocity, peak systolic velocity, and the resistive index. Studies were performed immediately pre-operatively and then 3 months after surgery. No differences were found between the pre-operative and postoperative measurements.

Laboratory Models

Several experimental studies in varying animal models have been published with mixed conclusions. The more widely referenced are summarized to illustrate this point. One of the studies was published in the Journal of Urology in 1999 by Uzzo and others [14]. Twelve male beagle dogs had inguinal hernia defects surgically created on one side of each animal. Six were repaired using a polypropylene TFR and the other six with a Shouldice technique. Study parameters included testicular temperature and volume, peripheral and testicular vein testosterone levels, testicular blood flow, vasography, testicular and cord histology, and sperm motility and morphology. The side without a hernia defect acted as a control. Postoperative testicular temperature, blood flow, and volume were similar to controls from both the mesh and Shouldice groups although there was a trend toward decreased volume in the TFR group(17.8 cc pre vs. 12.6 cc post, p = 0.17). Contralateral (control) testicular vein testosterone levels were higher in animals repaired with mesh than by Shouldice. There was a significant decrease in cross-sectional vasal luminal diameter in both repair groups compared to their respective contralateral controls. Microscopic examination disclosed a marked foreign-body reaction in the soft tissues surrounding the vas in the TFR group. All vasograms demonstrated patency. Three of the six TFR dogs had grossly abnormal pathology (two hydroceles and one ischemic testis). None of the Shouldice dogs demonstrated such findings. Sperm morphology and motility did not differ between the two groups.

Our group conducted a study to determine whether congenital indirect inguinal hernias in male pigs could be repaired by placing a polypropylene mesh prosthesis over the defect intra-abdominally [15]. The study design called for an assessment of the effect on fertility. The project differed from other mesh fertility studies in that the prosthesis was placed using an intraperitoneal onlay mesh technique (IPOM) meaning that peritoneum separated the prosthesis from the cord structures. Twenty-six healthy Yorkshire cross feeder male pigs weighing between 23 and 30 kg with congenital unilateral or bilateral indirect inguinal hernias were divided into two groups. In group 1, 13 pigs had a total of 19 indirect inguinal IPOM herniorrhaphies performed at the time of a laparotomy. Thirteen pigs in group 2 underwent the same operation laparoscopically and a total of 16 indirect inguinal hernias were repaired. All pigs were followed for 6 weeks postoperatively and allowed unrestricted physical activity and then sacrificed. There were no signs of erosion or damage to cord structures in any pig. There was normal flow of methylene blue without obstruction or extravasation (Fig. 31.1). A standard electrical transrectal ejaculation protocol employed in the livestock industry for artificial insemination was used to harvest sperm before sacrifice. Spermiograms were then performed and were normal.

Another evaluation of fertility was conducted by the respected group from Aachen, Germany, in pigs and rats [16]. Fifteen pigs underwent a TFR-type procedure on one side and a control operation Shouldice on the other. Three animals were sacrificed weekly until 35 days. On the TFR side, foreign-body reaction with diffuse infiltrating inflammatory cells was found in all. Five pigs were noted to have venous thrombosis of their spermatic veins and one animal was shown to have focal fibrinoid necrosis of the wall of the vas. On the control

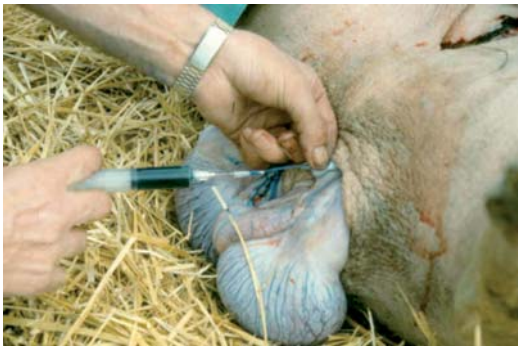

Fig. 31.1. Patency of the vas deferens was assessed with methylene blue injection

operated side, only minor postoperative changes were observed. The same operative scheme was used in eight chinchilla rabbits, but the study parameters in these animals included in addition to histological evaluation of the foreign-body reaction, testicular size, testicular temperature, testicular and spermatic cord perfusion, and spermatogenesis using the Johnsen scoring system. Just as in the pigs, there was much more foreign-body reaction on the mesh side than the Shouldice. In addition, there was decreased arterial perfusion and lower testicular temperature on the mesh side when compared to Shouldice. The TFR operation appeared to have adversely effected the Johnsen scale, which measures the rate of seminiferus tubules with regular spermatogenesis (TFR: 48.1%, Shouldice: 63.8%, controls: 65.8%). The authors voiced concern about this potential influence on spermatogenesis.

A study from Brazil included 18 dogs divided into three groups: group 1 (n = 7) underwent bilateral groin exploration with mesh being placed on the left side while the right had a non TFR repair [17]. In group 2 (n = 7), the sides were reversed (left side without mesh versus right side with mesh. Group 3 (n = 4) had no surgical manipulation (control group). The results were that there was increased chronic inflammatory reaction in all operated groups compared to controls, increased chronic inflammatory reaction on the mesh side compared to nonmesh, and decreased vas deferens diameter size on mesh side.

Taneli et al. examined testicular function, testicular nitric oxide metabolism, and germ cell-specific apoptosis in 40 rats who were divided into two groups consisting of a study group in whom a 0.5×1-cm polypropylene mesh patch was implanted behind the left inguinal spermatic cord and a sham-operated control group [18]. They concluded that long-term polypropylene mesh implantation has no effect on testicular hormonal function and only a limited effect on nitric oxide levels, and this effect is not sufficient to cause apoptosis in testis that could lead to infertility.

Another experimental study in rats evaluating how different types of mesh affect the spermatic cord was published in European Surgical Research by Berndsen and colleagues [19]. They divided 30 rats into 3 groups:

1. Conventional non-TFR repair,
2. TFR repair with a heavy-weight polypropylene mesh, and
3. TFR repair with large-pore, light-weight polypropylene/polyglactin composite.

Vasography was performed after 90 days. Study endpoints included cross-sectional area of the vas deferens and S-testosterone measured from the spermatic vein using the contralateral side as control. Light microscopy of the inguinal canal was performed and inflammation and fibrosis were graded. The vasography revealed patent vas deferens in all animals. In group III, there was a lower S-testosterone in the spermatic vein and a reduced cross-sectional area of the vas deferens on the operated compared to the control side. However, there was no difference in the other groups and there was no significant difference in S-testosterone levels between the groups. There was significantly more inflammation and fibrosis after mesh repair compared to suture repair, but there was no difference between the two mesh groups. The authors had no reason to believe that fertility would have been affected by any of these findings.

Conclusion

Infertility is a known complication of inguinal hernia surgery with or without mesh, and can be caused by a variety of mechanisms. The findings in the Shin manuscript which were the reason this review was undertaken are provocative and certainly provide an invitation for further study. However, careful analysis of the patients reported in that paper, as well as review of other pertinent literature, fails to unequivocally prove that polypropylene mesh can cause vasal obstruction as an independent aetiology. It seems logical that there might be a subset of patients in whom vasal obstruction will occur because of exquisite sensitivity to the fibroplastic response intended with the use of mesh material in hernia surgery. However, this subset must be quite small given that larger numbers of infertile patients are not being identified despite the fact that many patients having mesh hernia repairs are in an age group

still intending to father children. This is not just a matter of staunch TFR enthusiasts turning their backs and hiding their collective heads in the sand rather than face this "new revelation". On the contrary, the concern is overreaction to these level-4–5 evidenced based findings resulting in a return to the routine use of the Bassini operation or one of its nonprosthetic variants, which will inevitably lead to the need for more re-operative surgery for recurrence, which places the patient at the greatest risk of loss of fertility as a consequence of testicular atrophy.

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Discussion

Deysine: *I would like to start the discussion by telling the audience that when this paper arrived I lost some sleep. But I also read a commentary that Dr. Fitzgibbons wrote on the same issue of Annals of Surgery and that cleared the air completely. It was extremely well written to the point and with all the information necessary to take away the initial panic that people may have had and I have to congratulate you for that. Thank you!*

Kingsnorth: *I agree completely with the way you have analyzed this very difficult topic and the literature review you have done on the animals and so on. Thinking a bit laterally, because you know we are in a chronic pain session as well: do you think that damage to the vas deferens done either by the surgeon or by stenosis caused by the mesh is a source of chronic pain? It is something we don't consider. But do you think there are some patients in whom a transscrotal vasogramm may be beneficial in helping us to diagnose the cause of chronic pain?*

Fitzgibbons: *That's a very interesting question. As you know, Dr. Bendavid has described the dysejaculation syndrome, which is a specific syndrome obviously related to the vas. Whether there'll be patients that have just generalized pain not associated with the ejaculation is interesting. I suppose it's a possibility, but a speculation for me, though.*